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As filed with the Securities and Exchange Commission on June 20, 2016

Registration No. 333-211555

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**AMENDMENT NO. 2
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Selecta Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	2834 (Primary Standard Industrial Classification Code Number)	26-1622110 (I.R.S. Employer Identification No.)
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**480 Arsenal Street, Building One
Watertown, Massachusetts 02472
(617) 923-1400**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Werner Cautreels, Ph.D.
President and Chief Executive Officer
Selecta Biosciences, Inc.
480 Arsenal Street, Building One
Watertown, Massachusetts 02472
(617) 923-1400**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Peter N. Handrinos Brandon J. Bortner Latham & Watkins LLP John Hancock Tower 200 Clarendon Street Boston, Massachusetts 02116 (617) 948-6000	Divakar Gupta Marc Recht Joshua A. Kaufman Cooley LLP 500 Boylston Street, 14th Floor Boston, Massachusetts 02116 (617) 937-2300
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**Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement is declared effective.**

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer
(Do not check if a
smaller reporting company)

Smaller reporting company

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

4,250,000 Shares



Common stock

This is the initial public offering of our common stock. No public market for our common stock currently exists. We are offering all of the 4,250,000 shares of common stock offered by this prospectus. We expect the initial public offering price to be between \$14.00 and \$16.00 per share.

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "SELB."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common shares in "Risk Factors" beginning on page 15 of this prospectus.

Neither the Securities and Exchange Commission nor any other state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We refer you to "Underwriting" beginning on page 218 for additional information regarding total underwriting compensation.

Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The underwriters may also purchase up to an additional 637,500 shares of common stock from us at the public offering price, less the underwriting discounts payable by us, to cover over-allotments, if any, within 30 days from the date of this prospectus.

The underwriters expect to deliver the shares of common stock to investors on or about _____, 2016.

UBS Investment Bank

Stifel

Canaccord Genuity

Needham & Company



**Targeted
Immunotherapies** for
Rare and Serious Diseases

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We have not, and the underwriters have not, authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Through and including , 2016 (the 25th day after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Prospectus summary

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the "Risk factors" section beginning on page 15 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our" and "Selecta" refer to Selecta Biosciences, Inc. together with its consolidated subsidiaries.

OVERVIEW

We are a clinical-stage biopharmaceutical company using our proprietary synthetic vaccine particle, or SVP, technology to discover and develop targeted therapies that are designed to modulate the immune system to effectively and safely treat rare and serious diseases. Many such diseases are treated with biologic therapies that are foreign to the patient's immune system and, therefore, elicit an undesired immune response. Of particular concern are anti-drug antibodies, or ADAs, which are produced by the immune system in response to biologic therapy and can adversely affect the efficacy and safety of treatment. Our proprietary SVP technology encapsulates an immunomodulator in biodegradable nanoparticles to induce antigen-specific immune tolerance to mitigate the formation of ADAs in response to life-sustaining biologic drugs. We believe our SVP technology has the potential for broad applications to both enhance existing biologic drugs and enable novel therapies. Our lead product candidate, SEL-212, is a combination of a therapeutic enzyme and our SVP technology designed to be the first biologic treatment for gout that durably controls uric acid in refractory gout and dissolves and removes harmful deposits of uric acid crystals in chronic tophaceous gout, each a painful and debilitating disease with unmet medical need. SEL-212 is currently in a comprehensive Phase 1/2 clinical program. The Phase 1/2 clinical program is comprised of two Phase 1 clinical trials and a Phase 2 clinical trial, and is designed to evaluate the ability of SEL-212 to control uric acid levels and mitigate the formation of ADAs. Based on preliminary data from our ongoing Phase 1b clinical trial, we believe that SEL-212 has the potential to control serum uric acid levels for at least 30 days after a single dose by mitigating the formation of ADAs in response to the therapeutic enzyme. We expect to receive final data from both Phase 1 clinical trials and initiate the Phase 2 clinical trial in the second half of 2016.

Despite rapid advancement in biologic treatment of rare and serious diseases, many biologic therapies are not broadly effective because they are exogenous proteins that are foreign to the patient's immune system and, therefore, may elicit an immune response, known as immunogenicity. Undesired immunogenicity includes the formation of ADAs that can compromise the drug's efficacy and cause serious allergic reactions. The formation of ADAs is known to occur in established treatments such as enzyme and protein replacement therapies, as well as in novel technologies, such as gene therapy and antibody-drug conjugates. ADAs can start developing in the body with the first dose of a biologic therapy and can render subsequent doses ineffective or unsafe, potentially depriving patients of life-saving therapeutic options and limiting the likelihood of success for many otherwise promising novel biologic drugs and technologies. We believe the co-administration of our SVP technology with biologic treatments has the potential to overcome these limitations without requiring changes in dosing or formulation. We intend to build a platform based on our SVP technology applied to the mitigation of ADAs for a wide range of biologics.

OUR SVP TECHNOLOGY

Our SVP technology utilizes a biodegradable nanoparticle to selectively modulate an immune response in an antigen-specific manner. We believe that nanoparticles are uniquely suited to deliver precise

instructions to the immune system as a result of the natural predisposition of the immune system to interrogate nanoparticles, such as viruses.

Our SVP technology is a highly flexible nanoparticle platform, capable of incorporating a wide range of antigens and immunomodulators, allowing us to tailor our SVP products for specific applications across multiple indications. We are tailoring our SVP technology for:

- the treatment of chronic tophaceous and refractory gout;
- antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing;
- application with marketed products and novel biologic drugs that would otherwise be too immunogenic to develop;
- the treatment of a life threatening food allergy, celiac disease and type 1 diabetes under a collaboration with Sanofi; and
- immune stimulation programs to prevent and treat cancer, infectious diseases and other diseases.

SVP are designed to remain intact after injection into the body and accumulate selectively in lymphoid organs, which include lymph nodes and the spleen, where the immune response is coordinated. Depending on the type of immunomodulator encapsulated in the SVP, our technology is designed to induce either a:

- tolerogenic response to mitigate the formation of ADAs against a biologic drug or treat allergies and autoimmune diseases; or
- potent antigen-specific stimulatory response, such as an antibody response to a microbial antigen or a cytolytic T cell response to a tumor antigen.

A tolerogenic response is the induction of immune tolerance or non-responsiveness to a specific antigen. Cytolytic T cells are specialized antigen-specific immune cells that target and kill cells that harbor a specific antigen.

Our antigen-specific SVP tolerance programs utilize SVP-Rapamycin, our biodegradable nanoparticle encapsulating the immunomodulator rapamycin. Rapamycin is a small molecule approved for the prevention of organ rejection in kidney transplant patients. In preclinical studies, we have observed that SVP-Rapamycin, unlike free rapamycin, can be co-administered at the beginning of therapy with a biologic drug to mitigate the formation of ADAs without altering the drug or its dose regimen. As a result, we believe that SVP-Rapamycin may provide us with significant growth opportunities in the area of tolerance because SVP-Rapamycin can be co-administered at the beginning of therapy with many different biologic drugs.

In addition, we believe our SVP technology has the potential to be used for therapies that stimulate the immune system to treat cancer, infectious diseases and other diseases. Our SVP immune stimulation programs are designed to encapsulate an antigen and a toll-like receptor, or TLR, agonist. Activation of TLRs alert the immune system that a potential pathogen is present and that the immune system should mount a response. TLR agonists can be used as supplements, or adjuvants, to vaccines to increase the immune response to the vaccine by activating the TLRs in antigen-presenting cells. We currently finance these programs primarily through grants.

Our SVP technology is based in part on the pioneering research performed by our co-founders at Harvard University, Massachusetts Institute of Technology, or MIT, and Brigham and Women's Hospital, or Brigham. In connection with our company's founding, we licensed 17 patent families

related to certain aspects of our SVP technology as applied to nanoparticles for use in vaccines from our co-founders' institutions pursuant to an agreement with MIT.

OUR PRODUCT CANDIDATE AND DISCOVERY PIPELINES

The following chart summarizes our current SVP product candidate pipeline.

Program	Description	Development status	Program strategy
<i>SVP for immune tolerance</i>			
Refractory and chronic tophaceous gout (SEL-212)	SVP-Rapamycin co-administered with pegsiticase	Final data from Phase 1a and Phase 1b trials and initiation of Phase 2 trial expected in the second half of 2016	Own development
Gene therapy for an autosomal recessive metabolic, or ARM, disorder	SVP-Rapamycin co-administered with the Anc80 gene therapy vector, or Anc80	Investigational New Drug Application, or IND, filing for first indication expected by the end of 2017	Own development
Gene therapy for an X-linked metabolic, or XLM, disorder	SVP-Rapamycin co-administered with an adeno-associated virus, or AAV	IND filing for first indication expected in 2018	Own development
<i>SVP for immune stimulation</i>			
Smoking cessation and relapse prevention (SEL-070)	SVP-adjuvant and SVP-nicotine	Good laboratory practice, or GLP, toxicology studies ongoing	Own development, with grant from the National Institute on Drug Abuse, or NIDA
HPV-associated cancer (SEL-701)	SVP-adjuvant and SVP-HPV antigen	Preclinical	Own development, with grant from the Russian-based Development Fund of New Technologies Development and Commercialization Center, or the Skolkovo Foundation

The following chart summarizes our current discovery pipeline.

Program	Description	Development status	Program strategy
<i>SVP for immune tolerance</i>			
Food allergy	SVP-adjuvant and SVP-food allergen	Discovery	Sanofi worldwide exclusive license
Celiac disease	SVP-Rapamycin and SVP-gluten	Discovery	Sanofi worldwide exclusive license
Type 1 diabetes	SVP-Rapamycin and SVP-insulin	Discovery	Sanofi and Juvenile Diabetes Research Foundation, or JDRF, sponsored research program
<i>SVP for immune stimulation</i>			
Malaria	SVP-adjuvant and SVP-malaria antigen	Discovery	The Bill and Melinda Gates Foundation sponsored research program

SEL-212 FOR THE TREATMENT OF REFRACTORY AND CHRONIC TOPHACEOUS GOUT

Our lead product candidate, SEL-212, consists of SVP-Rapamycin co-administered with pegsiticase, our proprietary pegylated uricase, for the treatment of refractory and chronic tophaceous gout. Our preclinical data indicate that SVP-Rapamycin, when co-administered with pegsiticase, induces antigen-specific immune tolerance to pegsiticase and substantially reduces the formation of associated ADAs. We believe that our SEL-212 has the potential to offer a uniquely effective treatment for patients with refractory or chronic tophaceous gout, while also demonstrating the clinical effectiveness of our SVP technology. We completed the patient treatment portion of our Phase 1a trial in November 2015, initiated a Phase 1b trial in December 2015 and expect final data from both Phase 1 clinical trials in the second half of 2016.

Approximately 8.3 million and 10 million patients in the United States and the European Union, respectively, suffer from gout, which is caused by elevated levels of serum uric acid. Excessive uric acid levels result in harmful deposits of uric acid crystals in joints and tissues, causing joint damage and painful inflammation. High concentrations of serum uric acid also increase the risk for other conditions, including cardiovascular, cardiometabolic, joint and kidney disease. No treatment has been approved to remove uric acid deposits from joints and tissues. Approximately 50,000 patients in the United States have been diagnosed with chronic refractory gout, an orphan indication defined by uric acid levels that cannot be controlled by available oral therapies. The U.S. Food and Drug Administration, or FDA, may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a disease or condition with a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of greater than 200,000 individuals in the United States but for which there is no reasonable expectation that the cost of developing and making available in the United States the drug or biologic will be recovered from sales in the United States. Although we expect to seek orphan drug designation for one or more of our product candidates, we have not yet applied for or obtained such designation.

In addition, approximately 500,000 patients in the United States suffer from chronic tophaceous gout in which patients develop nodular insoluble masses of uric acid crystals referred to as tophi, which can occur either in joints such as fingers, toes or elbows or in the tissues that make up organs such as the kidney and heart. Both refractory and chronic tophaceous gout are severe diseases that can cause pain,

arthritis and organ failure. Krystexxa, a pegylated uricase, is the only product approved by the FDA for the treatment of chronic refractory gout. There is no approved product for chronic tophaceous gout.

SEL-212 was designed specifically to overcome the challenges faced by Krystexxa. In clinical trials, Krystexxa demonstrated the ability to significantly reduce uric acid levels in serum upon initial dosing. However, despite these results, Krystexxa has not achieved broad commercial adoption. We believe this is primarily due to the product's undesired immunogenicity. The package insert information for Krystexxa indicates that during Phase 3 clinical trials, 92% of patients developed ADAs. The package insert information also indicates that during the drug's Phase 3 clinical trials, high Krystexxa-specific ADA levels in patients were associated with a failure to maintain normalization of uric acid levels. Similarly, in 2011, The Journal of the American Medical Association published the results of clinical trials finding that 58% of Krystexxa patients who received biweekly doses of Krystexxa were non-responders as measured by the high uric acid levels in patients, which was associated with the Krystexxa-specific ADA levels.

GENE THERAPY PROGRAMS

We are also applying our SVP technology to antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing. Gene therapies often use a viral vector, such as an AAV vector, to place corrective genetic material into cells to treat genetic diseases. One of the key hurdles for the gene therapy field is to overcome immunogenicity against the viral vector, which can manifest itself in three ways. First, pre-existing ADAs that were induced following a natural AAV infection can neutralize the viral vector and block gene transfer. Up to 50% of patients are ineligible for gene therapy due to the presence of pre-existing ADAs. Second, ADAs form in response to the first administration of a gene therapy vector and prevent effective subsequent doses of gene therapy. Subsequent doses are particularly necessary for pediatric indications due to cellular turnover in young patients. The ability to readminister gene therapies is also important for diseases where the goal is to transfect a high number of cells. Moreover, the third way in which immunogenicity can manifest itself against the viral vector is that the cellular immune system can respond to the transduced cells, which can reduce efficacy and pose safety concerns.

We have in-licensed Anc80 from the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc., collectively referred to as MEE. In preclinical studies, Anc80 has been observed to be a potent gene therapy vector that has demonstrated the capability of yielding superior gene expression levels in the liver compared to naturally occurring AAVs that are currently evaluated in clinical trials. As a synthetic vector, we believe Anc80 has limited cross-reactivity to naturally-occurring AAVs and therefore has the potential to treat patients with pre-existing AAV-specific ADAs. By combining SVP-Rapamycin and Anc80, we intend to develop highly differentiated gene therapies to address all three of the immunogenicity issues associated with the use of viral vectors. In collaboration with the clinical and gene therapy laboratory at the National Institutes of Health and MEE, we plan to develop a product candidate utilizing the Anc80 vector for the treatment of an ARM disorder resulting from an inborn error of metabolism. This ARM disorder can cause severe developmental defects and premature death as a result of an accumulation of toxic metabolites. Under our license agreement with MEE, we also have the option to develop gene therapies using Anc80 for several additional diseases including lysosomal storage, muscular and genetic metabolic diseases. We plan to develop another product candidate for the treatment of an XLM disorder, which is a metabolic disorder similar to ARM disorder. We are pursuing this second indication through collaborations with third parties with preclinical and clinical experience in this area.

OTHER PROGRAMS FOR AUTOIMMUNE DISEASES, ALLERGIES AND MARKETED BIOLOGICS

We are also applying our SVP technology to the treatment of autoimmune diseases, allergies and marketed biologics. Currently, most autoimmune diseases are treated with broadly immunosuppressive therapies that indiscriminately affect the function of the entire immune system. Our SVP technology is designed to re-program the immune system to elicit tolerance to a specific antigen that is causing the autoimmune disease, without impacting the rest of the immune system. We believe that our preclinical data may support potential applications of SVP-Rapamycin to both marketed products, such as monoclonal antibodies against human tumor necrosis factor-alpha, or TNF-alpha, which are known to induce undesired immunogenicity, and novel biologic drugs that would otherwise be too immunogenic to develop. Since 2012, we have established three collaborations with Sanofi to research novel SVP products for the treatment of a life-threatening food allergy, celiac disease and type 1 diabetes. We intend to continue our strategy of out-licensing our SVP technology for antigen-specific immune tolerance for applications that are outside our areas of focus.

IMMUNE STIMULATION PROGRAMS

We also believe our SVP technology, by encapsulating antigens and adjuvants, has the potential to be used for therapies that stimulate the immune system to prevent and treat cancer, infectious diseases and other diseases. We have early-stage research programs for therapeutic vaccines for human papilloma virus, or HPV, associated cancers and for antibody-based vaccine programs for nicotine addiction and malaria. We currently finance these programs primarily through grants.

OUR STRATEGY

Our goal is to become the first biopharmaceutical company to develop and commercialize targeted therapies that are designed to modulate the immune system to effectively and safely treat rare and serious diseases. In addition, we intend to maximize the value of our SVP technology by collaborating with biopharmaceutical companies on programs that can benefit from our technology but that are outside our area of focus. The key elements of our strategy include the following.

- **Rapidly advance the development of our lead product candidate, SEL-212, for the treatment of refractory and chronic tophaceous gout.** We believe SEL-212 has the potential to be the first biologic treatment for gout that durably controls uric acid in refractory gout and dissolves and removes harmful deposits of uric acid crystals in chronic tophaceous gout in a majority of patients. We are currently conducting a comprehensive Phase 1/2 clinical program, comprised of two Phase 1 clinical trials, for which we expect to receive final data in the second half of 2016, and a Phase 2 clinical trial, which we expect to initiate in the second half of 2016 and for which we expect to receive data in the first half of 2017. We plan to advance this program through regulatory approval and commercialization.
- **Leverage our SVP technology for immune tolerance to develop novel uses and classes of non-immunogenic biologics.** We intend to use our SVP technology to develop gene therapies designed to mitigate the formation of ADAs and therefore enable repeat administration and first-in-class non-immunogenic versions of therapeutic enzymes or proteins for human therapy. We have several programs in various stages of discovery and we plan to continue to identify opportunities to utilize with our technology. In addition, we intend to pursue opportunities to in-license proprietary enzymes that we can co-administer with SVP-Rapamycin to address the issues of immunogenicity and develop effective proprietary products.
- **Establish infrastructure and capabilities to commercialize our products in rare and orphan diseases.** While we believe our SVP technology may be broadly applicable across disease areas, we

intend to focus our efforts on developing and commercializing proprietary SVP-enabled products for rare and serious diseases where there is high unmet medical need. Therapies for treating rare and serious diseases require focused commercial efforts and coordination with patient groups and investigators. As our product candidates advance towards commercialization, we intend to build a commercial infrastructure to market our products to capture the full value of our proprietary SVP products.

- **Selectively pursue collaborations and maximize the value of our SVP programs for immune tolerance.** In addition to our own proprietary product development efforts, we are in discussions with potential collaborators and licensees to pursue novel gene therapies and are collaborating with Sanofi on programs for a food allergy, celiac disease and type 1 diabetes. We also intend to selectively pursue additional collaborations with biopharmaceutical companies to further leverage our SVP technology.
- **Utilize our expertise in SVP to stimulate the immune system to fight disease.** We are currently developing prophylactic and therapeutic vaccines that activate the immune system to fight disease through our SVP immune stimulation programs, which are primarily funded by grants. Our current product pursuits include a SVP product to treat HPV-associated cancers, a SVP nicotine vaccine for smoking cessation and relapse prevention and a SVP product for the prevention of malaria. We are developing our programs for HPV-associated cancers and smoking cessation and relapse prevention on our own with grant funding from the Skolkovo Foundation for our HPV program and NIDA for our nicotine program. We are developing our malaria program under a sponsored research arrangement with The Bill and Melinda Gates Foundation.

RISKS FACTORS

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk factors" immediately following this prospectus summary. Some of these risks are:

- we are a development-stage company, have incurred significant losses since our inception, expect to incur losses for the foreseeable future and may never achieve or maintain profitability;
- even if this offering is successful, we will need additional funding in order to complete development of our product candidates and commercialize our products, if approved, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts;
- we are very early in our clinical development efforts and may not be successful in our efforts to use our SVP technology to build a pipeline of product candidates and develop marketable drugs;
- our product candidates are based on our SVP technology, which is an unproven approach designed to induce antigen-specific immune tolerance to biologic drugs or stimulate the immune system;
- clinical drug development involves a lengthy and expensive process, with an uncertain outcome, and we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates;
- we rely, and expect to continue to rely, on Shenyang Sunshine Pharmaceutical Co., Ltd., or 3SBio, in China for pepsitase and other third parties for the manufacture of our product candidates for preclinical and clinical testing, which increases the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts;

- our existing collaborations are important to our business and future licenses may also be important to us, and if we are unable to maintain any of these collaborations, or if these arrangements are not successful, our business could be adversely affected;
- if we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, others could compete against us more directly, which would negatively impact our business; and
- our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

IMPLICATIONS OF BEING AN EMERGING GROWTH COMPANY

As a company with less than \$1.0 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. An "emerging growth company" may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management's discussion and analysis of financial condition and results of operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until the last day of our fiscal year following the fifth anniversary of the completion of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenue exceeds \$1.0 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

CORPORATE INFORMATION

We were incorporated under the laws of the state of Delaware in 2007. Our principal executive offices are located at 480 Arsenal Street, Building One, Watertown, Massachusetts 02472 and our telephone number is (617) 923-1400. Our website address is www.selectabio.com. The information contained in, or accessible through, our website does not constitute a part of this prospectus.

The offering

Common stock offered by us	4,250,000 shares (or 4,887,500 shares if the underwriters exercise their option to purchase additional shares in full).
Common stock to be outstanding after this offering	16,914,048 shares (or 17,551,548 shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and estimated offering expenses payable by us, will be approximately \$55.4 million, or approximately \$64.3 million if the underwriters exercise their option to purchase additional shares in full, based on an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus. We expect that we will use the net proceeds from this offering to support the clinical development and manufacturing scale-up of SEL-212, advance the development of our other SVP product candidates and for working capital and general corporate purposes. See "Use of proceeds" beginning on page 69.
Directed share program	At our request, the underwriters have reserved up to 5% of the common stock being offered by this prospectus for sale at the initial public offering price to our directors, officers, employees and other individuals associated with us and members of their families. These sales will be made by UBS Financial Services Inc., a selected dealer affiliated with UBS Securities LLC, an underwriter of this offering, through a directed share program. We do not know if these persons will choose to purchase all or any portion of these reserved shares, but any purchases they do make will reduce the number of shares available to the general public. Any reserved shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares of common stock. Participants in the directed share program who purchase more than \$1,000,000 of shares shall be subject to a 25-day lock-up with respect to any shares sold to them pursuant to that program. Any shares sold in the directed share program to our directors or executive officers shall be subject to a 180-day lock-up. All of these lock-up agreements will have similar restrictions to the lock-up agreements described herein. See "Shares eligible for future sale—Lock-up agreements."
Risk factors	See "Risk factors" beginning on page 15 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock.
NASDAQ Global Market symbol	"SELB"

Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price. However, because

indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The number of shares of our common stock to be outstanding after this offering is based on 2,773,468 shares of our common stock outstanding as of May 31, 2016, which included 4,415 shares of unvested restricted stock and gives effect to the conversion of our outstanding preferred stock into 9,890,580 shares of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering, and excludes:

- 1,723,704 shares of common stock issuable upon exercise of stock options outstanding as of May 31, 2016, at a weighted average exercise price of \$4.92 per share;
- 112,789 shares of common stock issuable upon the exercise of warrants outstanding as of May 31, 2016, including outstanding warrants to purchase shares of preferred stock that will become warrants to purchase common stock upon the closing of this offering, at a weighted average exercise price of \$17.43 per share;
- 10,163 shares of our common stock available for future issuance under our 2008 Equity Incentive Plan;
- 390,796 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2016 Incentive Award Plan, or the 2016 Plan, which will become effective in connection with this offering, to some of our executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering;
- 819,460 shares of our common stock available for future issuance under our 2016 Plan, which will become effective in connection with this offering, as well as shares of our common stock that become available pursuant to provisions in our 2016 Plan on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Incentive Award Plan"; and
- 173,076 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, or the 2016 ESPP, which will become effective in connection with this offering, as well as shares of our common stock that become available pursuant to provisions in our 2016 ESPP that automatically increase the share reserve under our 2016 ESPP on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Employee Stock Purchase Plan."

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 1-for-3.9 reverse stock split of our common stock effected on June 7, 2016;
- the automatic conversion of all shares of our preferred stock outstanding into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock;
- outstanding warrants to purchase shares of our series D preferred stock becoming warrants to purchase shares of our common stock upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering;

- no exercise of outstanding options or warrants after May 31, 2016;
- the filing of our restated certificate of incorporation and the adoption of our restated bylaws, which will occur upon the closing of this offering; and
- no exercise by the underwriters of their option to purchase additional shares of our common stock.

Upon the closing of this offering, our series E preferred stock will automatically convert into a number of shares of common stock determined, in part, by the initial public offering price for this offering. Assuming an initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, our series E preferred stock will automatically convert into 3,297,480 shares of common stock upon closing of this offering. A \$1.00, \$2.00 and \$3.00 increase in the assumed initial public offering price of \$15.00 per share would decrease the number of shares of common stock issuable upon conversion of our series E preferred stock by 206,093 shares, 387,938 shares and 549,581 shares, respectively. A \$1.00, \$2.00 and \$3.00 decrease in the assumed initial public offering price of \$15.00 per share would increase the number of shares of common stock issued upon conversion of our series E preferred stock by 235,538 shares, 507,308 shares and 824,372 shares, respectively. Accordingly, the number of shares of our common stock issuable upon conversion of all of our preferred stock outstanding would correspondingly decrease or increase, as applicable.

Similarly, upon the closing of this offering, outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock determined, in part, by the initial public offering price for this offering. Assuming an initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, warrants to purchase shares of our series E preferred stock will become warrants to purchase 14,088 shares of our common stock upon closing of this offering. A \$1.00, \$2.00 and \$3.00 increase in the assumed initial public offering price of \$15.00 per share would decrease the number of shares of common stock issuable upon the exercise of these warrants by 880 shares, 1,658 shares and 2,348 shares, respectively. A \$1.00, \$2.00 and \$3.00 decrease in the assumed initial public offering price of \$15.00 per share would increase the number of shares of common stock issuable upon the exercise of these warrants by 1,006 shares, 2,168 shares and 3,522 shares, respectively.

Summary consolidated financial data

The following tables set forth, for the periods and as of the dates indicated, our summary consolidated financial data. You should read the following information together with the more detailed information contained in "Selected consolidated financial data," "Management's discussion and analysis of financial condition and results of operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus. We have derived the consolidated statements of operations data for the years ended December 31, 2014 and 2015 from our audited consolidated financial statements included elsewhere in this prospectus. The consolidated statement of operations data for the three months ended March 31, 2015 and 2016 and the consolidated balance sheet data as of March 31, 2016 have been derived from our unaudited condensed consolidated financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that should be expected in the future, and results for the three months ended March 31, 2016 are not necessarily indicative of the results to be expected for the full year ending December 31, 2016.

Consolidated statement of operations data:

	Years ended December 31,		Three months ended	
	2014	2015	2015	2016
	(in thousands, except share and per share data)			
			(unaudited)	(unaudited)
			March 31,	
Grant and collaboration revenue	\$ 3,040	\$ 6,011	\$ 1,034	\$ 2,088
Operating expenses:				
Research and development	10,486	22,980	4,972	6,648
General and administrative	7,953	8,335	1,872	2,381
Total operating expenses	18,439	31,315	6,844	9,029
Loss from operations	(15,399)	(25,304)	(5,810)	(6,941)
Other income (expense):				
Investment income	111	171	62	13
Foreign currency (loss) gain	3,004	933	194	(220)
Interest expense	(552)	(948)	(179)	(310)
Other expense	(44)	(26)	—	(18)
Total other income (expense), net	2,519	130	77	(535)
Net loss	(12,880)	(25,174)	(5,733)	(7,476)
Accretion of redeemable convertible preferred stock	(4,951)	(7,335)	(1,561)	(2,356)
Net effect of extinguishment of Series SRN redeemable convertible preferred stock	1,459	—	—	—
Net loss attributable to common stockholders	\$ (16,372)	\$ (32,509)	\$ (7,294)	\$ (9,832)
Net loss per share attributable to common stockholders(1)				
Basic and diluted	\$ (7.84)	\$ (15.13)	\$ (3.43)	\$ (4.52)
Weighted average common shares outstanding(1)				
Basic and diluted	2,090,677	2,150,422	2,126,878	2,175,037
Pro forma net loss per share attributable to common stockholders (unaudited)				
Basic and diluted(1)(2)		\$ (2.53)		\$ (0.59)
Pro forma weighted average common shares of common stock outstanding (unaudited)				
Basic and diluted(1)(2)		9,980,469		12,632,923

- (1) See Note 3 to our consolidated financial statements included elsewhere in this prospectus for additional information regarding the method used to calculate the historical and pro forma basic and diluted net loss per common share and the number of shares used in the computation of the per share amounts.
- (2) Pro forma basic and diluted net loss per common share and weighted average common shares outstanding give effect to: (i) the automatic conversion of all shares of our preferred stock into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock, (ii) outstanding warrants to purchase series D preferred stock becoming warrants to purchase shares of our common stock, upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering and (iii) the automatic cashless exercise of warrants, or the series E common warrants, for 567,306 shares of our common stock. Upon the closing of this offering, (a) our series E preferred stock will automatically convert into a number of shares of common stock and (b) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share.

the midpoint of the price range set forth on the cover page of this prospectus. See "Prospectus summary—The offering" for a related offering price per share sensitivity analysis.

Consolidated balance sheet data:

	As of March 31, 2016		
	Actual	Pro forma(1) (unaudited) (in thousands)	Pro forma as adjusted(2) (unaudited)
Cash, cash equivalents and short-term investments	\$ 25,979	\$ 25,979	\$ 81,367
Total assets	\$ 34,723	\$ 34,723	\$ 90,111
Loan payables, net of current portion	\$ 11,169	\$ 11,169	\$ 11,169
Redeemable convertible preferred stock	\$ 139,837	\$ —	\$ —
Total stockholders' equity (deficit)	\$ (125,805)	\$ 14,342	\$ 69,730

- (1) The pro forma balance sheet data give effect to: (i) the automatic conversion of all shares of our preferred stock into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock, (ii) outstanding warrants to purchase series D preferred stock becoming warrants to purchase shares of our common stock, upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering and (iii) the automatic cashless exercise of the series E common warrants for 567,306 shares of our common stock. Upon the closing of this offering, (a) our series E preferred stock will automatically convert into a number of shares of common stock and (b) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. See "Prospectus summary—The offering" for a related offering price per share sensitivity analysis.
- (2) The pro forma as adjusted consolidated balance sheet data give further effect to our issuance and sale of 4,250,000 shares of our common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total assets, additional paid-in capital and total stockholders' equity (deficit) by \$4.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price of \$15.00 per share would increase (decrease) each of cash and cash equivalents, total assets, additional paid-in capital and total stockholders' equity (deficit) by \$14.0 million. The pro forma information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of our initial public offering determined at pricing.

Risk factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our consolidated financial statements and the related notes and "Management's discussion and analysis of results of operations and financial condition," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment.

RISKS RELATED TO OUR FINANCIAL POSITION AND NEED FOR ADDITIONAL CAPITAL

We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was \$12.9 million for the year ended December 31, 2014, \$25.2 for the year ended December 31, 2015 and \$5.7 million and \$7.5 million for the three months ended March 31, 2015 and 2016, respectively. As of March 31, 2016, we had an accumulated deficit of \$121.1 million. To date, we have financed our operations primarily through issuances of preferred stock, debt, research grants and a research collaboration. We currently have no source of product revenue, and we do not expect to generate product revenue for the foreseeable future. All of our revenue to date has been collaboration and grant revenue. We have devoted substantially all of our financial resources and efforts to developing our SVP technology, identifying potential product candidates and conducting preclinical studies and our clinical trials. We are in the early stages of development of our product candidates, and we have not completed development of any SVP therapies. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We expect that our expenses will increase substantially as we:

- conduct additional clinical trials of SEL-212, our lead product candidate;
- continue the research and development of our other product candidates, including completing preclinical studies and commencing trials for such product candidates;
- seek to enhance our SVP technology and discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- potentially establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio, including through licensing arrangements;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our transition to a public company; and
- experience any delays or encounter any issues with any of the above, including, but not limited to, failed studies, complex results, safety issues or other regulatory challenges.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval and securing reimbursement for these product candidates, manufacturing, marketing and selling any products for

Risk factors

which we may obtain regulatory approval, and establishing and managing our collaborations at various stages of a product candidate's development. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical and biological product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the U.S. Food and Drug Administration, or FDA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase and revenue could be further delayed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations.

In addition, we have recurring losses and negative cash flows from operations and will require additional capital to fund planned operations. There can be no assurance that we will be able to raise additional capital on reasonable terms, if at all, which could prevent us from continuing our operations. These conditions cast substantial doubt about our ability to continue as a going concern. In this regard, our independent registered public accounting firm's report on our December 31, 2014 and 2015 financial statements included an explanatory paragraph referring to our ability to continue as a going concern. Our financial statements do not include any adjustments that may result from the outcome of this uncertainty.

Even if this offering is successful, we will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our clinical trials of SEL-212, and continue research and development for our other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Accordingly, we will need to obtain substantial additional funding to continue operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that our existing cash, cash equivalents and investments, and funding that we expect to receive under our existing collaborations, together with the expected net proceeds from this offering, will enable us to fund our operating expenses and capital expenditure requirements through at least December 31, 2017. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of SEL-212;
- our collaboration agreements remaining in effect, our entering into additional collaboration agreements and our ability to achieve milestones under these agreements;
- the cost of manufacturing clinical supplies of our product candidates;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;

Risk factors

- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders, and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in 2007, and our operations to date have been limited to developing and researching our SVP technology and related products and programs, building our intellectual property portfolio, developing our supply chain, planning our business, raising capital and providing general and administrative support for these operations. All but one of our product candidates, SEL-212, are still in preclinical development. We completed the patient treatment portion of our Phase 1a clinical trial of pegsiticase, a component of SEL-212, our lead product candidate, but have not yet completed any other clinical trials for SEL-212 or any other product candidates. We have not yet demonstrated our ability to successfully complete any Phase 2 clinical trial or any Phase 3 or other pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Consequently, any predictions you make about our

Risk factors

future success or viability may not be as accurate as they could be if we had a longer operating history.

The terms of our credit facility and subsidiary's charter place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

We have a \$12.0 million credit facility with Oxford Finance LLC, or Oxford, and Pacific Western Bank, as successor in interest to Square 1 Bank, that is secured by a lien covering substantially all of our personal property, excluding intellectual property. As of March 31, 2016, the outstanding principal balance under the credit facility was \$12.0 million. The credit facility contains customary affirmative and negative covenants and events of default applicable to us and our subsidiaries. The affirmative covenants include, among others, covenants requiring us (and us to cause our subsidiaries) to maintain our legal existence and governmental approvals, deliver certain financial reports and notifications, maintain proper books of record and account, timely file and pay tax returns, maintain inventory and insurance coverage, maintain unrestricted cash in a control account equal to or greater than the lesser of 105% of all outstanding amounts under the credit facility and 100% of the cash and cash equivalents of our company and our wholly-owned subsidiary, Selecta Biosciences Security Corporation, and protect material intellectual property. The negative covenants include, among others, restrictions on us and our subsidiaries transferring collateral, changing businesses, dissolving, liquidating, engaging in mergers or acquisitions, adding new offices or locations, making certain organizational changes, incurring additional indebtedness, encumbering collateral, paying cash dividends or making other distributions, making investments, selling assets, undergoing a change in control, engaging in certain non-ordinary course material transactions with affiliates, and making certain payments or transfers to our subsidiary Selecta (RUS) LLC, or Selecta RUS, in each case subject to certain exceptions. If we default under the credit facility, Oxford, as collateral agent for the lenders, may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lenders' right to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. The lenders could declare a default upon the occurrence of any event that they interpret as a material adverse effect as defined under the credit facility, thereby requiring us to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by the lenders of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

In addition, the charter of our subsidiary, Selecta RUS, prohibits distributions to us in violation of Russian law or if, as a result of such distribution, Selecta RUS would be insolvent or its net assets would be less than its charter capital and statutory reserves. Selecta RUS held \$4.2 million of total cash in Russian banks as of March 31, 2016, including \$1.5 million of cash and cash equivalents, \$2.0 million of short-term deposits and \$0.7 million of restricted cash.

Our ability to use our net operating loss and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

As of December 31, 2015, we had net operating loss carryforwards, or NOLs, for federal and state income tax purposes of \$82.4 million and \$76.3 million, respectively, which may be available to offset our future taxable income, if any, at various times through 2035. At December 31, 2015, we had available federal and state research and development income tax credits of approximately \$1.6 million

Risk factors

and \$1.1 million, respectively, which may be available to reduce future income taxes, if any, at various times through 2035. Our federal NOLs begin to expire in 2028. In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to use its pre-change NOLs to offset future taxable income. If the U.S. Internal Revenue Service, or IRS, challenges our analysis that existing NOLs will not expire before utilization due to previous ownership changes, or if we undergo an ownership change in connection with or after this public offering, our ability to use our NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to use NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to use a material portion of the NOLs reflected on our balance sheet, even if we attain profitability.

RISKS RELATED TO THE DISCOVERY, DEVELOPMENT AND REGULATORY APPROVAL OF OUR PRODUCT CANDIDATES

We are very early in our clinical development efforts and may not be successful in our efforts to use our SVP technology to build a pipeline of product candidates and develop marketable drugs.

We are primarily using our SVP technology to improve and enable biologics that treat rare and serious diseases, with an initial focus on developing SEL-212 for the treatment of refractory and chronic tophaceous gout. While we believe our preclinical and clinical data to date, together with our collaborative relationships, have validated our technology to a degree, we are at an early stage of development and our technology has not yet led to, and may never lead to, approvable or marketable drugs. We are developing additional product candidates to address the problem of anti-drug antibodies, or ADAs, and immunogenicity in biologic therapy and to treat cancer and other infectious diseases and conditions that are not responsive to currently available vaccines. We may have problems applying our technologies to these other areas, and our new product candidates may not be as effective as our initial product candidates. Even if we are successful in identifying additional product candidates, they may not be suitable for clinical development, including as a result of harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with positive results;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third party manufacturers for, or establishing, commercial manufacturing capabilities, or establishing such capabilities ourselves;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- our existing collaboration agreements remaining in effect and our entering into new collaborations throughout the development process as appropriate, from preclinical studies through to commercialization;
- acceptance of our products, if and when approved, by patients and the medical community;
- effectively competing with other therapies;

Risk factors

- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our products, if approved;
- protecting our rights in our intellectual property portfolio;
- operating without infringing or violating the valid and enforceable patents or other intellectual property of third parties;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our product candidates and technology.

If we do not successfully develop and commercialize product candidates based upon our technological approach, we will not be able to obtain future revenues, which would result in significant harm to our financial position and adversely affect our stock price.

Our product candidates are based on our SVP technology, which is an unproven approach designed to induce antigen-specific immune tolerance to biologic drugs or stimulate the immune system.

All of our product candidates are derived from our SVP technology, which is an unproven approach to inducing antigen-specific tolerance or stimulating the immune system. In addition, SEL-212, our lead product candidate, uses pegsiticase, a biologic, which we source from Shenyang Sunshine Pharmaceutical Co., Ltd., or 3SBio, in China. We have not, nor to our knowledge has any other company, received FDA approval for a therapeutic based on SVP or for a biologic product manufactured in China. In addition, we may use biologics other than pegsiticase with our SVP technology.

As a result, we cannot be certain that our approach, or our development of SEL-212, will lead to the development or approval of marketable products. In addition:

- due to the unproven nature of our SVP therapeutics, they may have different efficacy and safety rates in various indications;
- the FDA or other regulatory agencies may lack experience in evaluating the efficacy and safety of products based on SVP or a biologic sourced from China or other jurisdictions, which could result in a longer-than-expected regulatory review process, increase our expected development costs or delay or prevent commercialization of our product candidates; and
- in the event of a biologics license application for SEL-212 or another product and a pre-approval inspection by the FDA of the facilities of 3SBio or any other manufacturer of biologics we may use, the FDA may not approve the facility for production or may make observations that will take significant time for 3SBio or such other provider to address.

The occurrence of any of the foregoing, would effectively prevent or delay approval of our lead and other product candidates.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and management resources, we focus on a limited number of research programs and product candidates and are currently principally focused on SEL-212. As a result, we may forego or delay our pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource-allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our

Risk factors

spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may not pursue such product candidate, or we may relinquish valuable rights to that product candidate through future collaboration, licensing or other arrangements, in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Aside from SEL-212, our other product candidates are in preclinical development. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval, and the risk of failure through the development process is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its outcome is inherently uncertain. A failed clinical trial can occur at any stage of testing. Moreover, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

SEL-212 is currently being evaluated in a Phase 1/2 clinical program that includes a Phase 1a and Phase 1b clinical trial. As of June 3, 2016, on a combined basis, we had dosed a total of 70 subjects with either SEL-212 (SVP-Rapamycin and pegsiticase), SVP-Rapamycin alone or pegsiticase alone in the Phase 1a and Phase 1b clinical trials. We expect to receive final data from both Phase 1 clinical trials in the second half of 2016. Based on preliminary results from the Phase 1 clinical trials, we have generally observed that SEL-212 and its components, SVP-Rapamycin and pegsiticase, have been well tolerated. There can be no assurance, however, that these preliminary results will be predictive of the final results of the trial. Moreover, the biological effect observed in this trial has been observed only in the subjects of the trial, and is not statistically significant and might not be observed in any other patients treated with SEL-212 or its components, SVP-Rapamycin and pegsiticase. As of June 16, 2016, there have been three serious adverse events, or SAEs, in the Phase 1 clinical trials. One SAE occurred in a 62 year-old male who received a dose level of pegsiticase alone of 0.4 mg/kg. This subject developed atrial fibrillation 13 days after administration of pegsiticase. The subject was treated and the medical records from the principal investigator indicate that this subject has recovered. The principal investigator has deemed this SAE to not have been related to the study drug, pegsiticase. The second SAE occurred in a 59 year-old male who developed a pruritic rash on his lower extremities and joint pain approximately 12 days after being dosed with SEL-212, consisting of a dose level of SVP-Rapamycin of 0.1 mg/kg and a dose level of pegsiticase of 0.4 mg/kg. This subject was treated with steroids, analgesics, anti-nausea medications and topical antihistamine cream. Following treatment, the medical records from the principal investigator indicate that the rash and joint pain experienced by the subject have been resolved. The principal investigator classified this second SAE as having been possibly related to the study drug, SEL-212. A third observation was classified by the principal investigator on June 15, 2016 as an SAE after a 59 year-old male from Cohort #7 (SVP-Rapamycin Cohort) of the Phase 1b clinical trial developed stomatitis approximately seven days after being dosed with 0.5 mg/kg of SVP-Rapamycin, the highest dose of SVP-Rapamycin in the SVP-Rapamycin Cohorts of the Phase 1b clinical trial, and experienced 4.3 kg of weight loss. Stomatitis is a form of mouth sores and inflammation of the mouth and lips that often limits food intake and, according to the label for rapamycin, is a common adverse reaction to rapamycin itself.

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This subject was treated with oral over-the-counter and topical antihistamines followed by a steroid gel. As of June 16, 2016, the principal investigator indicated that the subject's stomatitis was improving. The principal investigator classified this third SAE as having been possibly related to the study drug, SVP-Rapamycin. We can provide no assurance that additional SAEs or similar events will not arise in the course of our development of SEL-212 or other product candidates.

We had a prior SVP-nicotine product candidate, which entered clinical development after a promising preclinical program. However, results from a Phase 1 clinical trial conducted in smokers and non-smokers with this product candidate showed that nicotine-specific antibodies were induced at sub-therapeutic levels. In this regard, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical development or early-stage clinical trials, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. Moreover, preclinical and clinical data is often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or other regulatory authority approval. If we fail to produce positive results in our clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be negatively impacted.

In addition, we cannot be certain as to what type and how many clinical trials the FDA will require us to conduct before we may successfully gain approval to market SEL-212 or any of our other product candidates in the United States or other countries. Prior to approving a new therapeutic product, the FDA generally requires that safety and efficacy be demonstrated in two adequate and well-controlled clinical trials. In some situations, evidence from a Phase 2 trial and a Phase 3 trial or from a single Phase 3 trial can be sufficient for FDA approval, such as in cases where the trial or trials provide highly reliable and statistically strong evidence of an important clinical benefit. We expect to conduct more than one Phase 3 trial for SEL-212 in the refractory gout indication in order to gain approval. Additional clinical trials could cause us to incur significant development costs, delay or prevent the commercialization of SEL-212 or otherwise adversely affect our business.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval for, or commercialize, our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with contract research organizations, or CROs, or clinical trial sites;
- we may be unable to recruit suitable patients to participate in a clinical trial, the number of patients required for clinical trials of our product candidates may be larger than we expect, enrollment in these clinical trials may be slower than we expect or participants may drop out of these clinical trials at a higher rate than we expect;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- investigators, regulators, data safety monitoring boards or institutional review boards may require that we or our investigators suspend or terminate clinical research, or we may decide to do so

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ourselves, for various reasons including noncompliance with regulatory requirements, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues such as a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions;

- the cost of clinical trials of our product candidates may be greater than we expect;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we expect; and
- regarding trials managed by our existing or any future collaborators, our collaborators may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but potentially suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- lose the support of collaborators, requiring us to bear more of the burden of research and development;
- not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have a product removed from the market after obtaining marketing approval.

Our product development costs will increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, from time to time our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

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We are initially developing our lead product candidate, SEL-212, for the treatment of chronic refractory gout, which affects approximately 50,000 patients in the United States. Accordingly, there is a limited number of patients who could enroll in our clinical studies.

In addition to the size of the patient population, patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the availability of other treatments for the disease under investigation;
- the existence of competing clinical trials;
- our efforts to facilitate timely enrollment in clinical trials;
- our payments for participating in clinical trials;
- the patient referral practices of physicians;
- the nature of the trial protocol;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which could cause the value of our common stock to decline and limit our ability to obtain additional financing.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, adverse event reporting, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing that product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third parties to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval for, or prevent or limit the commercial use of, such product candidates.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years. If additional clinical trials are required for certain jurisdictions, these trials can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved, and may ultimately be unsuccessful. Changes in marketing approval

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policies during the development period, changes in or the enactment or promulgation of additional statutes or regulations, respectively, or changes in the regulatory review process for each submitted product application, may cause delays in the review and approval of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept a marketing application as deficient or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Although the FDA and other regulatory authorities have approved nanotechnology-based therapeutics in the past, they are monitoring whether nanotechnology-based therapeutics pose any specific health and human safety risks. While they have not issued any regulations to date, it is possible that the FDA and other regulatory authorities could issue regulations in the future regarding nanotechnology-based therapeutics that could adversely affect our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may not be able to obtain orphan drug designation for our product candidates, and even if we do, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. We expect to seek orphan drug designation for several of our product candidates, although we have not yet applied for or obtained such designation. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full biologics license application, or BLA, or full new drug application, or NDA, to market the same biologic or drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. Our competitors, including Horizon Pharma plc, may seek orphan drug status for the same biologic or drug for the same indication as our product candidates. In this regard, Krystexxa previously obtained orphan drug status for chronic refractory gout, although the exclusivity period has lapsed. However, Krystexxa could in the future obtain orphan drug status for chronic tophaceous gout, an indication we plan to pursue.

The applicable exclusivity period is ten years in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

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Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care.

Any breakthrough therapy designation that we may receive from the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may in the future seek breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. The availability of breakthrough therapy designation was established recently with the passage of the Food and Drug Administration Safety and Innovation Act of 2012. We cannot be sure that any evaluation we may make of our product candidates as qualifying for breakthrough therapy designation will meet the FDA's expectations. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Further, therapies such as those we are developing involve unique side effects that could be exacerbated compared to side effects from other types of therapies with singular components. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient enrollment in our clinical trials or the ability of any enrolled patients to complete such trials or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

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Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

In addition, if our product candidates are associated with undesirable side effects in certain patient populations, such as pediatric patients or the elderly, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would harm our business.

RISKS RELATED TO OUR DEPENDENCE ON THIRD PARTIES AND MANUFACTURING

We rely on 3SBio in China as our sole supplier of pegsiticase and on other third parties for the manufacture of our product candidates for preclinical and clinical testing, and expect to continue to do so for the foreseeable future. Our reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We obtain the biologic pegsiticase, a component of SEL-212, our lead product candidate, from 3SBio in China. Under our license agreement with 3SBio, we are not permitted to manufacture pegsiticase and, as a result, expect to continue to rely on 3SBio for our supply of pegsiticase for the foreseeable future. Although we intend to seek to secure a backup supplier outside of China, we cannot assure you that we will be able to do so on acceptable terms.

Any disruption in production or inability of 3SBio in China to produce adequate quantities of pegsiticase to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our research and development of our future product candidates. Furthermore, since 3SBio is located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the Chinese government, political unrest or unstable economic conditions in China. Any of these matters could materially and adversely affect our business and results of operations. Any issues related to the manufacturing lots or similar action regarding pegsiticase used in preclinical studies or clinical trials could delay the studies or trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by 3SBio could significantly delay our clinical development of potential products and reduce third-party or clinical researcher interest and support of our proposed trials. These interruptions or failures could also impede commercialization of our future product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the

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value of the local currency in China. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in China.

In addition to 3SBio, we rely, and expect to continue to rely, on other third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. Our reliance on such third parties increases the risk that we will not have sufficient quantities of our product candidates on a timely basis or at all, or that such quantities will be available at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish any agreements with third-party manufacturers on acceptable terms or at all. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including the:

- inability, failure or unwillingness of third-party manufacturers to comply with regulatory requirements, maintain quality assurance, meet our needs, specifications or schedules or continue to supply products to us;
- reduced control we have over product development, including with respect to our lead product candidate, due to our reliance on such third-party manufacturers,
- breach of manufacturing agreements by the third-party manufacturers;
- misappropriation or disclosure of our proprietary information, including our trade secrets and know-how;
- relationships that the third party manufacturer may have with others, some of which may be our competitors, and, if it does not successfully carry out its contractual duties, does not meet expectations, experiences work stoppages, or needs to be replaced, we may need to enter into alternative arrangements, which may not be available, desirable or cost-effective; and
- termination or nonrenewal of agreements by third-party manufacturers at times that are costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current Good Manufacturing Practices, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. If our contract manufacturer is unable to comply with cGMP regulations or if the FDA does not approve their facility upon a pre-approval inspection, our product candidate may not be approved or may be delayed in obtaining approval. In addition, there are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing our products. Therefore, our product candidates and any future products that we may develop may compete with other products for access to manufacturing facilities. Any failure to gain access to these limited manufacturing facilities could severely impact the clinical development, marketing approval and commercialization of our product candidates.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for required raw materials used in the manufacture of our product candidates or for the manufacture of finished product. Moreover, we often rely on one contract

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manufacturer to produce multiple product components. For instance, one of our contract manufacturers produces polymers used in our SVP technology. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and expected future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts.

Our existing collaborations are important to our business, and future licenses may also be important to us. If we are unable to maintain any of these collaborations, or if these arrangements are not successful, our business could be adversely affected.

We have entered into collaborations with other parties, including pharmaceutical companies and universities, to develop products based on our SVP technology, and such collaborations and licensing arrangements currently represent a significant portion of our product pipeline. Our collaboration and license agreements include those with Sanofi, Massachusetts Institute of Technology, or MIT, 3SBio, BIND Therapeutics, Inc. and the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc. Our collaborations with Sanofi also provided us with important funding for some of our development programs and we expect to receive additional funding under collaborations in the future. Our existing collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

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- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we would potentially lose the right to pursue further development or commercialization of the applicable product candidates;
- collaborators may learn about our technology and use this knowledge to compete with us in the future;
- there may be conflicts between different collaborators that could negatively affect those collaborations and potentially others;
- the number and type of our collaborations could adversely affect our attractiveness to future collaborators or acquirers; and
- we currently have, and in the future may have, a limited number of collaborations and the loss of, or a disruption in our relationship with, any one or more of such collaborators may could harm our business.

If our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research and development funding or milestone or royalty payments under such collaborations. If we do not receive the funding we expect under these agreements, our continued development of our SVP technology and product candidates could be delayed and we may need additional resources to develop additional product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of our therapeutic program collaborators and there can be no assurance that our collaborations will produce positive results or successful products on a timely basis or at all.

Additionally, subject to its contractual obligations to us, if one of our collaborators is involved in a business combination or otherwise changes its business priorities, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of our business in the business and financial communities, and our stock price, could be adversely affected. In addition, we have a limited number of collaborations and if our relationship with any one or more of such collaborators were to cease, our business would be harmed as a result.

We may in the future collaborate with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may not be able to access specific antigens that would be suitable to development with our technology, have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and

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undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our programs, and our business may be materially and adversely affected.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including by failing to meet deadlines for the completion of such trials.

We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct and manage our clinical trials, including our Phase 1b clinical trial of SEL-212.

Our reliance on these third parties for research and development activities will reduce our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practice, or GCP, regulations, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and welfare of trial participants are protected. Other countries' regulatory agencies also have requirements for clinical trials. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, *ClinicalTrials.gov*, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, do not meet expected deadlines, experience work stoppages, terminate their agreements with us or need to be replaced, or do not conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated, or may need to be repeated. If any of the foregoing occur, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates or in commercializing our product candidates.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of such product candidates, producing additional losses and depriving us of potential product revenue.

We have no experience manufacturing our product candidates at commercial scale, and if we decide to establish our own manufacturing facility, we cannot assure you that we can manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have a pilot manufacturing facility at our Watertown, Massachusetts location where we conduct process development, scale-up activities and the manufacture of SVP product candidates for preclinical use. We rely on the scale equipment at our CMOs for the manufacture of the clinical supply of all of our product candidates. If our facility, or our CMOs' facilities, were damaged or destroyed, or otherwise subject to disruption, it would require substantial lead-time to replace our manufacturing

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capabilities. In such event, we would be forced to identify and rely entirely on alternative third-party contract manufacturers for an indefinite period of time. Any disruptions or delays at our facility or its failure to meet regulatory compliance would impair our ability to develop and commercialize our product candidates, which would adversely affect our business and results of operations.

In addition, the FDA and other comparable foreign regulatory agencies must, pursuant to inspections that are conducted after submitting a BLA or relevant foreign marketing submission, confirm that the manufacturing processes for the product candidate meet cGMP regulations. We do not currently have any of our own manufacturing facilities that meet the FDA's cGMP requirements for the production of any product candidates used in humans, and rely on our CMOs for clinical production.

We may choose to establish a manufacturing facility for our product candidates for production at a commercial scale. However, we have no experience in commercial-scale manufacturing of our product candidates. We currently intend to develop our manufacturing capacity in part by expanding our current facility or building additional facilities. This activity will require substantial additional funds and we would need to hire and train significant numbers of qualified employees to staff these facilities. We may not be able to develop commercial-scale manufacturing facilities that are adequate to produce materials for additional later-stage clinical trials or commercial use.

The equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of such facilities, equipment, systems, processes and analytics. We may be subject to lengthy delays and expense in conducting validation studies, if we can meet the requirements at all.

RISKS RELATED TO COMMERCIALIZATION OF OUR PRODUCT CANDIDATES AND OTHER LEGAL COMPLIANCE MATTERS

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if any, will depend on a number of factors, including:

- their efficacy, safety and other potential advantages compared to alternative treatments;
- the clinical indications for which our product candidates are approved;
- our ability to offer them for sale at competitive prices;
- their convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for our product candidates;
- the prevalence and severity of their side effects and their overall safety profiles;
- any restrictions on the use of our product candidates together with other medications;
- interactions of our product candidates with other medicines patients are taking;

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- our ability to create awareness with patients and physicians about the harmful effects of uric acid deposits;
- inability of certain types of patients to take our product candidates; and
- their ability to remain attractive in the event of changing treatment guidelines.

The research, development and commercialization of our product candidates depends upon our maintaining strong working relationships with the medical community. We rely on these professionals to provide us with considerable knowledge and experience regarding the development, marketing and commercialization of our product candidates. If we are unable to maintain our strong relationships with these professionals and continue to receive their advice and input, our products and product candidates may not be developed and marketed in line with such professionals' needs and expectations. Accordingly, the development and commercialization of our products and product candidates could suffer, which could have a material adverse effect on our business and results of operations.

We currently have no sales organization. If we are unable to establish effective sales, marketing and distribution capabilities, or enter into agreements with third parties with such capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product candidate for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform sales and marketing functions and we may not be successful in doing so.

In the future, we expect to build a focused sales and marketing infrastructure to market or co-promote our product candidates in the United States and potentially elsewhere, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or educate physicians on the benefits of our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies for our product candidates.

Outside the United States, we may rely on third parties to sell, market and distribute our product candidates. We may not be successful in entering into arrangements with such third parties or may be

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unable to do so on terms that are favorable to us. In addition, our product revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Our product candidates, if approved, may fail to offer material commercial advantages over other treatments.

The therapeutic advantages that we believe may be offered by our product candidates, if approved, may fail to materialize, or may not be recognized by physicians, hospital administrators, patients, caregivers, healthcare payors and others in the medical community. For example, physicians may be skeptical to use SEL-212 for the treatment of refractory and chronic tophaceous gout. Patients may also be skeptical of using a product based on our SVP technology. The therapeutic advantages of our product candidates may not be sufficient to either move market share to us or expand the population of patients using our treatments.

We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The development and commercialization of new drug and biologic products and technologies is highly competitive and is characterized by rapid and substantial technological development and product innovations. We protect our products and technologies by filing patent applications in major pharmaceutical markets as well as leading emerging growth markets. We have either been granted patents or filed patent applications covering our SVP technology, our immune tolerance programs and our SEL-212 product candidate. To the extent that our product candidates and technologies are protected by such intellectual property rights, they will be protected from competition for the life of the applicable patents. However, many companies offer pharmaceutical products or technologies that may address one or more indications that our product candidates target. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

In this regard, SEL-212 may compete with Krystexxa, recently acquired by affiliates of Horizon Pharma plc, which contains a pegylated uricase similar to the pegsiticase component of SEL-212 and is indicated for the treatment of refractory gout. Large companies with active research to prevent the formation of ADAs and treat allergies and autoimmune diseases include Sanofi, Pfizer Inc., or Pfizer, and Merck & Co., Inc., or Merck. Small early-stage biopharmaceutical companies active in the research for new technologies to achieve antigen-specific tolerance include Anokion SA, Cour Pharmaceutical Development Company, Inc., or Cour Pharmaceutical, Apitope International NV, Evotec AG and Dendright International, Inc. Large pharmaceutical companies, including Astra Zeneca PLC, or Astra Zeneca, Roche Holding AG, Pfizer, Merck, Bristol-Myers Squibb Company, and Amgen Inc., as well as smaller biopharmaceutical companies, including Immune Design Corp., are active in the research and development of cancer vaccines. Clinical stage companies with vaccine approaches to treating HPV-associated cancer include VGX3100 from Inovio Pharmaceuticals, Inc., or Inovio, ISA-101 from ISA Pharmaceuticals B.V., GTL001 from Genticel, INO-3112 licensed by Astra Zeneca from Inovio, and others. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others may be based on entirely different approaches. For example, Anokion SA targets to induce antigen-specific tolerance by

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attaching an antigen to red blood cells and Cour Pharmaceutical is working on a nanoparticle encapsulating antigen without any immunomodulator to treat celiac disease. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement for product candidates and in marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors.

These third parties compete with us in recruiting and retaining qualified scientific, sales and marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a microbiome therapeutic which will likely share our same regulatory approval requirements. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations or third-party coverage or reimbursement policies, any of which would harm our business.

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Obtaining and maintaining adequate reimbursement for our products may be difficult. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and adequate reimbursement for the product. We cannot be certain if and when we will obtain an adequate level of reimbursement for our products by third-party payors. Even if we do obtain adequate levels of reimbursement, third-party payors, such as government or private healthcare insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for, products. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that pharmaceutical companies

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provide them with predetermined discounts from list prices and are challenging the prices charged for products. We may also be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control, including possible price reductions, even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically necessary for a specific indication or cost-effective, or that coverage or an adequate level of reimbursement will be available.

Product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for any product candidates or products that we may develop;

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- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold \$10 million in product liability insurance coverage in the aggregate, with no per occurrence limit, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

Although we do not have any current plans to market and sell our products in other jurisdictions outside of the United States, we may decide to do so in the future and either we or our collaborators would need to obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in foreign countries may differ substantially from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product candidate be approved for reimbursement before the product candidate can be approved for sale in that country. We or our collaborators may not obtain approvals for our product candidates from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions, or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in any market.

Although we are not currently marketing our product candidates, including to healthcare providers, if and when we do, our relationships with healthcare providers, customers and third-party payors may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, customers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with third party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products

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for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation; in addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act);
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to certain payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or

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case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom will recommend, purchase and/or prescribe our product candidates, if approved, could be subject to challenge under one or more of such laws.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, in the United States, in 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the PPACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the PPACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

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- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA's regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unexpected problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to the continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to continual review and periodic inspections to assess compliance with cGMP. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy, or REMS, which could include requirements for a medication guide, physician communication plans or additional

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elements to ensure safe use, such as restricted distribution methods, patient registries and other risk mitigation tools. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our product, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. The FDA closely regulates the post-approval marketing and promotion of drugs and biologics to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products outside of their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDA's restrictions relating to the promotion of prescription products may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, if a regulatory agency or we later discover previously unknown problems with our products, such as adverse events of unexpected severity or frequency, problems with manufacturers or manufacturing processes, or failure to comply with regulatory requirements, the regulatory agency may impose restrictions on the products or us, including requiring withdrawal of the product from the market. Any failure to comply with applicable regulatory requirements may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- withdrawal of products from the market;
- suspension or termination of ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with existing and potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions; or
- imposition of civil or criminal penalties.

Noncompliance with other requirements in foreign jurisdictions regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with

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U.S. and foreign regulatory requirements regarding the development of products for pediatric populations and the protection of personal health information can also lead to significant penalties and sanctions.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues. If regulatory sanctions are applied or if regulatory approval is withheld or withdrawn, the value of our company and our operating results will be adversely affected.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other partners from authorizing, promising, offering or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our product candidates abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Our violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidates. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing

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negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

If we or our contract manufacturers or other third parties fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and our contract manufacturers and other third parties with whom we do business are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including biological materials and chemicals, such as trichloroethylene. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. The failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or compromise our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target and prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Our product candidates, including our products that utilize viral delivery systems, could produce adverse events. Adverse events in our clinical trials or following approval of any of our product candidates, even if not ultimately attributable to our product candidates, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the

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testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, others could compete against us more directly, which would negatively impact our business.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or in all jurisdictions. Prosecution of our patent portfolio is at a very early stage, and we are just beginning to reach the statutory deadlines for deciding whether and where to initiate prosecution in specific foreign jurisdictions by filing national stage applications based on our Patent Cooperation Treaty, or PCT, applications. As those deadlines come due, we will have to decide whether and where to pursue patent protection for the various inventions claimed in our patent portfolio, and we will only have the opportunity to obtain patents in those jurisdictions where we pursue protection. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as, with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, we have obligations under our licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license could have a material adverse impact on our business.

We currently own nine issued U.S. patents. Although we have patent applications pending, we cannot provide any assurances that any of these pending patent applications will mature into issued patents and, if they do, that such patents or our current patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. Further, it is possible that a patent claim may provide coverage for some but not all parts of a product candidate or third-party product. These and other factors may provide opportunities for our competitors to design around our patents, should they issue.

Moreover, other parties may have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications, and may have received or may receive

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patents, that may overlap or conflict with our patent applications, either by claiming similar methods or by claiming subject matter that could dominate our patent position. In addition, given the early stage of prosecution of our portfolio, it may be some time before we understand how patent offices react to our patent claims and whether they identify prior art of relevance that we have not already considered.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in any owned patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we may license patents were the first to make the inventions claimed or were the first to file. For these and other reasons, the issuance, scope, validity, enforceability and commercial value of our patent rights are subject to a level of uncertainty. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. The issuance, scope, validity, enforceability and commercial value of our patents are subject to a level of uncertainty.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering biotechnological and pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Even if issued, a patent's validity, inventorship, ownership or enforceability is not conclusive. Accordingly, rights under any existing patent or any patents we might obtain or license may not cover our product candidates, or may not provide us with sufficient protection for our product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any other third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary

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know-how, and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how, and other information and technology. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could adversely affect our business and operations.

Intellectual property rights do not prevent all potential threats to competitive advantages we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage.

The following examples are illustrative:

- others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or any of our licensors or collaborators might not have been the first to make the inventions covered by the patents or pending patent applications that we own or have exclusively licensed;
- we or any of our licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- the prosecution of our pending patent applications may not result in granted patents;
- granted patents that we own or have licensed may not cover our products or may be held not infringed, invalid or unenforceable, as a result of legal challenges by our competitors;
- with respect to granted patents that we own or have licensed, especially patents that we either acquire or in-license, if certain information was withheld from or misrepresented to the patent examiner, such patents might be held to be unenforceable;
- patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product candidates;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in markets where we intend to market our product candidates;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and

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- we may choose not to file a patent application for certain technologies, trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

We may not identify relevant patents or may incorrectly interpret the relevance, scope or expiration of a patent, which might adversely affect our ability to develop and market our product candidates.

We cannot guarantee that any of our patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete and thorough, nor can we be certain that we have identified each and every patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products or pipeline molecules. We may incorrectly determine that our product candidates are not covered by a third-party patent.

Many patents may cover a marketed product, including but not limited to the composition of the product, methods of use, formulations, cell line constructs, vectors, growth media, production processes and purification processes. The identification of all patents and their expiration dates relevant to the production and sale of an originator product is extraordinarily complex and requires sophisticated legal knowledge in the relevant jurisdiction. It may be impossible to identify all patents in all jurisdictions relevant to a marketed product. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect which may negatively impact our ability to develop and market our product candidates.

Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

If we are unable to protect the confidentiality of our trade secrets and know-how, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also seek to enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to, or independently developed by, a competitor, our competitive position would be harmed.

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Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, recent patent reform legislation could further increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, in particular the first to file provisions, became effective on March 16, 2013. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This requires us to be cognizant of the time from invention to filing of a patent application. Thus, for our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law. Moreover, some of the patent applications in our portfolio will be subject to examination under the pre-Leahy-Smith Act law and regulations, while other patents applications in our portfolio will be subject to examination under the law and regulations, as amended by the Leahy-Smith Act. This introduces additional complexities into the prosecution and management of our portfolio.

In addition, the Leahy-Smith Act limits where a patentee may file a patent infringement suit and provides opportunities for third parties to challenge any issued patent in the USPTO. These provisions apply to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a federal court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims because it may be easier for them to do so relative to challenging the patent in a federal court action. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. From time to time, the U.S. Supreme Court, other federal courts, the U.S. Congress or the USPTO may change the standards of patentability, and any such changes could have a negative impact on our business.

Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change or be interpreted in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue to us in the future. In addition, these events may adversely affect our ability to defend any patents that may issue in procedures in the USPTO or in courts.

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We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and ultimately unsuccessful.

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that one of our patents is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which could materially and adversely affect us and our collaborators.

Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. Even if we are successful, domestic or foreign litigation, or USPTO or foreign patent office proceedings, may result in substantial costs and distraction to our management. We may not be able, alone or with our licensors or potential collaborators, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such litigation has been brought against us and we have not been held by any court to have infringed a third party's intellectual property rights, we cannot guarantee that our technology, product candidates or use of our product candidates do not infringe third-party patents.

We are aware of numerous patents and pending applications owned by third parties, and we monitor patents and patent applications in the fields in which we are developing product candidates, both in the United States and elsewhere. However, we may have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications

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or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference or derivation proceedings before the USPTO and similar bodies in other countries. Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our product candidates or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, to infringe a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our product candidates and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Even if we are successful in such proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our product candidates. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. There could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing our product candidates;
- pay substantial damages for past use of the asserted intellectual property;

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- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign or rename some or all of our product candidates, or other brands to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Any of these risks coming to fruition could harm our business.

Issued patents covering our product candidates could be found invalid or unenforceable or could be interpreted narrowly if challenged in court.

Competitors may infringe our intellectual property, including our patents or the patents of our licensors. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time-consuming. If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement, or failure to claim patent-eligible subject matter. Grounds for unenforceability assertions include allegations that someone connected with the prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Moreover, even if not found invalid or unenforceable, the claims of our patents could be construed narrowly or in a manner that does not cover the allegedly infringing technology in question. Such a loss of patent protection would have a material adverse impact on our business.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and, in some jurisdictions, during the pendency of a patent application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions

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during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have an adverse effect on our business.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

It is our policy to enter into confidentiality and intellectual property assignment agreements with our employees, consultants, contractors and advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to multiple license agreements that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. For example, we currently rely on certain intellectual property rights licensed to us from MIT, and have licensed additional intellectual property rights under agreements with 3SBio, BIND Therapeutics, Inc. and The Massachusetts Eye and Ear Infirmary and the Schepens Eye Research Institute, Inc. Under our existing licensing agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreement. Our results of operations will be affected by the level of royalty payments that we are required to pay to third parties. We cannot precisely predict the amount, if any, of royalties that we will be required to pay to third parties in the future. Any disagreements with the counterparty over the amount of royalties owed could lead to litigation, which is costly. In addition, if we fail to comply with our obligations under current or future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of product candidates being developed using rights licensed to us under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or

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reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Furthermore, our counterparties may allege that we are operating outside the scope of the licenses granted and terminate our license or otherwise require us to alter development, manufacturing or marketing activities. For more information on our license agreements and associated obligations, please see "Business—Licenses and collaborations."

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties and under patents and patent applications that we own, to develop our product candidates. Because we may find that our programs require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may also engage advisors and consultants who are concurrently employed at universities or other organizations or who perform services for other entities. Although we try to ensure that our employees, advisors and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, advisors or consultants have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such party's former or current employer or in violation of an agreement with another party. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

In addition, while it is our policy to require our employees, consultants, advisors and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Similarly, we may be subject to claims that an employee, advisor

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or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources, and could adversely impact our financial condition or results of operations.

We will need to obtain FDA approval for any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any proprietary name or trademark we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies certain medical claims or contributes to an overstatement of efficacy. If the FDA objects to any product names we propose, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some

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countries outside the United States could be less extensive than in the United States, assuming that rights are obtained in the United States and assuming that rights are pursued outside the United States. In this regard, in addition to the United States, we also seek to protect our intellectual property rights in other countries, including Russia. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For all of the patent families in our portfolio, including the families that may provide coverage for our lead product candidate, the relevant statutory deadlines have not yet expired. Therefore, for each of the patent families that we believe provide coverage for our lead product candidate, we will need to decide whether and where to pursue additional protection outside the United States or Russia. In addition, the laws of some foreign countries, do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, for our existing patent rights outside the United States and any foreign patent rights we may decide to pursue in the future, we may not be able to obtain relevant claims and/or we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

If our ability to obtain and, if obtained, enforce our patents to stop infringing activities is inadequate, third parties may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property we develop or license.

If we do not obtain additional protection under the Hatch-Waxman Act and similar foreign legislation extending the terms of our patents for our product candidates, our business may be harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years

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as compensation for patent term lost during product development and the FDA regulatory review process. Patent term restorations, however, are limited to a maximum of five years and cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened, our competitors may obtain earlier approval of competing products and our ability to generate revenues could be materially adversely affected.

We may face competition from biosimilars, which may have a material adverse effect on the future commercial prospects of our product candidates.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. This new pathway could allow competitors to reference data from innovative biological products 12 years after the time of approval of the innovative biological product. This data exclusivity does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator's application to support the biosimilar product's approval. In his proposed budget for fiscal year 2017, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." While President Obama has proposed these measures in previous years without success, it is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity. The Biologics Price Competition and Innovation Act of 2009 is complex and only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning is subject to uncertainty. Although it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our product candidates.

RISKS RELATED TO EMPLOYEE MATTERS AND MANAGING GROWTH AND OTHER RISKS RELATED TO OUR BUSINESS

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Werner Cautreels, Ph.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements or offer letters with Dr. Cautreels and certain of our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key

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employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of lead discovery and product development, regulatory affairs, clinical affairs and manufacturing and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our expected future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such expected growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

A variety of risks associated with operating in Russia and internationally could adversely affect our business.

In addition to our U.S. operations, we have operations in Russia through our wholly owned subsidiary, Selecta RUS, and may expand international operations in the future, including by conducting clinical trials of our product candidates in countries outside the United States, including Russia and Belgium. We face risks associated with our operations in Russia, including possible unfavorable regulatory, pricing and reimbursement, legal, political, tax and labor conditions, which could harm our business. For example, one of our principal shareholders, RUSNANO, is a Russian Federation controlled entity and, according to press reports, in 2015 and 2016 several current and former RUSNANO managers were under investigation for embezzlement. While we and our officers and directors were not accused of any wrongdoing, further investigations or other accusations could adversely affect us.

We may also rely on collaborators to commercialize any approved product candidates outside of the United States. Doing business in Russia and internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;

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- failure by us to obtain and maintain regulatory approvals for the use of our product candidates in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection of and enforcing our intellectual property rights;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple-payor reimbursement regimes, government payors or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our product candidates and exposure to foreign currency exchange rate fluctuations, which could result in increased operating expenses and reduced revenues;
- natural disasters, political and economic instability, including wars, events of terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions and economic weakness, including inflation;
- changes in diplomatic and trade relationships;
- challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- certain expenses including, among others, expenses for travel, translation and insurance;
- legal risks, including use of the legal system by the government to benefit itself or affiliated entities at our expense, including expropriation of property; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the FCPA its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

Sanctions against Russia, and Russia's response to those sanctions, could adversely affect our business.

Due to Russia's recent military intervention in Ukraine, the United States and the European Union have imposed sanctions on certain individuals and six financial institutions in Russia and have proposed the use of broader economic sanctions. In response, Russia has imposed entry bans on certain U.S. lawmakers and officials. Our wholly owned subsidiary, Selecta RUS, held \$4.2 million of total cash in Russian banks as of March 31, 2016, including \$1.5 million of cash and cash equivalents, \$2.0 million of short-term deposits and \$0.7 million of restricted cash. If the United States and European Union were to impose sanctions on Russian businesses, or if Russia were to take retaliatory action against U.S. companies operating in Russia, our research and development activities with respect to our program for HPV-associated cancers currently conducted by Selecta RUS, or any other research and development activities with respect to our other immune stimulation programs conducted by Selecta RUS in the future, could be adversely affected.

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Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could expose us to liability and hurt our reputation.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA laws and regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, (2) manufacturing standards, (3) healthcare fraud and abuse laws, or (4) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Acquisitions or joint ventures could disrupt our business, cause dilution to our stockholders and otherwise harm our business.

We may acquire other businesses, product candidates or technologies as well as pursue strategic alliances, joint ventures, technology licenses or investments in complementary businesses. We have not made any acquisitions to date, and our ability to do so successfully is unproven. Any of these

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transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with future customers or with current or future distributors or suppliers as a result of such a transaction;
- unexpected liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- diversion of management time and focus from operating our business to acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses;
- possible write-offs or impairment charges relating to acquired businesses; and
- inability to develop a sales force for any additional product candidates.

Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the expected benefit of any acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

RISKS RELATED TO OUR COMMON STOCK AND THIS OFFERING

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although our common stock has been approved for listing on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;

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- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk factors" section and elsewhere in this prospectus.

After this offering, our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to stockholders for approval.

Upon the closing of this offering, based on the number of shares of common stock outstanding as of May 31, 2016, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering and their respective affiliates will, in the aggregate, hold shares representing approximately 45% of our outstanding voting stock, which does not take into account any potential participation by such parties in this offering. See "Certain relationships and related person transactions—Participation in this offering." As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation or sale of all or substantially all of our assets.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in

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this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares subsequently are issued under outstanding options or warrants, you will incur further dilution. Based on an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of \$10.88 per share as of March 31, 2016, representing the difference between our pro forma as adjusted net tangible book value per share, after giving effect to this offering, and the assumed initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately 35.0% of the aggregate price paid by all purchasers of our stock but will own only approximately 25.0% of our common stock outstanding after this offering.

Upon the closing of this offering, (i) our series E preferred stock will automatically convert into a number of shares of common stock and (ii) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. Accordingly, the number of shares of our common stock issuable upon conversion of all of our preferred stock and exercise of our warrants outstanding would correspondingly increase or decrease, as applicable, in the event of any change in the initial public offering price per share. See "Prospectus summary—The offering."

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. We expect that we will use the net proceeds of this offering to support the clinical development of SEL-212, conduct preclinical studies of our other SVP product candidates in order to advance such product candidates into clinical development and for working capital and general corporate purposes. However, our use of these proceeds may differ substantially from our current plans. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding 16,914,048 shares of common stock based on the number of shares outstanding as of May 31, 2016. This includes the 4,250,000 shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates, existing stockholders that are required to file reports pursuant to Section 16 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or participants in our directed share program who purchase more than \$1,000,000 of shares. See "Prospectus summary—Directed share program" and "Shares eligible for future sale." The remaining 12,664,048 shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times beginning 180 days after this offering, unless held by one of our affiliates, in which case the resale of those securities will be subject to

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volume limitations under Rule 144 of the Securities Act of 1933, as amended, or Rule 144. Moreover, after this offering, holders of 12,016,162 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenues exceed \$1.0 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of

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this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event

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we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target animal studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our restated certificate of incorporation and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our restated bylaws, which will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which

Risk factors

may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our restated certificate of incorporation, which will become effective upon the closing of this offering, specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

Because we do not expect paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, our credit facility with Oxford and Pacific Western Bank currently prohibits us from paying cash dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Special note regarding forward-looking statements

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products and product candidates, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of expected products and product candidates, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of factors, risks, uncertainties and assumptions described under the sections in this prospectus entitled "Risk factors" and "Management's discussion and analysis of financial condition and results of operations" and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Industry and other data

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they frequently involve a number of assumptions and limitations and therefore do not guarantee the accuracy or completeness of such information. Our estimates also involve risks and uncertainties and are subject to change based on various factors, including those discussed under the headings "Risk factors," "Special note regarding forward-looking statements" and "Management's discussion and analysis of financial condition and results of operations" in this prospectus.

Trademarks, service marks and tradenames

We own or have rights to use a number of registered and common law trademarks, service marks and trade names in connection with our business in the United States and in certain foreign jurisdictions, including, but not limited to, "SELECTA."

Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus are included without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and trade names. This prospectus contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this prospectus are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies or third parties.

Use of proceeds

We estimate that the net proceeds from our sale of 4,250,000 shares of our common stock in this offering will be approximately \$55.4 million, assuming an initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, we estimate that our net proceeds will be \$64.3 million. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share would increase (decrease) the net proceeds to us from this offering by approximately \$4.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by \$14.0 million, assuming the assumed initial public offering price stays the same.

We expect that we will use the net proceeds from this offering for the following purposes:

- approximately \$23 million to support the clinical development and manufacturing scale-up of SEL-212, including SEL-212's Phase 2 clinical trial;
- approximately \$10 million to fund the start of a Phase 1 clinical trial and manufacturing scale-up of our first gene therapy program; and
- the remainder, if any, to fund preparations for the Phase 3 clinical trial of SEL-212 and the further advancement of our second gene therapy program as well as other potential future development programs, early-stage research and development and continued development of our SVP technologies, and for working capital and general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to develop product candidates can be difficult and we expect that we will need additional funds to complete the development of SEL-212 and any other product candidates we identify. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

Dividend policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not expect to pay any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, our ability to pay cash dividends is currently prohibited by the terms of our credit facility.

Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2016, as follows:

- on an actual basis;
- on a pro forma basis to reflect the (i) the automatic conversion of all shares of our preferred stock into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock, (ii) outstanding warrants to purchase series D preferred stock becoming warrants to purchase shares of our common stock, upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering, (iii) the automatic cashless exercise of the series E common warrants for 567,306 shares of our common stock and (iv) the filing of our restated certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 4,250,000 shares of common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes appearing

Capitalization

at the end of this prospectus and the "Management's discussion and analysis of financial condition and results of operations" section and other financial information contained in this prospectus.

	As of March 31, 2016		
	Actual (unaudited) (in thousands, except for share data)	Pro forma (unaudited) (in thousands, except for share data)	Pro forma as adjusted (unaudited) (in thousands, except for share data)
Cash, cash equivalents and short-term investments	\$ 25,979	\$ 25,979	\$ 81,367
Other long-term liabilities	310	—	—
Loans payable, net of current portion	11,169	11,169	11,169
Redeemable convertible preferred stock (Series A, B, C, D, E and SRN), par value \$0.0001 per share; 37,835,623 shares authorized, 34,127,186 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	139,837	—	—
Preferred stock, par value \$0.0001 per share; no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, par value \$0.0001 per share; 62,164,377 shares authorized, 2,183,541 shares issued and 2,177,858 shares outstanding (5,683 shares subject to repurchase), actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted; 12,641,402 shares issued and 12,635,719 shares outstanding, pro forma; 16,891,402 shares issued and 16,885,719 shares outstanding, pro forma as adjusted	—	1	1
Additional paid in capital	1	140,147	195,535
Accumulated deficit	(121,051)	(121,051)	(121,051)
Accumulated other comprehensive loss	(4,755)	(4,755)	(4,755)
Total stockholders' equity (deficit)	(125,805)	14,342	69,730
Total capitalization	<u>\$ 25,511</u>	<u>\$ 25,511</u>	<u>\$ 80,899</u>

The number of shares in the table above does not include:

- 1,736,682 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2016, at a weighted average exercise price of \$4.84 per share;
- 112,789 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2016, including outstanding warrants to purchase shares of preferred stock that will become warrants to purchase common stock upon the closing of this offering, at a weighted average exercise price of \$17.43 per share;
- 7,091 shares of our common stock available for future issuance under our 2008 Equity Incentive Plan as of March 31, 2016;
- 390,796 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2016 Plan, which will become effective in connection with this offering, to some of our executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering;
- 819,460 shares of our common stock available for future issuance under our 2016 Plan, which will become effective in connection with this offering, as well as shares of our common stock that become available pursuant to provisions in our 2016 Plan on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Incentive Award Plan"; and
- 173,076 shares of our common stock reserved for future issuance under our 2016 ESPP, which will become effective in connection with this offering, as well as shares of our common stock that

Capitalization

become available pursuant to provisions in our 2016 ESPP that automatically increase the share reserve under our 2016 ESPP on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Employee Stock Purchase Plan."

In addition, upon the closing of this offering, (i) our series E preferred stock will automatically convert into a number of shares of common stock and (ii) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. Accordingly, the number of shares of our common stock issuable upon conversion of all of our preferred stock and exercise of our warrants outstanding would correspondingly increase or decrease, as applicable, in the event of any change in the initial public offering price per share. See "Prospectus summary—The offering."

Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of March 31, 2016, we had a historical net tangible book value (deficit) of \$(125.8) million, or \$(57.76) per share of common stock. Our historical net tangible book value per share is the amount of our total tangible assets less our total liabilities and redeemable convertible preferred stock, which is not included within stockholders' equity (deficit), divided by the number of shares of our common stock outstanding as of March 31, 2016.

Our pro forma net tangible book value as of March 31, 2016 was \$14.3 million, or \$1.13 per share. Pro forma net tangible book value is the amount of our total tangible assets less our total liabilities and redeemable convertible preferred stock, which is not included within stockholders' equity (deficit), after giving effect to the (i) the automatic conversion of all shares of our preferred stock into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock, (ii) outstanding warrants to purchase series D preferred stock becoming warrants to purchase shares of our common stock, upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering, (iii) the automatic cashless exercise of the series E common warrants for 567,306 shares of our common stock and (iv) the filing of our restated certificate of incorporation; and the pro forma net tangible book value per share represents our pro forma net tangible book value divided by the total number of shares outstanding as of March 31, 2016, after giving effect to the pro forma adjustments described above as if they had occurred on such date.

After giving further effect to the sale of 4,250,000 shares of common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2016 would have been approximately \$69.7 million, or approximately \$4.12 per share. This amount represents an immediate increase in pro forma net tangible book value of \$2.99 per share to our existing stockholders and an immediate dilution of approximately \$10.88 per share to new investors participating in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the

Dilution

amount of cash that a new investor paid for a share of common stock. The following table illustrates this dilution:

Assumed initial public offering price per share	\$ 15.00
Historical net tangible book value (deficit) per share as of March 31, 2016	\$ (57.76)
Increase per share attributable to the conversion of our preferred stock and cashless exercise of our series E common warrants	58.89
Pro forma net tangible book value per share as of March 31, 2016	1.13
Increase per share attributable to this offering	2.99
Pro forma as adjusted net tangible book value per share after this offering	\$ 4.12
Dilution per share to new investors in this offering	<u>\$ 10.88</u>

A \$1.00, \$2.00 and \$3.00 increase in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would, in each case, increase the pro forma as adjusted net tangible book value per share after this offering by \$0.24 and increase dilution per share to new investors participating in this offering by \$0.76, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A \$1.00, \$2.00 and \$3.00 decrease in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by \$0.23, \$0.23 and \$0.22 and decrease dilution per share to new investors by \$0.77, \$0.77 and \$0.78, respectively, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1.0 million shares in the number of shares offered by us would increase our pro forma as adjusted net tangible book value per share after this offering by \$0.78 per share and decrease the dilution to new investors by \$0.78 per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. Each decrease of 1.0 million shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by approximately \$0.88 and increase the dilution per share to new investors participating in this offering by approximately \$0.88, assuming no change in the assumed initial public offering price and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares of our common stock in full, the pro forma as adjusted net tangible book value after this offering would be \$4.52 per share, the increase in pro forma net tangible book value per share would be \$0.40 and the dilution per share to new investors would be \$10.48 per share, in each case assuming an initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus.

The following table summarizes on the pro forma as adjusted basis described above, as of March 31, 2016, the differences between the number of shares purchased from us, the total consideration paid to us in cash and the average price per share that existing stockholders and new investors paid. The calculation below is based on an assumed initial public offering price of \$15.00 per share, which is the

Dilution

midpoint of the price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders(1)	12,641,402	75%	\$ 118,547,735	65%	\$ 9.38
New investors	4,250,000	25	63,750,000	35	\$ 15.00
Total	16,891,402	100%	\$ 182,297,735	100%	

(1) Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such stockholders.

The foregoing tables and calculations are based on 2,183,541 shares of our common stock outstanding as of March 31, 2016, which included 5,683 shares of unvested restricted stock, reflect the issuance of 567,306 shares of common stock issued in connection with the automatic cashless exercise of the series E common warrants on May 24, 2016, and give effect to the conversion of our outstanding preferred stock into 9,890,580 shares of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering, and exclude:

- 1,736,682 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2016, at a weighted average exercise price of \$4.92 per share;
- 112,789 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2016, including outstanding warrants to purchase shares of preferred stock that will become warrants to purchase common stock upon the closing of this offering, at a weighted average exercise price of \$17.43 per share;
- 7,091 shares of our common stock available for future issuance under our 2008 Equity Incentive Plan as of March 31, 2016;
- 390,796 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2016 Plan, which will become effective in connection with this offering, to some of our executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering;
- 819,460 shares of our common stock available for future issuance under our 2016 Plan, which will become effective in connection with this offering, as well as shares of our common stock that become available pursuant to provisions in our 2016 Plan on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Incentive Award Plan"; and
- 173,076 shares of our common stock reserved for future issuance under our 2016 ESPP, which will become effective in connection with this offering, as well as shares of our common stock that become available pursuant to provisions in our 2016 ESPP that automatically increase the share reserve under our 2016 ESPP on January 1 of each subsequent calendar year as described in "Executive and director compensation—Incentive plans—2016 Employee Stock Purchase Plan."

Dilution

To the extent any of these outstanding options or warrants is exercised, there will be further dilution to new investors. If all of such outstanding options and warrants had been exercised as of March 31, 2016, the pro forma as adjusted net tangible book value per share after this offering would be \$4.12, and total dilution per share to new investors would be \$10.88.

If the underwriters exercise their option to purchase additional shares of our common stock in full:

- the percentage of shares of common stock held by existing stockholders will decrease to approximately 72% of the total number of shares of our common stock outstanding after this offering; and
- the number of shares held by new investors will increase to 4,887,500, or approximately 28% of the total number of shares of our common stock outstanding after this offering.

In addition, upon the closing of this offering, (i) our series E preferred stock will automatically convert into a number of shares of common stock and (ii) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. See "Prospectus summary—The offering" for a related offering price per share sensitivity analysis.

Selected consolidated financial data

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the "Management's discussion and analysis of financial condition and results of operations" section of this prospectus. We have derived the consolidated statement of operations and comprehensive loss data for the years ended December 31, 2014 and 2015 and the consolidated balance sheet data as of December 31, 2014 and 2015 from our audited consolidated financial statements appearing elsewhere in this prospectus. The consolidated statement of operations data for the three months ended March 31, 2015 and 2016 and the consolidated balance sheet data as of March 31, 2016 have been derived from our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus and have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that should be expected in the future, and results for the three months ended March 31, 2016 are not necessarily indicative of the results to be expected for the full year ending December 31, 2016.

Selected consolidated financial data
Consolidated statement of operations data:

	Years ended December 31,		Three months ended March 31,	
	2014	2015	2015	2016
	(in thousands, except share and per share data)			
Grant and collaboration revenue	\$ 3,040	\$ 6,011	\$ 1,034	\$ 2,088
Operating expenses:				
Research and development	10,486	22,980	4,972	6,648
General and administrative	7,953	8,335	1,872	2,381
Total operating expenses	18,439	31,315	6,844	9,029
Loss from operations	(15,399)	(25,304)	(5,810)	(6,941)
Other income (expense):				
Investment income	111	171	62	13
Foreign currency (loss) gain	3,004	933	194	(220)
Interest expense	(552)	(948)	(179)	(310)
Other expense	(44)	(26)	—	(18)
Total other income (expense), net	2,519	130	77	(535)
Net loss	(12,880)	(25,174)	(5,733)	(7,476)
Accretion of redeemable convertible preferred stock	(4,951)	(7,335)	(1,561)	(2,356)
Net effect of extinguishment of Series SRN redeemable convertible preferred stock	1,459	—	—	—
Net loss attributable to common stockholders	\$ (16,372)	\$ (32,509)	\$ (7,294)	\$ (9,832)
Net loss per share attributable to common stockholders(1)				
Basic and diluted	\$ (7.84)	\$ (15.13)	\$ (3.43)	\$ (4.52)
Weighted average common shares outstanding(1)				
Basic and diluted	2,090,677	2,150,422	2,126,878	2,175,037
Pro forma net loss per share attributable to common stockholders (unaudited)				
Basic and diluted(1)(2)		\$ (2.53)		\$ (0.59)
Pro forma weighted average common shares of common stock outstanding (unaudited)				
Basic and diluted(1)(2)		9,980,469		12,632,923

- (1) See Note 3 to our consolidated financial statements included elsewhere in this prospectus for additional information regarding the method used to calculate the historical and pro forma basic and diluted net loss per common share and the number of shares used in the computation of the per share amounts.
- (2) Pro forma basic and diluted net loss per common share and weighted average common shares outstanding give effect to: (i) the automatic conversion of all shares of our preferred stock into common stock upon closing of this offering, which, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, would result in the issuance of 9,890,580 shares of our common stock, (ii) outstanding warrants to purchase series D preferred stock becoming warrants to purchase shares of our common stock, upon the closing of this offering, and outstanding warrants to purchase shares of our series E preferred stock becoming warrants to purchase 14,088 shares of our common stock, at a weighted average exercise price of \$17.55 per share of common stock, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, upon the closing of this offering and (iii) the automatic cashless exercise of the series E common warrants for 567,306 shares of our common stock. Upon the closing of this offering, (a) our series E preferred stock will automatically convert into a number of shares of common stock and (b) outstanding warrants to purchase shares of our series E.

Selected consolidated financial data

preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. See "Prospectus summary—The offering" for a related offering price per share sensitivity analysis.

Consolidated balance sheet data:

	<u>As of December 31,</u>		<u>As of</u>
	<u>2014</u>	<u>2015</u>	<u>March 31,</u>
			<u>2016</u>
	(in thousands)		
Cash, cash equivalents and short-term investments	\$ 16,592	\$ 36,462	\$ 25,979
Total assets	\$ 22,228	\$ 42,824	\$ 34,723
Loan payables, net of current portion	\$ 4,824	\$ 11,855	\$ 11,169
Redeemable convertible preferred stock	\$ 94,033	\$ 137,482	\$ 139,837
Total stockholders' equity (deficit)	\$ (87,755)	\$ (116,493)	\$ (125,805)

Management's discussion and analysis of financial condition and results of operations

You should read the following discussion and analysis of our financial condition and results of operations together with "Selected consolidated financial data" and our consolidated financial statements and related notes thereto included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

OVERVIEW

We are a clinical-stage biopharmaceutical company using our proprietary synthetic vaccine particle, or SVP, technology to discover and develop targeted therapies that are designed to modulate the immune system to effectively and safely treat rare and serious diseases. Many such diseases are treated with biologic therapies that are foreign to the patient's immune system and, therefore, elicit an undesired immune response. Our proprietary SVP technology encapsulates an immunomodulator in biodegradable nanoparticles to induce antigen-specific immune tolerance to mitigate the formation of anti-drug antibodies, or ADAs, in response to life-sustaining biologic drugs. We believe our SVP technology has the potential for broad applications to both enhance existing biologic drugs and enable novel therapies. Our lead product candidate, SEL-212, is a combination of a therapeutic enzyme and our SVP technology designed to be the first biologic treatment for gout that durably controls uric acid in refractory gout and dissolves and removes harmful deposits of uric acid crystals in chronic tophaceous gout, each a painful and debilitating disease with unmet medical need. SEL-212 is currently in a comprehensive Phase 1/2 clinical program. The Phase 1/2 clinical program is comprised of two Phase 1 clinical trials and a Phase 2 clinical trial, and is designed to evaluate the ability of SEL-212 to control uric acid levels and mitigate the formation of ADAs. Based on preliminary data from our ongoing Phase 1b clinical trial, we believe that SEL-212 has the potential to control serum uric acid levels for at least 30 days after a single dose by mitigating the formation of ADAs in response to the therapeutic enzyme. We expect to receive final data from both Phase 1 clinical trials and initiate the Phase 2 clinical trial in the second half of 2016.

We were incorporated in 2007 under the laws of the State of Delaware and our corporate headquarters is in Massachusetts. Our operations to date have been limited to organizing and staffing our company, business planning, acquiring operating assets, raising capital, developing our technology, identifying potential nanoparticle immunomodulatory product candidates, research and development, undertaking preclinical studies and conducting clinical trials. To date, we have financed our operations primarily through private placements of our preferred stock, common stock and debt securities, funding received from research grants and collaboration arrangements and our credit facility. We do not have any products approved for sale and have not generated any product sales. All of our revenue to date has been generated from research grants and contracts.

Since our inception and through March 31, 2016, we have raised an aggregate of \$151.6 million to fund our operations, of which \$118.5 million was from the sale of preferred stock, \$7.8 million was from government grants, \$14.3 million was from the issuance of debt securities and \$11.0 million was from grants and collaboration arrangements. As of March 31, 2016, we had cash and cash equivalents

Management's discussion and analysis of financial condition and results of operations

totaling \$17.1 million, of which \$1.5 million of such cash and cash equivalents was held by our wholly owned Russian subsidiary and designated solely for use in its operations.

In August and September 2015, we issued and sold 8,888,888 shares of series E preferred stock for \$40.0 million in gross proceeds which included 1,619,550 shares of series E preferred stock that were issued as a result of the conversion of convertible notes. As part of the series E preferred stock issuance, we also issued 569,791 common stock warrants to the stockholders who participated in that round of financing.

All shares of our redeemable convertible preferred stock will automatically convert into shares of common stock in connection with this offering, and as a result, our common stock will be the only class of stock outstanding following this offering.

Since inception, we have incurred significant operating losses. We incurred net losses of \$12.9 million and \$25.2 million for the years ended December 31, 2014 and 2015, respectively. Our net loss was \$5.7 million and \$7.5 million for the three months ended March 31, 2015 and 2016, respectively. As of March 31, 2016, we had an accumulated deficit of \$121.1 million. We expect to continue incurring significant expenses and operating losses for at least the next several years as we:

- conduct and expand clinical trials for SEL-212, our lead product candidate;
- continue the research and development of our other product candidates;
- seek regulatory approval for any product candidates that successfully complete clinical trials;
- potentially establish a sales, marketing and distribution infrastructure and scale-up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, operational and financial personnel, to execute our business plan; and
- add personnel and clinical, scientific, operational, financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, license and collaboration agreements with partners, and research grants. We may be unable to raise capital when needed or on reasonable terms, if at all, which would force us to delay, limit, reduce or terminate our product development or future commercialization efforts. We will need to generate significant revenues to achieve profitability, and we may never do so.

The consolidated financial information presented below includes the accounts of Selecta Biosciences Inc. and our wholly owned subsidiaries, Selecta (RUS) LLC, a Russian limited liability company, or Selecta RUS, and Selecta Biosciences Security Corporation, a Massachusetts securities corporation. All intercompany accounts and transactions have been eliminated.

FINANCIAL OVERVIEW

Grant and collaboration revenue

To date, we have not generated any product sales. Our revenue consists of grant and collaboration revenue, which includes amounts recognized related to upfront and milestone payments for research

Management's discussion and analysis of financial condition and results of operations

and development funding under collaboration and license agreements. In addition, we earn revenue under the terms of government contracts or grants, which require the performance of certain research and development activities. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of fees, research and development reimbursements and other payments from collaborators. We do not expect to generate revenue from product sales for at least the next several years. If we or our collaborators fail to complete the development of our product candidates in a timely manner or fail to obtain regulatory approval as needed, our ability to generate future revenue will be harmed, and will affect the results of our operations and financial position. For a further description of the agreements underlying our collaboration and grant-based revenue, see Notes 2 and 12 to our consolidated financial statements included elsewhere in this prospectus.

Research and development

Research and development expenses consist of costs incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses, manufacturing process-development and scale-up activities, clinical trial and related clinical manufacturing expenses, fees paid to contract research organizations, or CROs, and investigative sites, payments to partners under our license agreements and other outside expenses. Our research and development costs are often devoted to expanding our programs and are not necessarily allocable to a specific target.

Our research and development expenses consist of external research and development costs, which we track on a program-by-program basis and primarily include contract manufacturing organization and CRO-related costs, and internal research and development costs, which are primarily compensation expenses for our research and development employees, lab supplies, analytical testing, allocated overhead costs and other related expenses. As we expand the clinical development of SEL-212, we expect our research and development expenses to increase. The increase in external research and development spending is expected to outpace internal research and development spending. We have incurred a total of \$82.1 million in research and development expenses from inception through March 31, 2016, with a majority of the expenses being spent on the development of SEL-212 and a prior nicotine vaccine, and the remainder being spent on our various discovery and preclinical stage product candidate programs and the general expansion of our technology.

We expense research and development costs as incurred. Conducting a significant amount of research and development is central to our business model. Product candidates in clinical development generally have higher development costs than those in earlier stages of development, primarily due to the size and duration of clinical trials. We plan to increase our research and development expenses for the foreseeable future as we seek to complete development of SEL-212, and to further advance our preclinical and earlier stage research and development projects. The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the development of SEL-212 or any of our preclinical programs or the period, if any, in which material net cash inflows from these product candidates may commence. Clinical development timelines, the probability of success and development costs can differ materially from our expectations. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently expect will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time to complete any clinical development.

Management's discussion and analysis of financial condition and results of operations

The following table sets forth the components of our research and development expenses during the periods indicated (in thousands, except percentages):

	Years ended December 31,		Increase (decrease)	Three months ended March 31,		Increase (decrease)		
	2014	2015		2015	2016			
External research and development expenses:								
SEL-212	\$ 474	\$ 9,335	\$ 8,861	—%	\$ 2,305	\$ 2,182	\$ (123)	(5)%
Discovery and preclinical stage product programs, collectively	38	856	818	2,153%	259	1,081	822	317%
Internal research and development expenses	9,974	12,789	2,815	28%	2,408	3,385	977	41%
Total research and development expenses	<u>\$ 10,486</u>	<u>\$ 22,980</u>	<u>\$ 12,494</u>	<u>119%</u>	<u>\$ 4,972</u>	<u>\$ 6,648</u>	<u>\$ 1,676</u>	<u>34%</u>

General and administrative

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, business development and support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expenses, travel expenses for our general and administrative personnel and professional fees for auditing, tax and corporate legal services, including intellectual property-related legal services. We expect that our general and administrative expenses will increase in future periods, reflecting an expanding infrastructure and increased professional fees associated with being a public reporting company.

Investment income

Investment income consists primarily of interest income earned on our cash and cash equivalents and short term investments.

Interest expense

Interest expense consists of interest expense on amounts borrowed under our credit facility.

Other expense

Other expense for the years ended December 31, 2014 and 2015 was de minimis.

Foreign currency

The functional currency of our Russian subsidiary is the ruble. In addition to holding cash denominated in rubles, our Russian bank accounts also hold cash balances denominated in U.S. dollars to facilitate payments to be settled in U.S. dollars or other currencies. At December 31, 2014 and 2015, and March 31, 2016, we maintained cash of \$7.3 million, \$3.8 million and \$4.2 million, respectively, in Russian banks, of which \$3.0 million was denominated in U.S. dollars for the period ended March 31, 2016. The amounts denominated in U.S. dollars and used in transacting the day to day operations are subject to transaction gains and losses, which are reported as incurred.

Management's discussion and analysis of financial condition and results of operations**RESULTS OF OPERATIONS****Three months ended March 31, 2015 compared to the three months ended March 31, 2016****Revenue**

The following is a comparison of revenue for the three months ended March 31, 2015 and 2016 (in thousands, except percentages):

	Three months ended March 31,		Increase (decrease)	
	2015	2016		
	<i>(unaudited)</i>			
Grant revenue	\$ 531	\$ 1,926	\$ 1,395	263%
Collaboration revenue	503	162	(341)	(68)%
Total revenue	\$ 1,034	\$ 2,088	\$ 1,054	102%

During the three months ended March 31, 2016, total revenue increased by \$1.1 million, or 102%, as compared to the same period in the prior year, of which \$1.3 million was related to a National Institute on Drug Abuse, or NIDA, grant, or the NIDA grant, awarded to us in 2014 and recognized as revenue throughout the three months ended March 31, 2016, offset by a reduction of \$0.3 million related to the amortization of upfront payments from the license and research collaboration agreement with Sanofi executed in November 2012 and supplemented in May 2015. We recognized revenue increases of \$0.1 million from various other grants and collaborations during the three months ended March 31, 2016 over the three months ended March 31, 2015.

Research and development

The following is a comparison of research and development expenses for the three months ended March 31, 2015 and 2016 (in thousands, except percentages):

	Three months ended March 31,		Increase (decrease)	
	2015	2016		
	<i>(unaudited)</i>			
Research and development	\$ 4,972	\$ 6,648	\$ 1,676	34%

During the three months ended March 31, 2016, our research and development expenses increased by \$1.7 million, or 34%, as compared to the same period in the prior year, due to the timing of the toxicology expenses associated with the NIDA grant, and the addition of research and development staffing to support the SEL-212 clinical trial.

General and administrative

The following is a comparison of general and administrative expenses for the three months ended March 31, 2015 and 2016 (in thousands, except percentages):

	Three months ended March 31,		Increase (decrease)	
	2015	2016		
	<i>(unaudited)</i>			
General and administrative	\$ 1,872	\$ 2,381	\$ 509	27%

Management's discussion and analysis of financial condition and results of operations

For the three months ended March 31, 2016, our general and administrative expenses increased \$0.5 million, or 27%, as compared to the same period in the prior year, primarily due to an increase in costs for intellectual property filings and corresponding searches. Additionally, facility costs increased as a result of the termination of our sublease and subsequent utilization of the related space.

Investment income

Change in investment income during the three months ended March 31, 2016 as compared to the prior year period reflects reduced interest bearing account balances of cash and cash equivalents held by our company and our Russia subsidiary.

Foreign currency gain (loss)

We recognized a foreign currency gain of \$0.2 million and foreign currency loss of \$0.2 million during the three months ended March 31, 2015 and 2016, respectively, reflecting the fluctuation of the U.S. dollar to the ruble from the beginning to the end of each period.

Interest expense

Interest expense for the three months ended March 31, 2016 was \$0.3 million, an increase of \$0.1 million, or 50%, as compared to the same period in the prior year. The increase was primarily due to the amortization of loan issuance costs and interest accrued on the increase of the venture debt effective December 31, 2015.

Other income (expense)

Other income (expense) was de minimis for the three months ended March 31, 2015 and 2016.

Year ended December 31, 2014 compared to the year ended December 31, 2015**Revenue**

The following is a comparison of revenue for the years ended December 31, 2014 and 2015 (in thousands, except percentages):

	Years ended December 31,		Increase (decrease)	
	2014	2015		
Grant and collaboration revenue	\$ 3,040	\$ 6,011	\$ 2,971	98%

During the year ended December 31, 2015, total revenue increased by \$3.0 million, or 98%, as compared to the prior year, primarily due to revenue from our grants and collaborations associated with increased research and development activities, including an increase of \$1.9 million of revenue recognized during the year from the NIDA grant, \$0.1 million for our collaboration with JDRE, \$0.4 million of revenue recognized that was previously reported as contingently repayable grant funding, \$0.3 million from other collaborations initiated in 2015 and \$0.3 million from other agreements.

Management's discussion and analysis of financial condition and results of operations

Research and development

The following is a comparison of research and development expenses for the years ended December 31, 2014 and 2015 (in thousands, except percentages):

	Years ended December 31,		Increase (decrease)	
	2014	2015		
Research and development	\$ 10,486	\$ 22,980	\$ 12,494	119%

During the year ended December 31, 2015, our total research and development expenses increased by \$12.5 million from the prior year, reflecting the costs associated with the advancement of SEL-212 into clinical trials, including related headcount growth, as compared to the prior year during which research and development expenses primarily reflected costs associated with the general pre-clinical development of SEL-212.

General and administrative

The following is a comparison of general and administrative expenses for the years ended December 31, 2014 and 2015 (in thousands, except percentages):

	Years ended December 31,		Increase (decrease)	
	2014	2015		
General and administrative	\$ 7,953	\$ 8,335	\$ 382	5%

During the year ended December 31, 2015, our general and administrative expenses increased by \$0.4 million, or 5%, as compared to the prior year, primarily due to an increase in legal expense as a result of initiating and reviewing potential collaboration agreements and expanding intellectual property protections.

Investment income

Change in investment income was de minimis during the year ended December 31, 2015 as compared to the prior year as cash and cash equivalent balances held in interest bearing accounts and the prevailing interest rates remained relatively consistent during both years.

Foreign currency gain

We recognized a foreign currency gain of \$0.9 million during the year ended December 31, 2015 as compared to \$3.0 million during the year ended December 31, 2014 reflecting the continued strength of the U.S. dollar to the ruble occurring between December 31, 2014 (beginning of the period) to December 31, 2015 (end of period).

Interest expense

Interest expense was \$0.9 million during the year ended December 31, 2015, as compared to \$0.6 million in the prior year. The increase was primarily due to outstanding borrowings throughout 2015 as well as incremental amounts borrowed during the year. As of January 2014, we had outstanding borrowings of \$3.0 million under our credit facility. In July 2014, we drew the remaining \$4.5 million of available borrowings under the credit facility. As of December 31, 2015, we expanded

Management's discussion and analysis of financial condition and results of operations

the credit facility to a total of \$12.0 million and drew all of the remaining borrowings available under the credit facility. Additionally, the increase included the amortization of loan issuance costs and interest accrued on convertible notes issued in April 2015 that were converted into our series E preferred stock in August 2015.

Other expense

Other expense for the years ended December 31, 2014 and 2015 was de minimis.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception and through March 31, 2016, we have raised an aggregate of \$151.6 million to fund our operations, of which \$118.5 million was from the sale of preferred stock, \$7.8 million was from government grants and \$14.3 million was from borrowings under our credit facility and \$11.0 million was through our collaborations and license agreements.

As of March 31, 2016, our cash and cash equivalents were \$17.1 million, of which \$1.5 million was held by our Russian subsidiary designated solely for use in its operations and is consolidated for financial reporting purposes. Additionally, our Russian subsidiary maintained \$2.0 million in short term deposits and \$0.7 million in restricted cash.

In addition to our existing cash and cash equivalents, we receive research and development funding and are eligible to earn a significant amount of milestone payments under collaboration agreements. Our ability to earn these milestone payments, and the timing of achieving these milestones, is dependent upon the outcome of our research and development and regulatory activities, and is uncertain at this time. Currently, funding from research grants and payments under collaboration agreements represent our only source of committed external funds.

To date, we have financed our operations primarily through private placements of our preferred stock and common stock, issuance of debt securities, funding received from grants and collaborative arrangements and through borrowings under our credit facility. We expect that we will continue to incur losses and that such losses will increase for the foreseeable future. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through a combination of equity offerings, debt financings, third-party funding and other collaborations and strategic alliances.

Indebtedness

In August 2013, we entered into a credit facility with Oxford Finance, LLC, or Oxford, and Pacific Western Bank, as successor in interest to Square 1 Bank, as co-lenders. The credit facility initially provided funding for an aggregate principal amount of up to \$7.5 million. The term loan A portion of the facility was funded on the facility's closing date in the aggregate principal amount of \$3.0 million. In July 2014, we borrowed the remaining \$4.5 million of the available capacity under a term loan B portion of the facility. On December 31, 2015, we expanded the credit facility to a total of \$12.0 million, and drew down all available funding at the closing, with the full amount borrowed referred to as the term loan.

Management's discussion and analysis of financial condition and results of operations

The credit facility is secured by substantially all of our personal property other than our intellectual property. The term loan under the credit facility bears interest at an annual rate equal to the greater of (i) 8.0% and (ii) the sum of (a) the 30-day U.S. LIBOR rate five business days prior to the applicable funding date plus (b) 7.68%. We are required to make interest payments through January 1, 2017, or the interest only period. Following the interest only period, all outstanding borrowings under the credit facility will begin amortizing with monthly payments of principal and interest being made over 30 consecutive monthly installments. All loans under the facility mature on July 1, 2019, and include a final payment fee equal to 6% of the total amount borrowed under the credit facility. This final payment has been recorded as a discount to the loan balance and is being amortized into interest expense over the life of the loan.

The term loan is prepayable at our option in whole, but not in part, subject to a prepayment fee of 3% if the term loan is prepaid prior to the first anniversary of the December 31, 2015 borrowing date, the borrowing date, 2% if the terms loans are prepaid between the first and second anniversary of the borrowing date and 1% if the term loan is prepaid after the second anniversary of the borrowing date. We are also required to prepay the term loan upon the occurrence of customary events of default set forth in the credit agreement. In addition, the term loan contains a subjective acceleration clause whereby an event of default and immediate acceleration of the borrowings under credit agreement occurs in the event of a material impairment of the perfection or priority of the lenders' lien in the collateral or the value of such collateral, a material adverse change in our business operations or condition (financial or otherwise) or a material impairment of the prospect of repayment of any portion of the obligations.

We were also required to issue the lenders warrants for the purchase of preferred stock equal to 4.0% of the term loan A and term loan B at each closing, and 2.5% for the additional borrowing on December 31, 2015. In connection with the term loan security and loan agreement, in August 2013, we issued a fully vested warrant to purchase 26,668 shares of our series D preferred stock, in July 2014, we issued an additional fully vested warrant to purchase 40,000 shares of our series D preferred stock, and in December 31, 2015, we issued an additional fully vested warrant to purchase 37,978 shares of our series E preferred stock. The exercise price for all warrants is \$4.50 per share, and they have a ten year life from date of issuance. These are recorded at the fair market value and expensed through the income statement.

The credit facility includes affirmative and negative covenants applicable to us and our subsidiaries. The affirmative covenants include, among others, covenants requiring us to (and to cause our subsidiaries to) maintain our legal existence and governmental approvals, deliver certain financial reports, maintain inventory and insurance coverage, maintain unrestricted cash in a control account equal to or greater than the lesser of 105% of all outstanding amounts under the credit facility and 100% of the cash and cash equivalents of our company and our wholly owned subsidiary, Selecta Biosciences Security Corporation, and protect material intellectual property. The negative covenants include, among others, restrictions on us and our subsidiaries transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, selling assets and allowing a change in control, in each case subject to certain exceptions. Additionally, the credit facility restricts us from making certain payments or transfers to our Russian subsidiary, Selecta RUS, subject to certain exceptions. The credit facility does not include any other financial covenants. As of March 31, 2016, we were in compliance with the covenants under our credit facility.

The credit facility also includes events of default, the occurrence and continuation of which provide the co-lenders with the right to exercise remedies against us and the collateral securing the loans under the credit facility, including our cash. These events of default include, among other things, our failure to pay any amounts due under the credit facility, a breach of covenants under the credit facility, our

Management's discussion and analysis of financial condition and results of operations

insolvency and the insolvency of our subsidiaries, the occurrence of a material adverse event, the occurrence of any default under certain other indebtedness, and a final judgment against us in an amount greater than \$100,000. As of March 31, 2016, there had been no such events of default and the lenders had not exercised their rights with respect to an event of default under the credit facility.

Plan of operations and future funding requirements

To date, we have not generated any product sales. We do not know when, or if, we will generate revenue from product sales. We will not generate significant revenue from product sales unless and until we obtain regulatory approval and commercialize one of our current or future product candidates. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses, and general overhead costs. We expect that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to risks in the development of our products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. We expect that we will need substantial additional funding in connection with our continuing operations. In their report on our consolidated financial statements for the years ended December 31, 2014 and 2015, our independent registered public accounting firm included an explanatory paragraph stating that we have recurring losses from operations since inception and negative cash flows from operating activities and will require additional capital to fund planned operations. These conditions raise substantial doubt about our ability to continue as a going concern.

We expect that the net proceeds from this offering, together with our cash and cash equivalents as of March 31, 2016, and funding that we expect to receive under our existing collaborations will fund our operating expenses and capital expenditure requirements through at least December 31, 2017. We have based these estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain. Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of SEL-212;
- our collaboration agreements remaining in effect, our ability to enter into additional collaboration agreements and our ability to achieve milestones under these agreements;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;

Management's discussion and analysis of financial condition and results of operations

- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products and technologies.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and revenue from license and collaboration arrangements. Except for any obligations of our collaborators to reimburse us for research and development expenses or to make milestone payments under our agreements with them, upon completion of this offering, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash flows

The following is a summary of cash flows for the years ended December 31, 2014 and 2015 and the three months ending March 31, 2016 (in thousands):

	Year ended December 31,		Three months ended March 31,	
	2014	2015	2015 (unaudited)	2016 (unaudited)
Beginning of the period	\$ 8,057	\$ 16,592	\$ 16,592	\$ 32,337
Net cash used in operating activities	(12,686)	(22,463)	(4,898)	(10,166)
Net cash used in investing activities	(227)	(4,679)	(123)	(3,555)
Net cash provided by (used in) financing activities	24,771	43,906	(207)	(1,677)
Effect of exchange rate changes on cash	(3,323)	(1,019)	(230)	112
End of the period	<u>\$ 16,592</u>	<u>\$ 32,337</u>	<u>\$ 11,134</u>	<u>\$ 17,051</u>

Net cash used in operating activities

Net cash used in operating activities was \$4.9 million for the three months ended March 31, 2015 as compared to \$10.2 million for the three months ended March 31, 2016. The increase in net cash used in operating activities of \$5.3 million reflected an increase of (i) \$1.7 million in net loss due to increased research and development expenses as we advanced from preclinical studies into the Phase 1 clinical trials, (ii) \$2.0 million of restricted cash and other deposits, (iii) \$1.0 million of receivables associated with pending receipts from the NIDA grant and (iv) \$2.2 million from the net payments of accounts payable and other liabilities, offset by (a) \$1.3 million of advance grant and collaboration receipts classified as deferred revenue and contingent repayable grant funding and (b) a \$0.3 million decrease in other assets.

Net cash used in operating activities was \$12.7 million for the year ended December 31, 2014, as compared to \$22.5 million for the year ended December 31, 2015. The increase of \$10.0 million in

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cash used in operating activities during the year ended December 31, 2015, was primarily related to the increased net loss position as a result of the incremental costs associated with the clinical trial.

Net cash used in investing activities

Net cash used in investing activities was \$0.1 million for the three months ended March 31, 2015 as compared to net cash used in investing activities of \$3.6 million of the three months ended March 31, 2016. The increase in cash used for investing activities of \$3.5 million was primarily caused by the purchase of \$3.5 million of short term government obligations.

Net cash used in investing activities was \$0.2 million for the year ended December 31, 2014, as compared to net cash used in investing activities of \$4.7 million for the year ended December 31, 2015. The increase in cash used for investing activities was caused by the purchase of \$3.5 million of short-term investments and an additional \$1.2 million of purchased equipment.

Net cash provided by (used in) financing activities

Net cash used in financing activities was \$0.2 million for the three months ended March 31, 2015 as compared to \$1.7 million for the three months ended March 31, 2016. The increase of \$1.5 million used in financing activities is caused by the increase in deferred costs related to this initial public offering.

Net cash provided by financing activities was \$24.8 million for the year ended December 31, 2014, as compared to net cash provided by financing activities of \$43.9 million for the year ended December 31, 2015. The increase of \$19.1 million reflected the difference in proceeds from the issuance of the series E preferred stock and the convertible notes (that converted into series E preferred stock) in 2015 versus the proceeds from the issuance of series D preferred stock and our series SRN preferred stock issued in 2014.

Effect of exchange rates on cash

The functional currency of our Russian subsidiary is the ruble. The statement of cash flows for our Russian subsidiary is translated using the average translation rate applicable during the period except that all cash and cash equivalents, short term investments and restricted cash at the beginning of the period is translated using the exchange rate as of the beginning balance sheet date, and short term investments and restricted cash at the end of the period is translated using the exchange rate as of the ending balance sheet date.

Contractual obligations and contingent liabilities

The following summarizes our significant contractual obligations as of March 31, 2016 (in thousands):

Contractual Obligations	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Operating leases(1)	\$ 1,188	\$ 1,188	\$ —	\$ —	\$ —
Research and development contract obligations(2)	240	60	120	60	—
Long term debt(3)	14,745	2,059	10,637	2,049	—
Total obligations	\$ 16,173	\$ 3,307	\$ 10,757	\$ 2,109	\$ —

(1) Represents future minimum lease payments under non-cancellable operating leases in effect as of March 31, 2016, including the remaining lease payments for our current facilities in Watertown, Massachusetts. The minimum lease payments above do not include common area maintenance charges, real estate taxes or any sublease payments we receive.

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- (2) Represents minimum annual license fees payable to universities or partners under our license agreements. Under our license agreement with the Massachusetts Institute of Technology, or MIT, milestone payments are due upon the occurrence of certain events and royalty payments commence upon our commercialization of a product. For the purposes of presenting our contractual obligations under the MIT agreement, we have assumed license payments are fully offset by royalty payments in 2020.
- (3) Represents payments of principal and interest under our credit facility assuming \$12.0 million of borrowings and no prepayments.

The contractual obligations table does not include any potential contingent payments upon the achievement by us of specified clinical, regulatory and commercial events, as applicable, or patent prosecution or royalty payments we may be required to make under license agreements we have entered into with various universities or partners pursuant to which we have in-licensed certain intellectual property, including our license agreement with MIT. We have excluded these potential payments in the contractual obligations table because the timing and likelihood of these contingent payments are not known. See "Business—Licenses and collaborations" for additional information about these license agreements, including with respect to potential payments thereunder.

We enter into agreements in the normal course of business with manufacturers and CROs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. As of March 31, 2016, we had approximately \$7.0 million of purchase orders under these agreements. However, these agreements generally provide for termination upon notice. As a result, we have excluded payments under these agreements because (i) the timing of these payments is uncertain and contingent upon completion of future activities and (ii) we believe that our non-cancelable obligations under these agreements are not material.

CRITICAL ACCOUNTING POLICIES AND USE OF ESTIMATES

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities in our consolidated financial statements, as well as the reported revenues and expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our consolidated financial statements and understanding and evaluating our reported financial results.

Revenue recognition

Collaborative research and development and multiple-deliverable arrangements

We enter into collaborative arrangements for the development and commercialization of product candidates utilizing our SVP technology. The terms of these agreements have typically included

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multiple deliverables by us (for example, license rights, research and development services and manufacturing of clinical materials) in exchange for consideration to us of some combination of non-refundable upfront payments, research and development funding, payments based upon achievement of clinical development or other milestones, and royalties in the form of a designated percentage of product sales or profits.

Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable and collection is reasonably assured. When one or more of the revenue recognition criteria are not met, we defer the recognition of revenue until such time as all such criteria are met. Multiple-deliverable arrangements, such as development agreements, are analyzed to determine whether the deliverables can be separated or whether they must be accounted for as a single unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit.

We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. We have used our best estimate of selling price to estimate the selling price for licenses related to our proprietary technology, since we do not have VSOE or TPE of selling price for these deliverables. In those circumstances, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the best estimate of selling price, we evaluate whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of consideration between multiple deliverables.

We may receive upfront payments when licensing our intellectual property in conjunction with a research and development agreement. When management believes the license to our intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, we generally recognize revenue attributed to the license over the contractual or estimated performance period. When management believes the license to our intellectual property has stand-alone value, we generally recognize revenue attributed to the license upon delivery. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue we record in future periods. We have not experienced any significant adjustments to our estimates to date.

Payments or reimbursements resulting from our research and development efforts are recognized and presented on a gross basis as the services are performed. The rationale for presenting on a gross basis is that we are the principal for such efforts, and as long as there is persuasive evidence of an arrangement, the fee is fixed or determinable and collection of the related amount is reasonably assured. Grant agreements generally provide for the reimbursement of direct costs, including salaries, benefits and supplies, as well as indirect costs.

At the inception of each agreement that includes milestones payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of

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the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized over the remaining period of performance.

Deferred revenue

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within one year following the balance sheet date are classified as non-current deferred revenue.

Accrued expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing contracts and purchase orders, reviewing the terms of our vendor agreements, communicating with our applicable personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include:

- fees payable to CROs and other third parties;
- fees payable to vendors in connection with preclinical or clinical development activities; and
- fees payable to vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows and expense recognition. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. Our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting changes in estimates in any particular period. We have not experienced any significant adjustments to our estimates to date.

Stock-based compensation

We issue stock-based awards to employees and non-employees, generally in the form of stock options and restricted stock. We account for our stock-based awards in accordance with the ASC 718, *Compensation—Stock Compensation*, or ASC 718. We account for stock-based awards to non-employees in accordance with ASC 505-50, *Equity-Based Payments to Non-Employees*, or ASC 505-50.

Pursuant to ASC 718, we measure stock options and other stock-based awards granted to employees and directors based on the fair value on the date of grant and recognize the corresponding compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue stock options and restricted stock awards with only service-based vesting conditions and record the expense for these awards using the straight-line method.

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Pursuant to ASC 505-50, we measure stock-based awards granted to consultants and non-employees based on the fair value of the award on the date at which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected terms of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Stock-based compensation for employees and non-employees were classified in the consolidated statements of operations and comprehensive loss as outlined below (in thousands):

	Year ended December 31,		Three months ended March 31,	
	2014	2015	2015	2016
			(unaudited)	
Research and development	\$ 384	\$ 495	\$ 132	\$ 167
General and administrative	840	630	170	115
Total	\$ 1,224	\$ 1,125	\$ 302	\$ 282

As of March 31, 2016, we had \$3.0 million of total unrecognized compensation expense, net of related forfeiture estimates, which is expected to be recognized over a weighted average remaining vesting period of approximately 3.0 years. We expect the impact of our stock-based compensation expense for stock options and restricted stock granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common stock and headcount.

Common stock valuation

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant, and factors that may have changed from the date of the most recent valuation through the date of the grant. We have periodically determined the estimated fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid.

The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, our board of directors considered the following methods.

- *Option Pricing Method.* Under the option pricing method, or OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.

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- *Probability-Weighted Expected Return Method.* The probability-weighted expected return method, or PWERM, is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Given the range of possible financing and exit events that existed at the time we completed our valuations, our board of directors concluded the PWERM to be the most appropriate for purposes of valuing our common stock given our expected time to a liquidity event, subjectivity with regards to estimating possible proceeds from a future liquidation event and subjectivity with regards to the ability to estimate the probability of an initial public offering, sale or other financing events. The PWERM explicitly considers the various terms of our investor related documents, including various rights of each class of our stock, at the date of the liquidity event when those rights will either be executed or abandoned.

We obtained valuations of our common stock on February 28, 2014, November 30, 2014, September 30, 2015, December 31, 2015, January 31, 2016, March 31, 2016 and April 30, 2016. All valuations utilized the PWERM methodology to allocate the enterprise value to the common stock. The fair value of our common stock was estimated using a probability-weighted analysis of the present value of the returns afforded to common stockholders under several future stockholder exit or liquidity event scenarios, either through (1) a near-term and longer-term initial public offering, or IPO, scenario; (2) a sale of our company at values deemed to be low, medium and high; or (3) a liquidation event where the value is well below the preferred stock preference levels.

The selected enterprise value in the near-term IPO scenario was based on the pre-money market data for IPOs between the median and the mean of the observed range given reasonably "like" stage companies. The selected aggregate enterprise value in the longer-term scenario was also based on the pre-money market data for IPOs of equivalent stage biotechnology companies, but with added consideration that the market may not be as robust in the near-term initial public offering time frame and we will have completed our proof-of-concept with positive findings. The selected enterprise values utilized for each of the three scenarios in the sale scenario considered management's best estimates considering program accomplishments towards one or more indications being in the clinic, the available cash runway and additional preclinical data from our other product candidates. In the liquidation scenario at a price below liquidation preference, the valuations assumed a value that would not allow the preferred stockholders to realize their full liquidation preference resulting in no value to common stockholders.

Under all the exit scenarios considered in the PWERM, the fair value of our common stock was calculated using the estimated future enterprise valuations and a risk-adjusted discount rate based on the inherent risk of a hypothetical investment in our common stock, and a discount for lack of marketability. The risk-adjusted discount rate was based on consideration of the weighted average cost of capital, or WACC, for comparable biotechnology companies adjusted for company-specific risk factors, the venture capital rates of return and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. We corroborated the discount based on the value of a put option compared to the value of common stock using Black-Scholes. We also considered the rights and privileges of our preferred stock as compared to our common stock, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing.

We performed these valuations, with the assistance of a third-party valuation specialist, on February 28, 2014, November 30, 2014, September 30, 2015, December 31, 2015, January 31, 2016, March 31, 2016 and April 30, 2016. The resulting estimated fair value of our common stock as of April 30, 2016 was \$8.97, March 31, 2016 was \$8.15, January 31, 2016 was \$7.02, December 31,

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2015 was \$6.79, September 30, 2015 was \$6.40, November 30, 2014 was \$9.36 and February 28, 2014 was \$8.97 per share. The changes in the assumptions used for the September 2015 valuation as compared to the November 2014 valuation reflected our progress towards proof of scientific concept and resulting technology advancement, the decision to advance towards an IPO, and the offering value of our series E preferred stock financing. This decrease in per share value was primarily due to then-current valuations for biotechnology companies, capital market conditions for biotechnology companies and the terms of our recent series E preferred stock financing. The valuations performed as of January 31, 2016 and December 31, 2015, as compared to September 30, 2015, reflected only the advancement of time between valuations towards the future stockholder exit or liquidity event scenarios. As there were no new significant clinical data, financial events or other changes in the business during that period, management believes the change in valuation is attributable to time progression. The valuations performed for April 30, 2016 and March 31, 2016 included consideration for the continued advancement of time towards an IPO in the second quarter of 2016, the apparent stabilization of the capital markets, the initial results of our Phase 1b clinical trial and analysis of the valuations for other biotechnology companies.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation could be materially different.

Following the closing of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock.

Stock option grants

The following table summarizes by grant date the number of shares subject to options granted since January 1, 2014, the per share exercise price of the options, the fair value of common stock underlying the options on date of grant and the per share estimated fair value of the options:

Grant date	Number of common shares underlying options granted	Exercise price per common share(1)	Fair value of common stock per share on grant date(2)	Per share estimated fair value of options
April 8, 2014	152,820	\$ 8.97	\$ 8.97	\$ 6.86
April 23, 2014	20,512	\$ 8.97	\$ 8.97	\$ 6.37
September 9, 2014	6,923	\$ 8.97	\$ 8.97	\$ 6.98
February 6, 2015	57,692	\$ 9.36	\$ 9.36	\$ 7.14
February 21, 2015	62,820	\$ 9.36	\$ 9.36	\$ 7.14
April 7, 2015	5,128	\$ 9.36	\$ 9.36	\$ 7.06
June 12, 2015	6,410	\$ 9.36	\$ 6.40	\$ 3.86
September 8, 2015	115,384	\$ 9.36	\$ 6.40	\$ 3.78
December 4, 2015	315,320	\$ 6.40	\$ 6.40	\$ 4.56
March 9, 2016	171,794	\$ 7.02	\$ 7.41	\$ 5.69
April 5, 2016	11,282	\$ 8.15	\$ 8.15	\$ 4.67
	<u>926,085</u>			

(1) Our board of directors determined at the time of grant of the stock options that the exercise price was based upon the fair value of our common stock calculated in the most recent valuation as of February 28, 2014, November 30, 2014, September 30, 2015, December 31, 2015, January 31, 2016 or March 31, 2016, as applicable.

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- (2) As described below, the fair value of common stock at the date of these grants was adjusted to recognize the decline in the per share valuation for the period between the November 30, 2014 and the December 31, 2015 valuations. The adjustments are made based on a reassessment of the events occurring between the two valuations, such as the value paid for the most recent venture funding, and the determination of the time in which the pricing of the funding would be known. The fair value of common stock per share on the March 9, 2016 grant date was based on the valuation performed as of January 31, 2016, and the fair value of the common stock per share on the April 5, 2016 grant date was based on the valuation performed as of March 31, 2016.

In the course of preparing for this offering, on January 31, 2016 and March 31, 2016, we performed a fair value assessment and concluded that the fair value of our common stock underlying the stock options we granted between April 8, 2014 and April 5, 2016 was between \$6.40 and \$9.36 per share for accounting purposes. These reassessed values, which we applied to determine the fair values of the option grants in determining the stock-based compensation expense for accounting purposes, were based in part upon the valuation of our common stock as of January 31, 2016 and March 31, 2016, performed with the assistance of a third-party specialist, taking into account an increased probability of executing a successful IPO during the first half of 2016, the recent IPO valuations for early-stage biotechnology companies and the probability of a successful result in our Phase 1/2 clinical trials of SEL-212. These revised common stock valuations were performed using the PWERM method noted above.

Initial public offering

In consultation with the underwriters for this offering, we determined the estimated price range for this offering, as set forth on the cover page of this prospectus. The midpoint of the price range is \$15.00 per share. In comparison, our estimate of the fair value of our common stock was \$8.97 per share as of the April 30, 2016 valuation. We note that, as is typical with IPOs, the estimated price range for this offering was not derived using a formal determination of fair value, but was determined by negotiation between us and the underwriters. Among the factors that were considered in setting this range were the following:

- an analysis of the typical valuation ranges seen in recent IPO for companies in our industry;
- the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies;
- an assumption that there would be a receptive public trading market for clinical and pre-commercial biotechnology companies such as us; and
- an assumption that there would be sufficient demand for our common stock to support an offering of the size contemplated by this prospectus.

In addition to these factors, we believe that the difference between the fair value of our common stock as of April 30, 2016 and the midpoint of the price range for this offering is primarily the result of our receipt in late May and early June 2016 of positive data from our Phase 1b clinical trial in respect of the safety and tolerability of our lead product candidate, SEL-212. See "Business—Our antigen-specific tolerance program SEL-212 for the treatment of refractory and chronic tophaceous gout-clinical development—Phase 1b clinical trial." In addition, the estimated IPO price range necessarily assumes that the IPO has occurred, a public market for our common stock has been created and that our preferred stock converted into common stock in connection with the IPO, and therefore excludes any discount for lack of marketability of our common stock, which was factored into the April 30, 2016 valuation.

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WARRANT VALUATION

We granted warrants to purchase shares of our series D preferred stock and series E preferred stock to the lenders under our loan and security agreement dated August 9, 2013, as amended on May 9, 2014, and as amended and restated on December 31, 2015. These warrants are classified as a liability as the warrants are free-standing financial instruments that may require us to transfer assets upon exercise. The warrants were initially recorded at their grant date fair value and are remeasured to fair value at each subsequent balance sheet date. Changes in fair value of these warrants are recognized as a component of other income (expense) in our consolidated statements of operations and comprehensive loss. We will continue to adjust the liability for changes in fair value of the warrants until the earlier of the exercise or expiration of the warrants.

The fair value of the warrants are estimated using Black-Sholes, which incorporates assumptions and estimates to value these warrants. We assess these assumptions and estimates on a quarterly basis based on information available to us on each valuation date. Such assumptions and estimates include: the fair value per share of the underlying series D preferred stock and series E preferred stock, the remaining contractual term of the warrants, risk-free interest rate applicable to the remaining contractual term, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determine the fair value per share of the underlying preferred stock by taking into consideration the most recent sales of our redeemable convertible preferred stock, results obtained from third-party valuations and additional factors that we deem relevant. We have historically been a private company and lack company-specific historical and implied volatility information of our stock. Therefore, we estimate expected stock volatility based on the historical volatility of publicly traded comparable companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods that approximately equal to the remaining contractual term of the warrants. We assumed no dividend yield based on the fact that we have never paid or declared dividends, and do not expect to pay or declare dividends in the future.

In connection with this offering, the underlying redeemable convertible preferred stock will be converted to common stock. The preferred warrants will therefore become exercisable into common stock instead of preferred stock and the fair value of the warrant liability will be reclassified to additional paid-in capital at that time.

OFF-BALANCE SHEET ARRANGEMENTS

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under Securities and Exchange Commission rules.

NET OPERATING LOSS AND RESEARCH AND DEVELOPMENT TAX CREDIT CARRYFORWARDS

As of December 31, 2015, we had net operating loss carryforwards, or NOLs, for federal and state income tax purposes of \$82.4 million and \$76.3 million, respectively, which expire at various times through 2035. In 2014, our wholly owned subsidiary, Selecta RUS, was granted a "Skolkovo designated" resident status in Russia. As a result, the subsidiary operates as a corporate tax exempt entity, with lower employee and employment taxes. All foreign net operating loss carryforwards have been eliminated. The state NOLs began expiring in 2015 and will continue to expire through 2035. At December 31, 2015, we had available federal and state research and development income tax credits of approximately \$1.6 million and \$1.1 million respectively, which may be available to reduce future income taxes, if any, at various times through 2035.

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Utilization of the NOLs and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Code. Specifically, this limitation may arise in the event of a cumulative change in our ownership of more than 50% within any three-year period. The amount of the annual limitation is determined based on our value immediately before the ownership change. Subsequent ownership changes may further affect the limitation in future years. The annual limitation may result in the expiration of our net operating losses and credits before we can use them. We have recorded a valuation allowance on all of our deferred tax assets, including our deferred tax assets related to our NOLs and research and development tax credit carryforwards. We plan to undertake a study to analyze and determine if any historical ownership changes have occurred to determine if there are any permanent limitations on our ability to utilize NOLs and other tax attributes in the future. In addition, we may experience ownership changes after this offering as a result of subsequent shifts in our stock ownership. As a result, we are unable to estimate the effect of these limitations, if any, on our ability to utilize NOLs and other tax attributes in the future.

JOBS ACT ACCOUNTING ELECTION

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

RECENTLY ISSUED ACCOUNTING PRONOUNCEMENTS

In May 2014, FASB issued Accounting Standards Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers*, or ASU 2014-09, which amends the guidance for revenue recognition to replace numerous industry-specific requirements. ASU 2014-09 implements a five-step process for customer contract revenue recognition that focuses on transfer of control, as opposed to transfer of risk and rewards. ASU 2014-09 also requires enhanced disclosures regarding the nature, amount, timing and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The amendments in ASU 2014-09 are effective for reporting periods beginning after December 15, 2017. Early adoption is permitted, but not before December 15, 2016. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. We are currently in the process of evaluating the effect the adoption of ASU 2014-09 may have on our financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 requires management to assess our ability to continue as a going concern and to provide related disclosures in certain circumstances. The requirements of ASU 2014-15 will be effective for the annual financial statement period beginning after December 15, 2016, with early adoption permitted. We are currently in the process of evaluating the impact of adopting ASU 2014-15.

In February 2016, FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"). ASU 2016-02 requires a lessee to separate the lease components from the non-lease components in a contract and recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. It also aligns lease

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accounting for lessors with the revenue recognition guidance in ASU 2014-09. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years, and is to be applied at the beginning of the earliest period presented using a modified retrospective approach. We are currently in the process of evaluating the impact of adopting ASU 2016-02.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2015 and March 31, 2016, we had cash equivalents of \$32.3 million and \$17.1 million, respectively, consisting of non-interest and interest-bearing money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term the low risk profile of our money market accounts, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

In addition, we are subject to currency risk for balances held in rubles in our foreign subsidiary. We hold portions of our funds in both U.S. dollars and rubles. The exchange rate between the U.S. dollar and ruble fluctuated significantly. As of December 31, 2013, the exchange rate was 32.7 rubles per U.S. dollar as compared to 56.26 rubles per U.S. dollar at December 31, 2014 and 72.89 rubles per U.S. dollar at December 31, 2015. As of March 31, 2016, the exchange rate was 67.61 rubles per U.S. dollar, under which we held \$4.2 million of total cash in Russian banks to support our Russian subsidiary, which includes \$1.5 million of cash and cash equivalents, \$2.0 million of short-term deposits and \$0.7 million of restricted cash, of which \$1.0 million of cash and cash equivalents and the \$2.0 million of short-term deposits were denominated in U.S. dollars. We do not hedge against foreign currency risks. We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

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OVERVIEW

We are a clinical-stage biopharmaceutical company using our proprietary synthetic vaccine particle, or SVP, technology to discover and develop targeted therapies that are designed to modulate the immune system to effectively and safely treat rare and serious diseases. Many such diseases are treated with biologic therapies that are foreign to the patient's immune system and therefore, elicit an undesired immune response. Of particular concern are anti-drug antibodies, or ADAs, which are produced by the immune system in response to biologic therapy and can adversely affect the efficacy and safety of treatment. Our proprietary SVP technology encapsulates an immunomodulator in biodegradable nanoparticles to induce antigen-specific immune tolerance to mitigate the formation of ADAs in response to life-sustaining biologic drugs. We believe our SVP technology has the potential for broad applications to both enhance existing biologic drugs and enable novel therapies. Our lead product candidate, SEL-212, is a combination of a therapeutic enzyme and our SVP technology designed to be the first biologic treatment for gout that durably controls uric acid in refractory gout and dissolves and removes the harmful deposits of uric acid in chronic tophaceous gout, each a painful and debilitating disease with unmet medical need. SEL-212 is currently in a comprehensive Phase 1/2 clinical program. The Phase 1/2 clinical program is comprised of two Phase 1 clinical trials and a Phase 2 clinical trial, and is designed to evaluate the ability of SEL-212 to control uric acid levels and mitigate the formation of ADAs. Based on preliminary data from our ongoing Phase 1b clinical trial, we believe that SEL-212 has the potential to control serum uric acid levels for at least 30 days after a single dose by mitigating the formation of ADAs in response to the therapeutic enzyme. We expect to receive final data from both Phase 1 clinical trials and initiate the Phase 2 clinical trial in the second half of 2016. We have submitted to the FDA two investigational new drug, or IND, applications, both of which are active. Each IND lists us as the named sponsor and is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Despite rapid advancement in biologic treatment of rare and serious diseases, many biologic therapies are not broadly effective because they are exogenous proteins that are foreign to the patient's immune system and, therefore, may elicit an immune response, known as immunogenicity. Undesired immunogenicity includes the formation of ADAs that can compromise the drug's efficacy and cause serious allergic reactions. The formation of ADAs is known to occur in established treatments such as enzyme and protein replacement therapies, as well as in novel technologies, such as gene therapy and antibody-drug conjugates. ADAs can start developing in the body with the first dose of a biologic therapy and can render subsequent doses ineffective or unsafe, potentially depriving patients of life-saving therapeutic options and limiting the likelihood of success for many otherwise promising novel biologic drugs and technologies. We believe the co-administration of our SVP technology with biologic treatments has the potential to overcome these limitations without requiring changes in dosing or formulation. We intend to build a platform based on our SVP technology applied to the mitigation of ADAs for a wide range of biologics.

Our lead product candidate, SEL-212, was designed specifically to overcome the challenges faced by Krystexxa, a pegylated uricase. Krystexxa, is the only product approved by the U.S. Food and Drug Administration, or the FDA, for the treatment of chronic refractory gout. In clinical trials, Krystexxa demonstrated the ability to rapidly reduce uric acid levels in serum upon initial dosing. However, despite these results, Krystexxa has not achieved broad commercial adoption. We believe this is largely attributable to undesired immunogenicity. The package insert information for Krystexxa indicates that during Phase 3 clinical trials, 92% of patients developed ADAs. The package insert information also indicates that during the drug's Phase 3 clinical trials, high Krystexxa-specific ADA levels in patients

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were associated with a failure to maintain Krystexxa-induced normalization of uric acid levels. Similarly, in 2011, The Journal of the American Medical Association published the results of clinical trials finding that 58% of Krystexxa patients who received biweekly doses of Krystexxa were non-responders.

SEL-212 consists of SVP-Rapamycin co-administered with pegsiticase, our proprietary pegylated uricase, for the treatment of refractory and chronic tophaceous gout. SVP-Rapamycin uses our SVP technology to encapsulate the approved immunomodulator rapamycin in biodegradable nanoparticles. Our preclinical data indicate that SVP-Rapamycin, when co-administered with pegsiticase, induces antigen-specific immune tolerance to pegsiticase and substantially reduces the formation of associated ADAs. We believe that SEL-212 has the potential to offer a uniquely effective treatment for patients with refractory or chronic tophaceous gout, while also demonstrating the clinical effectiveness of our SVP technology. Approximately 8.3 million patients in the United States suffer from gout, which is caused by elevated levels of serum uric acid. Excessive uric acid levels result in harmful deposits of insoluble uric acid crystals in joints and tissues, causing joint damage and painful inflammation. High concentrations of serum uric acid also increase the risk for other conditions, including cardiovascular, cardiometabolic, joint and kidney disease. No treatment has been approved to remove uric acid deposits from joints and tissues. Approximately 50,000 patients in the United States have been diagnosed with chronic refractory gout, an orphan indication defined as uric acid levels that cannot be controlled by available oral therapies. Approximately 500,000 patients in the United States suffer from chronic tophaceous gout, in which patients develop nodular insoluble masses of uric acid crystals referred to as tophi, which can occur either in joints, such as fingers, toes or elbows, or in the tissues that make up organs, such as the kidney and heart. Tophi are a source of inflammation and pain, and have been associated with diseases of the heart, vascular system, metabolic process, kidney and joints. There is no approved drug for chronic tophaceous gout.

We are also applying our SVP technology to antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing. Gene therapies often use a viral vector, such as an adeno-associated virus, or AAV, vector to place corrective genetic material into cells to treat genetic diseases. One of the key hurdles for the gene therapy field is to overcome immunogenicity against the viral vector, which can manifest itself in three ways. First, pre-existing ADAs that were induced following a natural AAV infection can neutralize the viral vector and block gene transfer. Up to 50% of patients are ineligible for gene therapy due to the presence of pre-existing ADAs. Second, ADAs form in response to the first administration of a gene therapy vector and prevent effective subsequent doses of gene therapy. Subsequent doses are particularly necessary for pediatric indications due to cellular turnover in young patients. The ability to readminister gene therapies is also important for diseases where the goal is to transfect a high number of cells. Moreover, the third way in which immunogenicity can manifest itself against the viral vector is that the cellular immune system can respond to the transduced cells, which can reduce efficacy and pose safety concerns.

We have in-licensed the Anc80 gene therapy vector, or Anc80, from the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc., collectively referred to as MEE. Developed by the laboratory of Luk H. Vandenberghe, Ph.D., of Massachusetts Eye and Ear Infirmary and Harvard Medical School, Anc80 was designed as a synthetic precursor of AAV1, AAV2, AAV8 and AAV9. In preclinical studies, Anc80 has been observed to be a potent gene therapy vector that has demonstrated the capability of yielding superior gene expression levels in the liver compared to naturally occurring AAVs that are currently evaluated in clinical trials. As a synthetic vector, we believe Anc80 has limited cross-reactivity to naturally-occurring AAVs and therefore has the potential to treat patients with pre-existing AAV-specific ADAs. By combining SVP-Rapamycin and Anc80, we intend to develop highly differentiated gene therapies to address all three of the immunogenicity issues associated with

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the use of viral vectors. We believe that any such potential proprietary gene therapy products utilizing SVP-Rapamycin and Anc80 would have significant advantages, including (i) applicability to patients with pre-existing ADAs to naturally occurring AAV, a current exclusion criteria for many clinical studies, and (ii) the potential development of gene therapies for diseases that require repeat dosing due to a younger patient population or need to reach higher levels of protein expression than can be achieved with a single dose.

In collaboration with the clinical and gene therapy laboratory at the National Institutes of Health, or NIH, and MEE, we plan to develop a product candidate utilizing the Anc80 vector for the treatment of an autosomal recessive metabolic, or ARM, disorder resulting from an inborn error of metabolism. This ARM disorder can cause severe developmental defects and premature death as a result of an accumulation of toxic metabolites. Under our license agreement with MEE, we also have the option to develop gene therapies using Anc80 for several additional diseases including lysosomal storage, muscular and genetic metabolic diseases. We plan to develop another product candidate for the treatment of an X-linked metabolic, or XLM, disorder, which is a metabolic disorder similar to ARM disorder. We are pursuing this second indication through collaborations with third parties with preclinical and clinical experience in this area.

In addition to developing proprietary non-immunogenic therapeutic enzymes and gene therapies, we intend to pursue out-licensing opportunities for select applications of our SVP technology. We believe that our preclinical data may support the potential application of SVP-Rapamycin to both marketed products, such as monoclonal antibodies against human tumor necrosis factor-alpha, or TNF-alpha, which are known to induce undesired immunogenicity, and novel biologic drugs that would otherwise be too immunogenic to develop, such as novel antibody-drug conjugates. We are also applying our SVP technology to the treatment of autoimmune diseases and allergies. Currently, most autoimmune diseases are treated with broadly immunosuppressive therapies that indiscriminately affect the function of the entire immune system. Our SVP technology is designed to re-program the immune system to elicit tolerance to a specific antigen without impacting the rest of the immune system. Since 2012, we have established three collaborations with Sanofi to research novel products for the treatment of a life-threatening food allergy, celiac disease and type 1 diabetes. We intend to continue a strategy of out-licensing our SVP technology for antigen-specific immune tolerance for applications that are outside our areas of focus.

We believe our SVP technology also has the potential to be used for therapies that stimulate the immune system to prevent and treat cancer, infectious diseases and other diseases. We have early-stage research programs for therapeutic vaccines for human papilloma virus, or HPV, associated cancers and for antibody-based vaccine programs for nicotine addiction and malaria. These programs use our SVP technology to encapsulate an immune-stimulatory agent in biodegradable nanoparticles in order to stimulate the immune system in response to a specific antigen. We currently finance these programs primarily through grants.

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The following chart summarizes our current SVP product candidate pipeline:

Program	Description	Development status	Program strategy
<i>SVP for immune tolerance</i>			
Refractory and chronic tophaceous gout (SEL-212)	SVP-Rapamycin co-administered with pegsitticase	Final data from Phase 1a and Phase 1b trials and initiation of Phase 2 trial expected in the second half of 2016	Own development
Gene therapy for an ARM disorder	SVP-Rapamycin co-administered with Anc80	Investigational New Drug Application, or IND, filing for first indication expected by the end of 2017	Own development
Gene therapy for an XLM disorder	SVP-Rapamycin co-administered with AAV	IND filing for first indication expected in 2018	Own development
<i>SVP for immune stimulation</i>			
Smoking cessation and relapse prevention (SEL-070)	SVP-adjuvant and SVP-nicotine	Good laboratory practice, or GLP, toxicology studies ongoing	Own development, with grant from the National Institute on Drug Abuse, or NIDA
HPV-associated cancer (SEL-701)	SVP-adjuvant and SVP-HPV antigen	Preclinical	Own development, with grant from the Russian-based Development Fund of New Technologies Development and Commercialization Center, or the Skolkovo Foundation

The following chart summarizes our current discovery pipeline.

Program	Description	Development status	Program strategy
<i>SVP for immune tolerance</i>			
Food allergy	SVP-adjuvant and SVP-food allergen	Discovery	Sanofi worldwide exclusive license
Celiac disease	SVP-Rapamycin and SVP-gluten	Discovery	Sanofi worldwide exclusive license
Type 1 diabetes	SVP-Rapamycin and SVP-insulin	Discovery	Sanofi and Juvenile Diabetes Research Foundation, or JDRF, sponsored research program
<i>SVP for immune stimulation</i>			
Malaria	SVP-adjuvant and SVP-malaria antigen	Discovery	The Bill and Melinda Gates Foundation sponsored research program

OUR STRATEGY

Our goal is to become the first biopharmaceutical company to develop and commercialize targeted therapies that are designed to modulate the immune system to effectively and safely treat rare and serious diseases. In addition, we intend to maximize the value of our SVP technology by collaborating

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with biopharmaceutical companies on programs that can benefit from our technology but that are outside our area of focus. The key elements of our strategy include the following.

- **Rapidly advance the development of our lead product candidate, SEL-212, for the treatment of refractory and chronic tophaceous gout.** We believe SEL-212 has the potential to be the first biologic treatment for gout that durably controls uric acid in refractory gout and dissolves and removes harmful deposits of uric acid crystals in chronic tophaceous gout in a majority of patients. We are currently conducting a comprehensive Phase 1/2 clinical program, comprised of two Phase 1 clinical studies, for which we expect to receive final data in the second half of 2016, and a Phase 2 clinical trial, which we expect to initiate in the second half of 2016 and for which we expect to receive data in the first half of 2017. We plan to advance this program through regulatory approval and commercialization.
- **Leverage our SVP technology for immune tolerance to develop novel uses and classes of non-immunogenic biologics.** We intend to use our SVP technology to develop gene therapies designed to mitigate the formation of ADAs and therefore enable repeat administration and first-in-class non-immunogenic versions of therapeutic enzymes or proteins for human therapy. We have several programs in various stages of discovery and we plan to continue to identify opportunities. In addition, we intend to pursue opportunities to in-license proprietary enzymes that we can co-administer with our SVP-Rapamycin to address the issues of immunogenicity and develop effective proprietary products. We also intend to use our SVP technology to develop AAV-based gene therapies designed to mitigate the formation of ADAs and therefore enable repeat administration.
- **Establish infrastructure and capabilities to commercialize our products in rare and orphan diseases.** While we believe our SVP technology may be broadly applicable across disease areas, we intend to focus our proprietary efforts on developing and commercializing proprietary SVP-enabled products for rare and serious diseases where there is high unmet medical need. Therapies for treating these diseases require focused commercial efforts and coordination with patient groups and investigators. As our product candidates advance towards commercialization, we intend to build a commercial infrastructure to market our products to capture the full value of our proprietary SVP products.
- **Selectively pursue collaborations and maximize the value of our SVP programs for immune tolerance.** In addition to our own proprietary product development efforts, we are in discussions with potential collaborators and licensees to pursue novel gene therapies and are collaborating with Sanofi on programs for a food allergy, celiac disease and type 1 diabetes. We also intend to selectively pursue additional collaborations with biopharmaceutical companies to further leverage our SVP technology.
- **Utilize our expertise in SVP to stimulate the immune system to fight disease.** We are currently developing prophylactic and therapeutic vaccines that activate the immune system to fight disease through our SVP immune stimulation programs, which are primarily funded by grants. Our current product pursuits include a SVP product to treat HPV-associated cancers, a SVP nicotine vaccine for smoking cessation and relapse prevention and a SVP product for the prevention of malaria. We are developing our programs for HPV-associated cancers and smoking cessation and prevention on our own with grant funding from the Skolkovo Foundation for our HPV program and from the National Institute for Drug Abuse for our nicotine program. We are developing our malaria program under a sponsored research arrangement with The Bill and Melinda Gates Foundation.

OVERVIEW OF THE HUMAN IMMUNE SYSTEM

The human immune system is an integrated system of specialized immune cells, cell products and tissues that protect against infectious disease and cancer. The immune system recognizes antigens, which are substances, such as proteins, enzymes or complex sugars. These antigens can be endogenous, or self-antigens, which are produced by the body, or exogenous antigens derived from foreign sources, such as viruses, fungi or bacteria. The human immune system has evolved to recognize and destroy potentially harmful substances. To function effectively, the immune system must discern between harmful antigens and innocuous antigens. The immune system maintains a delicate balance between effector cells, which mount immune responses to antigens that represent potential threats, and regulatory cells, which mitigate undesired and potentially harmful immune responses through immune tolerance. Depending upon the characteristics of the antigen and the context in which the antigen is encountered, the immune system must determine whether to mount a defensive (effector) or regulatory (tolerogenic) immune response.

Antigens are processed in lymphoid organs, such as lymph nodes and the spleen, where the immune system determines whether to mount a defensive or regulatory response through a process called "antigen presentation." In connection with antigen presentation, dendritic cells process the antigens and present them to T cells. When presented, antigens perceived as harmful induce a stimulatory response that can result in the activation of cytolytic T cells or helper T cells, the latter of which help to induce B cells to produce antibodies. The role of cytolytic T cells is to kill cells that harbor intracellular antigens, such as viruses. The role of antibodies is to neutralize or eliminate extracellular antigens on cell surfaces or in interstitial fluids, such as plasma. Figure 1 below depicts both antigen presentation and the related immune responses.

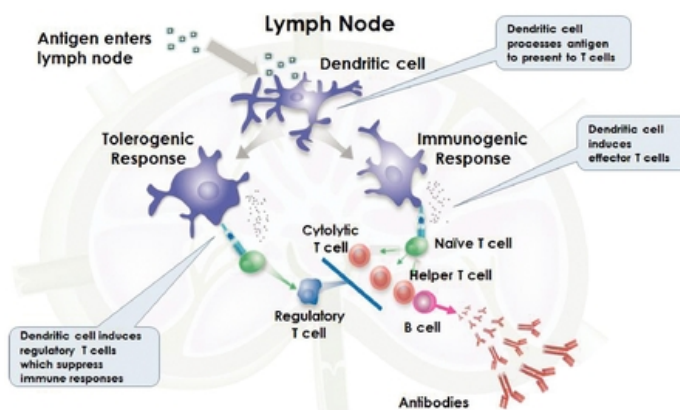


Figure 1. Antigen Presentation and Related Tolerogenic or Stimulatory Immune Response

There are a number of diseases that occur when the immune system mounts an undesired response to an innocuous foreign antigen or a self-antigen. For example, food allergy occurs when the immune system mounts an immune response to innocuous food particles. Another example of undesired immunogenicity occurs when the immune system is exposed to a biologic treatment, recognizes it as a foreign antigen and instructs the body to mount a defense by forming ADAs to the antigen, which can compromise a therapy's desired beneficial effect. Undesired immunogenicity is common with biologic therapies, such as in enzyme and protein replacement therapies, and in novel technologies, such as gene therapy and antibody-drug conjugates.

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A number of therapies have been developed to modulate an immune response. These therapies fall into two categories:

- *Immunosuppressive therapies.* Immunosuppressive therapies are designed to suppress the immune system and inhibit an undesired immune response. However, many current therapies are not antigen-specific and, as a result, broadly suppress the immune system leading to undesired side effects that include opportunistic infections, skin cancer and lymphomas. We believe there is an opportunity to develop therapies that instruct the immune system to remain tolerant to a specific antigen and thereby avoid off-target effects of systemic immunosuppression.
- *Immunostimulatory therapies.* Immunostimulatory therapies are designed to stimulate the immune system to prevent or treat infections and cancers. The most common class of immunostimulatory therapies are vaccines, which are designed to simulate the body's immune system to mount a defensive response to a specific antigen. While traditional vaccines have been successful for the prevention of infectious diseases, there has been limited success in developing therapeutic vaccines for the successful treatment of certain other diseases, including chronic infections and cancer. As a result, we believe there is a need for more effective vaccines to treat these diseases.

OUR SVP TECHNOLOGY

Our proprietary SVP technology encapsulates an immunomodulator in biodegradable particles to selectively modulate an immune response in an antigen-specific manner. Our SVP technology is based in part on the pioneering research performed by our co-founders at Harvard University, Massachusetts Institute of Technology, or MIT, and Brigham and Women's Hospital, or Brigham. In connection with our company's founding, we licensed 17 patent families related to certain aspects of our SVP technology as applied to nanoparticles for use in vaccines from our co-founders' institutions pursuant to an agreement with MIT, the party that administers licensing arrangements with respect to patents jointly owned by these institutions. We believe one of the key insights from this research is that nanoparticles are uniquely suited to deliver precise instructions to the immune system as a result of the natural predisposition of the immune system to interrogate nanoparticles, such as viruses. This research led to a portfolio of patents and patent applications covering aspects of our SVP technology, which we have exclusively in-licensed with respect to therapeutic or prophylactic vaccine products or processes. We have aggressively sought to extend and protect the proprietary intellectual property underlying the composition and use of SVP for antigen-specific immunomodulation.

Our SVP technology is a highly flexible nanoparticle platform, capable of incorporating a wide range of antigens and immunomodulators, allowing us to tailor our SVP products for specific applications across multiple indications. We are tailoring our SVP technology for:

- the treatment of chronic tophaceous and refractory gout;
- antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing;
- application with marketed products and novel biologic drugs that would otherwise be too immunogenic to develop;
- the treatment of a life-threatening food allergy, celiac disease and type 1 diabetes under a collaboration with Sanofi; and
- immune stimulation programs to prevent and treat cancer, infectious diseases and other diseases.

SVP are designed to remain intact after injection into the body and accumulate selectively in lymphoid organs, which include lymph nodes and the spleen, where the immune response is coordinated. SVP

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are designed to be processed by specialized immune cells, such as dendritic cells and other antigen-presenting cells that initiate and regulate immune responses, where they deliver the antigen and immunomodulator in a coordinated and targeted manner. Depending on the type of immunomodulator encapsulated in the SVP, our technology is designed to induce either a:

- tolerogenic response to mitigate the formation of ADAs against a biologic drug or treat allergies and autoimmune diseases; or
- potent antigen-specific stimulatory response, such as an antibody response to a microbial antigen or a cytolytic T cell response to a tumor antigen.

A tolerogenic response is the induction of immune tolerance or non-responsiveness to a specific antigen. Cytolytic T cells are specialized antigen-specific immune cells that target and kill cells that harbor a specific antigen.

Figure 2 below depicts the process by which SVP communicates with the immune system to induce either a tolerogenic or antigen-specific stimulatory response.

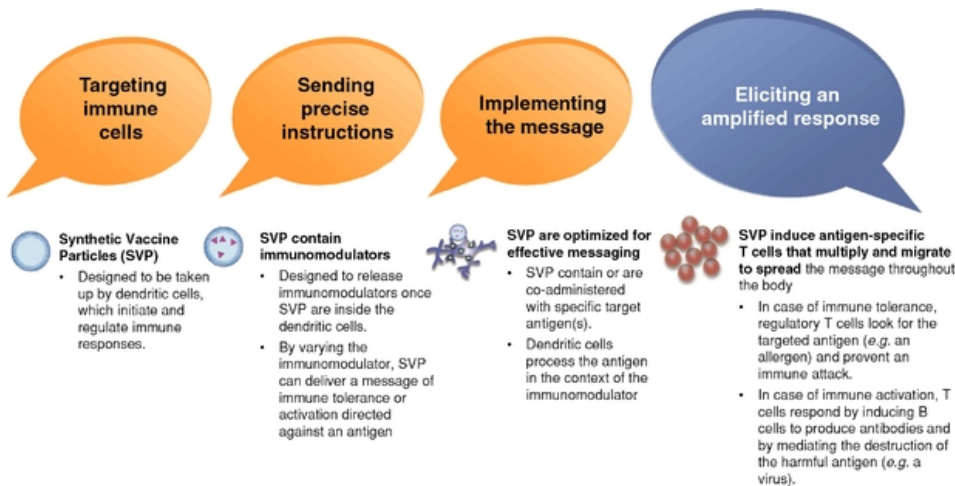


Figure 2. How SVP Communicate with the Immune System

OUR ANTIGEN-SPECIFIC TOLERANCE PROGRAM

Our antigen-specific SVP tolerance programs utilize SVP-Rapamycin, our biodegradable nanoparticle encapsulating the immunomodulator rapamycin. Rapamycin is a small molecule approved for the prevention of organ rejection in kidney transplant patients. To induce immune tolerance in the body, we co-administer our SVP-Rapamycin with a free antigen, such as a biologic drug, which is depicted in Figure 3 below.

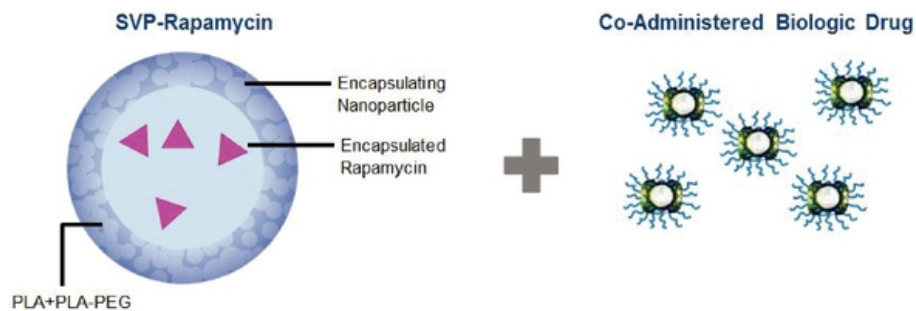


Figure 3. Co-Administration of SVP-Rapamycin with a Biologic Drug

SVP-Rapamycin is co-administered at the beginning of therapy with a biologic drug to mitigate the formation of ADAs without altering the drug or its dose regimen. As a result, we believe our SVP-Rapamycin may provide us with significant growth opportunities in the areas of immune tolerance because SVP-Rapamycin can be co-administered at the beginning of therapy with many different biologic drugs. Importantly, each pairing of SVP-Rapamycin with a biologic drug also offers us the opportunity to pursue another proprietary product candidate, which can be separately patented, approved and marketed. SVP-Rapamycin is manufactured under cGMP using well-defined commercial operations, which, we believe, further enhances the scalability of our tolerance programs.

During preclinical studies, we observed that delivering an antigen together with SVP-Rapamycin provided the appropriate signals *in vivo* to induce regulatory T cells, which, in turn, inhibited effector immune responses, such as the formation of ADAs. In our preclinical studies, we observed that SVP-Rapamycin labeled with a fluorescent dye selectively accumulated in lymphoid organs where it was processed by antigen-presenting cells. Figure 4 below depicts a model of how SVP-Rapamycin would enter a lymph node and be taken up by a dendritic cell. We believe that when delivered in the context of our SVP-Rapamycin, both the biologic drug and SVP-Rapamycin are taken up and processed by dendritic cells in a manner that induces regulatory T cells, which can block the activation of helper T cells, mitigating the formation of ADAs.

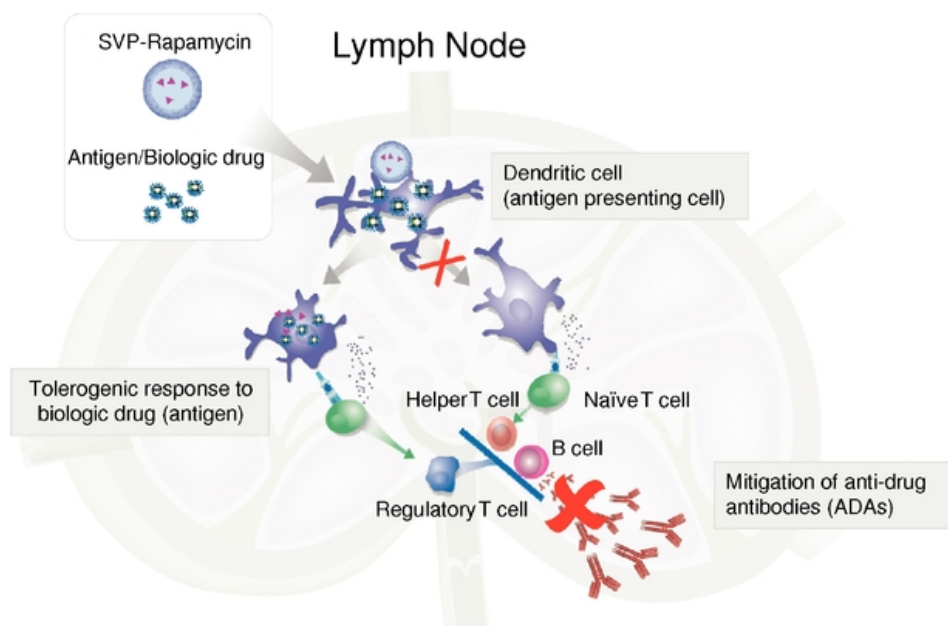


Figure 4. SVP-Rapamycin and Antigen/Biologic Drug Presentation and Related Immune Tolerance Induction

Limitations of existing therapies

All biologics, even those comprised of human protein sequences, have the potential to induce ADAs. Whether a biologic drug elicits an ADA response depends on both product-specific factors, such as propensity to form aggregates, route of administration and mechanism of action, as well as patient-specific factors, such as genetics, underlying disease and medications. Many enzyme and protein replacement therapies used in the treatment of rare and serious diseases have a particularly high rate of immunogenicity because patients are genetically deficient in the target protein and, as a result, the therapeutic protein can be recognized as foreign.

The induction of ADAs can lead to neutralization of efficacy, modification of pharmacokinetics and pharmacodynamics as well as allergic responses. Immunogenicity is a significant hurdle for the development of safe and effective biologic treatments and has become a key concern for regulators, as evidenced by over 100 approved biologics that describe immunogenicity in their labels or clinical literature. We believe that immunogenicity is a leading cause of treatment failure for patients and product development failure for biopharmaceutical companies. As depicted in Figure 5 below:

- for 36 currently marketed biologics, over 20% of the patients receiving the biologic are affected by immunogenicity, including Factor VIII products for hemophilia such as Advate and therapeutics with fully human protein sequences such as Humira, a human TNF-alpha antibody;
- promising novel biologics, such as recombinant erythropoetin and IgA protease, were abandoned during clinical or preclinical development due to immunogenicity issues;

- improved versions of biologics that are in the same pharmaceutical class as immunogenic marketed biologics, including pegsiticase, long-acting coagulation Factor VII and certain antibody drug conjugates, are affected by immunogenicity; and
- novel platform technologies, such as gene therapy and gene editing, are fundamentally restricted by immunogenicity.

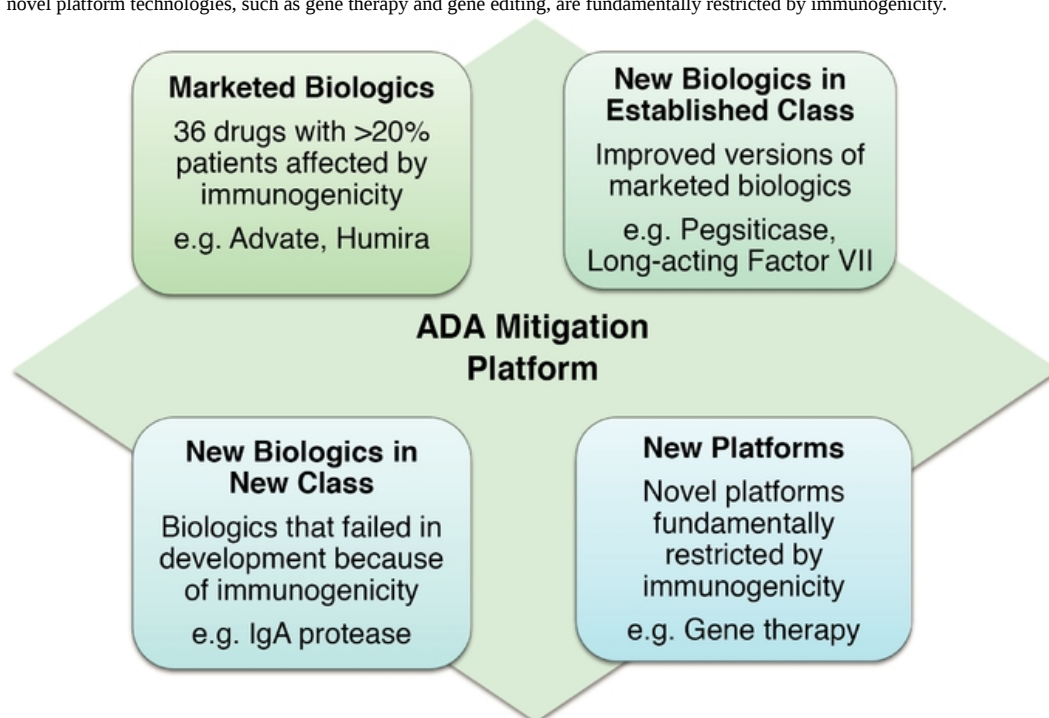


Figure 5. ADA Mitigation Platform Opportunities

Undesired immunogenicity represents a significant hurdle that can affect the clinical development of new biologic platforms. For example, in gene therapy, viral vectors are required to transport the genetic material into cells. The viral origin of these vectors explains their immunogenicity, which has led drug developers to limit applications to situations where the required frequency and site of administration are conducive to manageable immune responses.

Treatment and product development failure resulting from undesired immunogenicity has been recognized by regulators and patient advocacy organizations. Recently, the FDA and the National Organization for Rare Disorders, or NORD, co-sponsored a workshop on undesired immune responses to enzyme replacement therapies and called on the biopharmaceutical industry to take a more proactive approach to addressing immunogenicity to biologics.

Currently, we believe there are no comprehensive solutions to the complications of immunogenicity. Drug developers often stop the development of biologics that show an undesired immune response during preclinical or clinical development. In some cases, biopharmaceutical companies may attempt to reduce undesired immune responses by re-engineering the biologic through protein pegylation or

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removal of immunogenic epitopes. However, these approaches are limited in their effectiveness. Physicians may try to address the issue of undesired immune responses by increasing the dose of the biologic, which can be prohibitively expensive, or in life-threatening situations by using general immunosuppressive combination therapies. We believe that our tolerogenic SVP technology could offer an entirely new and effective treatment alternative for undesired immune responses, including with respect to the formation of ADAs, but potentially also for autoimmune diseases and allergies.

Immune tolerance preclinical studies

We have conducted several preclinical studies that we believe demonstrate the efficacy of our SVP technology in inducing immune tolerance.

Transfer of immune tolerance from mice treated with SVP-Rapamycin

In a preclinical study, we observed that *in vivo* administration of SVP resulted in induction of regulatory T cells, which, in turn inhibited effector immune responses. The objective of this study was to evaluate the ability to transfer tolerance from a tolerized animal to a naïve animal, a hallmark of tolerance induction. As depicted in Figure 6 below, we injected donor mice with two injections of either:

- an empty nanoparticle, or Empty Nanoparticle, as indicated in blue;
- a nanoparticle encapsulating rapamycin, or NP-Rapamycin, and administered without antigen, as indicated in red; or
- SVP-Rapamycin encapsulating a peptide sequence from proteolipoprotein, or PLP, a myelin antigen associated with multiple sclerosis, or SVP-Rapamycin.PLP, as indicated in green.

Two weeks after the second injection, cells from the spleens of the mice were harvested and expanded *in vitro*. These immune cells were then transferred into naïve recipient mice. The next day, all recipient mice were immunized with the PLP peptide in complete Freund's adjuvant, or CFA, a potent immune stimulating adjuvant, to induce experimental autoimmune encephalomyelitis, or EAE, a model of multiple sclerosis. As indicated by the increase in the mean clinical score for multiple sclerosis in Figure 6 below, the untreated control mice that were immunized but received no transferred cells developed EAE approximately ten days after immunization with PLP and CFA, as reflected in black in Figure 6 below. The mice receiving immune cells transferred from donor mice treated with either Empty Nanoparticle or NP-Rapamycin, as indicated in blue and red in Figure 6 below, respectively, also developed EAE approximately ten days after immunization. In contrast, mice that received immune cells transferred from donor mice treated with SVP-Rapamycin.PLP did not develop EAE during the course of the trial, as indicated in green in Figure 6 below. We believe that these results indicate that the SVP-Rapamycin treatment induces a population of antigen-specific regulatory cells that mediate immune tolerance, as evidenced by the ability of transferred cells to confer protection from disease to naïve animals, reflecting a hallmark of immune tolerance.

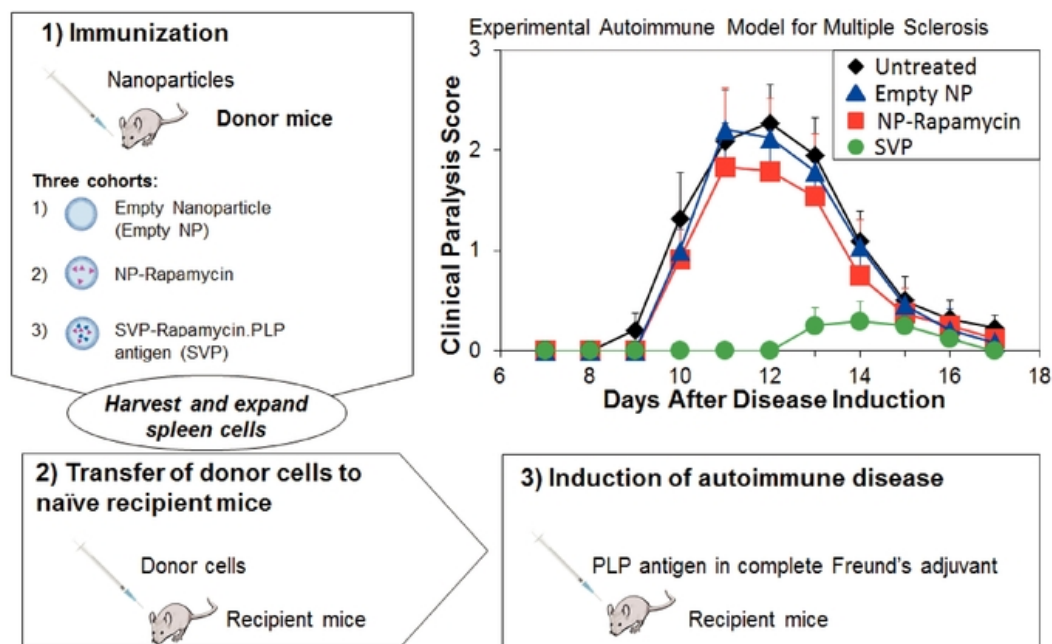


Figure 6. Preclinical Study: Transfer of Immune Tolerance from Mice Treated with SVP-Rapamycin to Naive Mice

Immune tolerance induction with SVP-Rapamycin

We conducted a preclinical study to test whether the encapsulation of rapamycin in SVP was necessary for immune tolerance induction by comparing weekly doses of SVP-Rapamycin with daily doses of free unencapsulated rapamycin. Our preclinical data indicated that SVP-Rapamycin, but not free unencapsulated rapamycin, induced antigen-specific tolerance that was resistant to subsequent challenges with the antigen alone. As depicted in Figure 7 below, study mice were separated into three groups during the course of a 21-day treatment period:

- the first group, referred to as the Delayed Immunization Group indicated in black, was not treated with anything during the treatment period;
- the second group, referred to as the Daily Free Rapamycin Group indicated in red, was treated with doses of free unencapsulated rapamycin five days per week and weekly doses of the highly immunogenic antigen keyhole limpet hemocyanin, or KLH; and
- the third group, referred to as the SVP-Rapamycin Group indicated in green, received three weekly doses of SVP-Rapamycin combined with KLH.

Following the treatment period, all of the mice were then challenged with three weekly injections of KLH alone to assess the durability of immune tolerance. As depicted in Figure 7 below, the mice in both the SVP-Rapamycin Group and Daily Free Rapamycin Group showed inhibition of the KLH-specific ADA responses after the treatment phase of the trial. However, only the SVP-Rapamycin Group maintained immune tolerance after the challenge phase. We believe that these results indicate that SVP-Rapamycin induced a population of regulatory T cells that maintained tolerance to challenge with antigen alone, whereas the administration of daily free rapamycin did not. Notably, the Daily

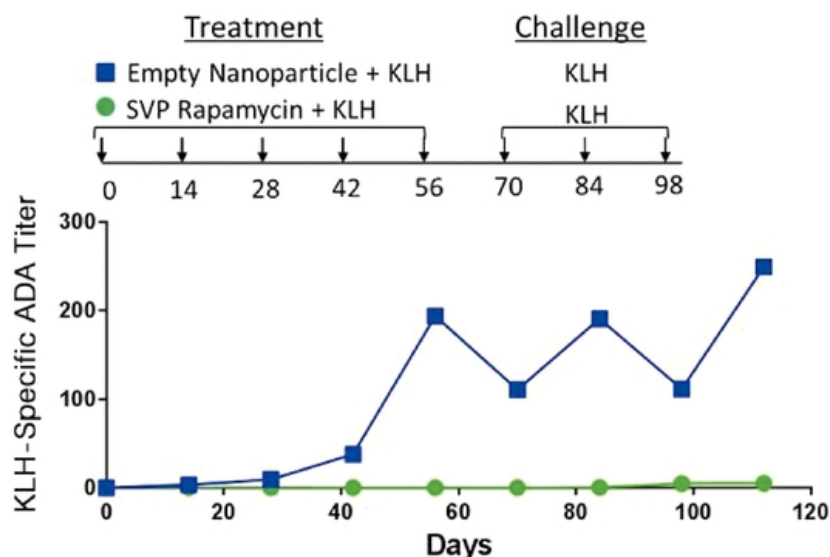


Figure 8. Preclinical Study: Inhibition of KLH-Specific ADA Response by SVP-Rapamycin in Nonhuman Primates

OUR SVP PROGRAMS TO INDUCE ANTIGEN-SPECIFIC TOLERANCE

We believe our SVP technology to induce antigen-specific tolerance has a broad range of applications. We are currently pursuing targeted product development strategies for four discrete applications in which we believe SVP products could be highly differentiated.

- Therapeutic enzymes.* Therapeutic enzymes are a frequently used class of biologic drugs to treat rare diseases. Through our analysis of biologic drugs, including our preclinical studies, we have observed that enzymes are especially prone to undesired immune responses. Our lead product candidate, SEL-212, includes pegsiticase, a pegylated uricase enzyme, which is an example of an immunogenic enzyme for which we are applying SVP-Rapamycin with the intention of improving the enzyme's efficacy and safety. Other examples of immunogenic enzymes include acid alpha-glucosidase for the treatment of Pompe disease, alpha galactosidase A for the treatment of Fabry's disease and microbial enzymes such as asparaginase for the treatment of cancers. We intend to seek opportunities to secure supply of and, if appropriate, licenses to, these or other enzymes that we would pair with SVP-Rapamycin to enhance their efficacy, safety and use in their treatment of diseases.
- Gene therapies.* We believe gene therapies have the potential to address key unmet medical needs for many rare genetic diseases, but that undesired immune responses to the viral vectors used for gene replacement, augmentation and editing may be restricting their broader use. Through our analysis of genetic diseases, we have identified applications and patient segments that we believe would benefit from our SVP technology. We intend to develop proprietary SVP-Rapamycin-enabled non-immunogenic gene therapies with viral vectors such as the Anc80 vector that we have licensed from MEE. We believe our product candidates have the potential to solve the problem of pre-existing immunogenicity to the gene therapy vector by using a novel engineered gene therapy vector, Anc80, and to prevent undesired immune responses to the vector and transgene that can occur with the first dose of gene therapy by using our SVP technology. Our initial areas of focus

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include lysosomal storage, genetic muscular and genetic metabolic diseases. Our proprietary gene therapy programs are focused on the use of vectors that have documented efficiency in delivery of the transgene in nonhuman primates such as Anc80. We believe we are the first company to systematically pursue the development of gene therapy products in combination with an immunotherapy with the goal of enabling repeat administration of the gene therapy. We have engaged third parties with experience in gene therapy and rare diseases to support the development of our proprietary products.

- *Other products and product candidates affected by undesired immune responses.* We have generated preclinical data demonstrating the breadth of the SVP program for immune tolerance. For many biologic drugs, undesired immune responses limit efficacy and cause safety concerns. This includes TNF-alpha-specific monoclonal antibodies for the treatment of rheumatoid arthritis and coagulation factor replacement therapies for the treatment of hemophilia. We intend to out-license SVP-Rapamycin technology for use with other products that are outside our focus to larger biopharmaceutical companies. We believe our SVP technology may also be of interest to biopharmaceutical companies with biologic product candidates in clinical development that have demonstrated initial efficacy but are experiencing issues with safety or sustained efficacy due to inhibitory ADAs.
- *Allergies and autoimmune diseases.* In addition to the formation of ADAs, undesired immunogenicity can take the form of allergies when the immune system reacts to allergens such as food and pollen, or autoimmune diseases when the immune system attacks the body's own proteins. We have three collaborations with Sanofi to advance our SVP programs in the area of allergies and autoimmune disease. As part of one of the collaborations, the Juvenile Diabetes Research Foundation and Sanofi have also awarded us with a grant to support the development of our SVP technology in the area of autoimmune disease by providing expertise and financial resources. Our SVP program in the area of allergies and autoimmune disease focuses on expanding our related product pipeline based on these collaborations and other out-licensing arrangements.

SEL-212 for the treatment of refractory and chronic tophaceous gout

Overview

SEL-212 is our proprietary product candidate for the treatment of refractory and chronic tophaceous gout. SEL-212 consists of SVP-Rapamycin co-administered with pegsiticase, a pegylated uricase. We believe that our SEL-212 has the potential to offer a uniquely effective treatment for patients with refractory or chronic tophaceous gout, while also demonstrating the clinical effectiveness of our SVP technology. Pegylated uricase, in the form of the approved drug Krystexxa, has demonstrated the ability to significantly reduce uric acid levels and dissolve the harmful uric acid crystals that are the manifestations of gout upon initial treatment in naïve patients. However, Krystexxa has not achieved broad commercial adoption, which we believe is primarily due to an undesired immune response that significantly restricts clinical use. Based on our preclinical studies, we believe that by leveraging our SVP technology to induce durable immune tolerance of our pegylated uricase, pegsiticase, SEL-212 may potentially overcome this undesired immune response and optimize pegsiticase's effectiveness in controlling uric acid levels and, as a result, enable the effective dissolution and removal of uric acid crystals.

The market for gout therapy

Gout is a painful and potentially disabling form of arthritis resulting from excess accumulation of uric acid and deposition of uric acid crystals in joints and soft tissues, including those of the kidney and

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heart, causing harmful inflammation. Gout is caused by an overproduction of uric acid, a natural byproduct of purine metabolism that is produced after consumption of food with high levels of purines such as seafood, meat, yeast and certain vegetables, or an inability of the kidneys to excrete adequate amounts of uric acid from the body. High concentrations of serum uric acid lead to formation of insoluble uric acid crystals in joints and tissues, causing pain, inflammation and joint damage, and increase the risk for other conditions, including cardiovascular, cardiometabolic, joint and kidney disease.

There are approximately 8.3 million and 10 million gout sufferers in the United States and the European Union, respectively. The first line of treatments for gout are allopurinol and febuxostat. Both drugs are xanthine oxidase inhibitors, oral drugs that reduce the synthesis of uric acid. Lesinurad and probenecid are oral gout drugs that increase the rate of excretion of uric acid through the kidneys, and are used almost exclusively in combination with these first line treatments. While both of these treatments are designed to prevent the formation of uric acid deposits, neither of these treatments effectively reduces existing uric acid deposits in joints and tissues. Additionally, neither of these first line treatments individually or in combination with lesinurad and probenecid are indicated for refractory or chronic tophaceous gout.

We estimate that approximately 50,000 patients in the United States suffer from chronic refractory gout, an orphan indication defined by uric acid levels that cannot be controlled by available oral therapies. Krystexxa, an injectable pegylated uricase enzyme, is indicated for the treatment of chronic refractory gout. In clinical trials, Krystexxa demonstrated the ability to rapidly reduce uric acid levels upon initial dosing. However, despite these clinical results, Krystexxa has not achieved broad commercial adoption. Because uricase is an enzyme foreign to humans, we believe this is primarily due to an undesired immune response. The package insert information for Krystexxa indicates that 92% of patients develop ADAs, 26% experience infusion site reactions and 6.5% experience anaphylaxis, a life-threatening allergic reaction typically involving itchy rash, throat swelling and low blood pressure. The package insert information also indicates that during the drug's clinical trials, high Krystexxa-specific ADA titer in patients was associated with a failure to maintain normalization of uric acid levels. Similarly, in 2011, The Journal of the American Medical Association published the results of clinical trials finding that 58% of Krystexxa patients who received biweekly doses of Krystexxa were non-responders with loss of efficacy starting as early as two weeks after treatment.

Gout is a spectrum of disease with the traditional diagnosis being the extraction of monosodium urate crystals with joint fluid or uric acid crystals from a visible tophus. Additionally, high concentrations of serum uric acid increase the risk of co-morbidities, including cardiovascular, cardiometabolic, joint and kidney disease. Patients who are unable to reduce their serum uric acids levels below 6 mg/dl with oral drugs are diagnosed with refractory gout. Patients who have uric acid deposits, or tophi, in soft tissues, joints, the urinary tract, the digestive tract or the heart and a persistently elevated uric acid level when left untreated are diagnosed with chronic tophaceous gout. Tophi are a source of inflammation and pain.

Figure 9 below illustrates the association between gout and diseases of the heart, vascular system, metabolic process, kidney and joints.

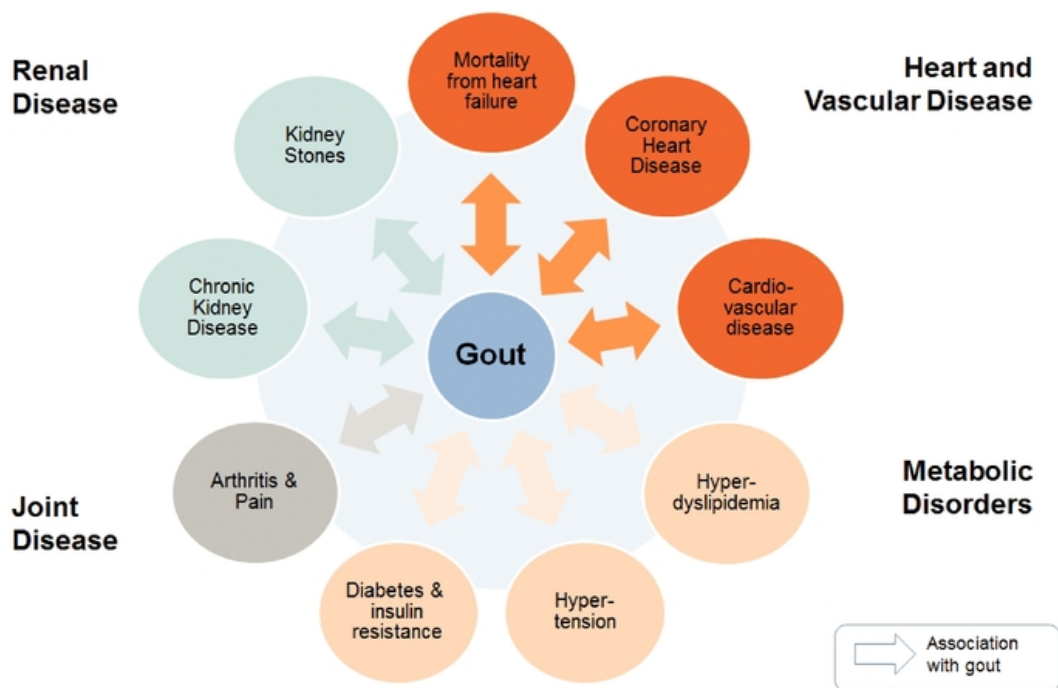


Figure 9. Co-Morbidities Associated with Gout

Approximately 500,000 patients in the United States suffer from chronic tophaceous gout. There is no approved drug for this patient group that resolves tophi, although clinical studies have indicated that Krystexxa is effective in clearing uric acid deposits in patients that do not develop inhibitory levels of ADAs. We believe that oral gout drugs cannot effectively remove tophi from joints and tissue due to their limited ability to affect existing uric acid deposits.

Based on our preclinical studies, our Phase 1b clinical data and market research, we believe that SEL-212 may potentially address two key unmet needs in the treatment of gout, the durable control of serum uric acid levels in patients with chronic refractory gout and removal of painful and damaging uric acid deposits for patients with chronic tophaceous gout.

Our product development strategy is designed to address these unmet medical needs while improving the dosing regimen compared to Krystexxa. We plan to initially seek regulatory approval for the treatment of refractory gout by demonstrating reduction of serum uric acid levels below the FDA-approved endpoint and clinical guideline of 6 mg/dl. We plan to conduct a clinical program to support a label extension for the treatment of patients with chronic tophaceous gout. During our market research, physicians expressed their preference for monthly dosing as well as for a subcutaneous route of administration. In response to this preference, we intend to develop SEL-212 as a monthly treatment and offer a subcutaneous formulation following the initial launch of the intravenous dosage form, if approved. We believe that Krystexxa has been developed as a bi-weekly intravenous-only formulation to avoid additional immunogenicity anticipated from a higher dose that would be required by a monthly regimen.

We believe that SEL-212 is ideally suited for patients diagnosed with chronic tophaceous gout. If approved, our strategy is to position SEL-212 as an induction therapy for gout that would remove harmful uric acid deposits over five monthly doses on average and allow patients to switch to oral gout maintenance therapy with xanthine oxidase inhibitors unless and until such patients experience a subsequent manifestation of uric acid deposits at which time a new course of SEL-212 would be required. We do not believe that oral therapy would completely prevent the build-up over time of uric acid crystals in patients with a history of chronic tophaceous gout. As a result, we anticipate that SEL-212 induction treatment, if approved, would be required intermittently in such patients. We believe that, in contrast to Krystexxa, SEL-212 induction treatment may be effective in removing harmful uric acid deposits in most patients with chronic tophaceous gout over multiple cycles of treatment. Figure 10 below depicts this positioning strategy as a sample diagram illustrating what we believe to be a shift in the treatment paradigm for chronic tophaceous gout.

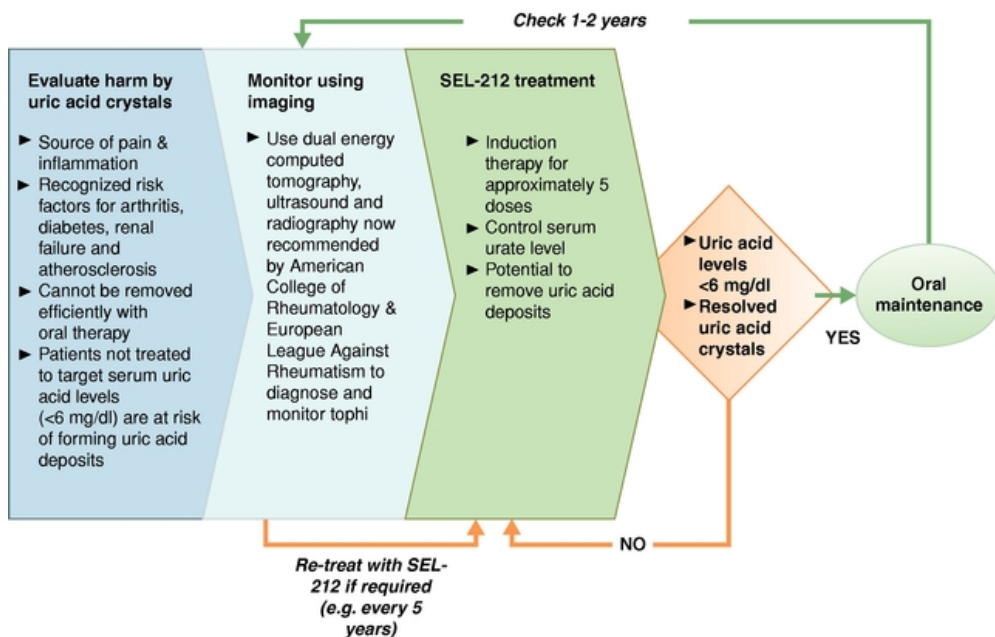


Figure 10. Sample Treatment Course for Chronic Tophaceous Gout.

We expect our clinical and marketing strategy for SEL-212 to initially focus on the estimated 160,000 patients in the United States diagnosed with refractory or chronic tophaceous gout being treated by rheumatologists, as well as approximately the same estimated number of patients in Europe. We believe that for these patients who are already being treated by rheumatologists and diagnosed with chronic tophaceous gout, the need for a new treatment is the highest. If SEL-212 is approved, we expect our strategy for marketing SEL-212 to rheumatologists will be to promote a switch from oral therapies to SEL-212 for patients with serum uric acid levels chronically above 6 mg/dl and diagnosed with chronic tophaceous gout. We intend to leverage imaging technologies recently recommended by the guideline writing associations for rheumatology, including the American College of Rheumatology and the European League Against Rheumatism. In particular, dual energy computed tomography can visualize uric acid deposits in joints and tissues as depicted in Figure 11 below in green and has the potential to become an important tool to manage chronic tophaceous gout and to visualize the efficacy

of SEL-212. We believe dual energy computed tomography imaging use could increase the market for SEL-212 by increasing the rate of diagnosis of chronic tophaceous gout.

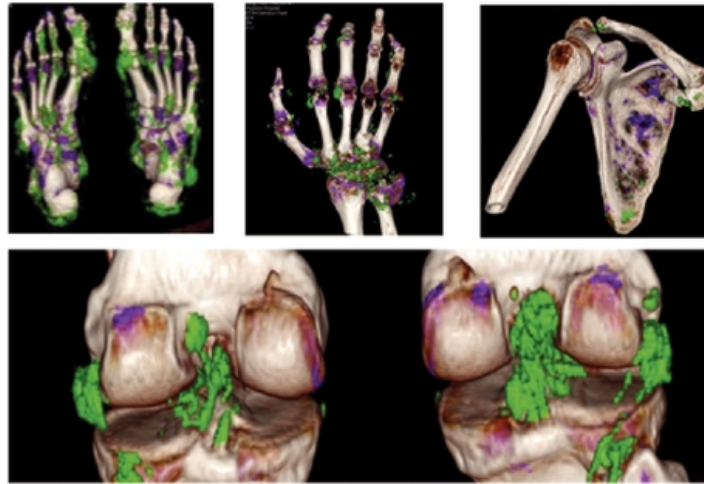


Figure 11. Tophi / Uric Acid Deposits (shown in green) Visualized Using Dual Energy Computed Tomography Imaging

SEL-212 components

Our SEL-212 consists of SVP-Rapamycin co-administered with pegsiticase. Our SVP-Rapamycin consists of nanoparticles composed of poly(D,L-lactide), or PLA, and poly(D,L-lactide)-block-poly(ethylene-glycol), or PLA-PEG, encapsulating rapamycin. Our pegsiticase consists of a uricase modified with poly(ethylene-glycol), or PEG. The components of SEL-212 are depicted in Figure 12 below.

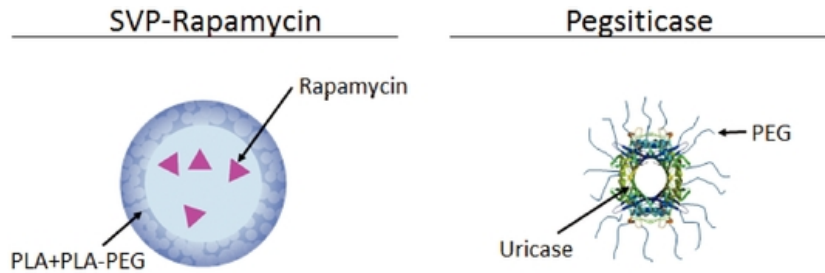


Figure 12. Components of SEL-212

Our pegsiticase is a pegylated version of the therapeutic enzyme uricase, which we have licensed from Shenyang Sunshine Pharmaceutical Co., Ltd., or 3SBio, exclusively for all markets, except Japan and Greater China, and exclusively for Japan only in combination with our SVP Platform technology. Uricase is an enzyme endogenous to all mammals, except for humans and certain primates, which converts uric acid to the more soluble metabolite, allantoin. There is a natural limit to the amount of uric acid that can be excreted by the kidneys, which decreases with age and can be reduced by some medications. By converting uric acid to allantoin, uricase provides an additional way for the body to reduce uric acid. Unlike other gout drugs, uricase is highly effective in lowering existing high uric acid levels within the first few hours of administration.

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SVP-Rapamycin is our biodegradable nanoparticle that encapsulates the tolerance-inducing immunomodulator rapamycin, also referred to as sirolimus. Rapamycin is the active ingredient of Rapamune, an immunosuppressant which has extensive prior use in humans and is currently FDA-approved for prophylaxis of organ rejection in kidney transplant patients aged 13 or older. PLA is part of the broader poly(lactic-co-glycolic acid), or PLGA, family of biodegradable polymers that have more than 30 years of commercial use and are formulation components in a number of approved products. Polyethylene glycol, or PEG, has been widely studied in clinical trials and is also a formulation component in many approved biologic products. In our preclinical studies, SVP-Rapamycin co-administered at the initiation of treatment with a biologic drug induced antigen-specific immune tolerance to the biologic drug, substantially reducing the formation of associated ADAs.

As depicted in Figure 13 below, SEL-212 is designed as a treatment course consisting of three doses of SVP-Rapamycin co-administered with pegsiticase followed by two doses of pegsiticase alone, with each dose administered every two to four weeks.

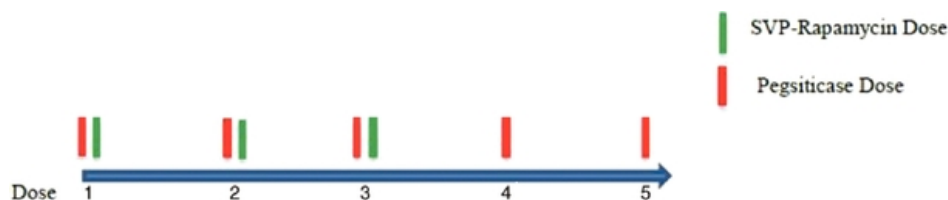


Figure 13. SEL-212 Treatment Course

Preclinical development

We have executed a comprehensive preclinical program of SEL-212 in uricase deficient mice and wild type mice, rats and nonhuman primates to evaluate efficacy, dose regimens and safety.

Proof-of-concept study in uricase-deficient mice

We conducted a pharmacology study in mice that were genetically deficient in endogenous uricase. The study evaluated the efficacy of a dose regimen consisting of three immunizations with SEL-212 followed by doses of pegsiticase alone in preventing the formation of ADAs to pegsiticase. The treatment period consisted of the first 14 days of the study. In the study, mice were separated into three treatment groups. As depicted in Figure 14 below, during the treatment period:

- the first group, referred to as the Untreated Group and indicated in black, received no treatment;
- the second group, referred to as the Pegsiticase Group and indicated in red, was treated with pegsiticase alone; and
- the third group, referred to as the SVP-Rapamycin + Pegsiticase Group and indicated in green, was treated with SVP-Rapamycin co-administered with pegsiticase.

The Pegsiticase Group and SVP-Rapamycin + Pegsiticase Group were treated on days zero, seven and 14 of the treatment period. Each group was then treated with pegsiticase alone on days 35 and 42 of the study, or the challenge period. Uricase-specific ADA levels were recorded to determine the formation of ADAs to pegsiticase. Uric acid levels were measured to determine effectiveness of SVP-Rapamycin co-administered with pegsiticase in lowering uric acid levels below 6 mg/dl, which is the treatment target for gout patients.

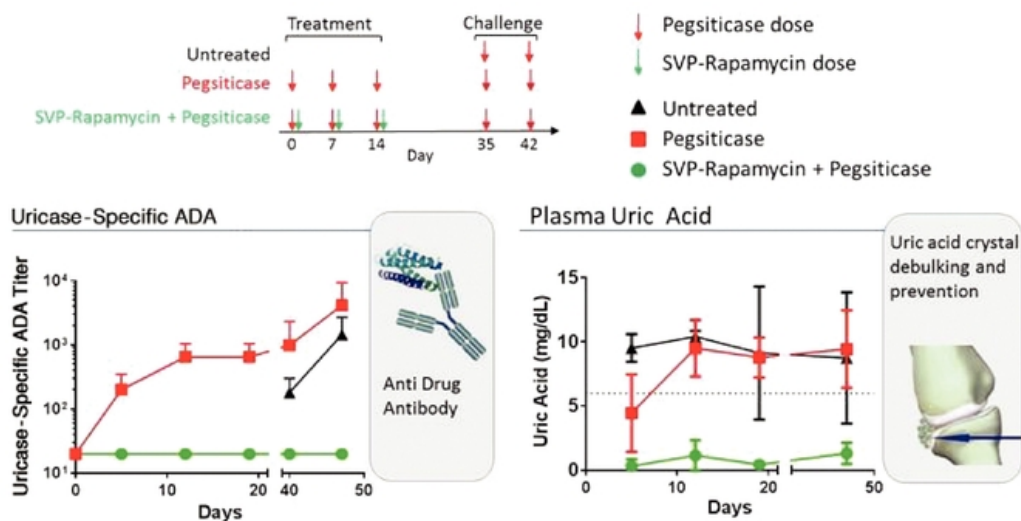


Figure 14. Preclinical Study: Proof-of-Concept in Uricase-Deficient Mice

Antibody formation. The Pegsiticase Group developed uricase-specific ADAs when exposed to pegsiticase during the treatment period. The Untreated Group also developed uricase-specific ADAs as soon as they were challenged with pegsiticase. Despite exposure to pegsiticase during both the treatment and challenge periods, the SVP-Rapamycin + Pegsiticase Group did not develop uricase-specific ADAs during either period.

Uric acid levels. After initial exposure to pegsiticase, the Untreated Group maintained high uric acid levels of approximately 10 mg/dl. The Pegsiticase Group recorded uric acid levels below 6 mg/dl after the first dose in the treatment period. However, during subsequent doses in the treatment period and challenge period, uric acid levels returned to levels well in excess of 6 mg/dl. In contrast, the SVP-Rapamycin + Pegsiticase Group maintained uric acid levels that were close to zero throughout the study.

Proof-of-concept study in nonhuman primates

We also conducted a preclinical study to evaluate the ability of SVP-Rapamycin to mitigate the formation of uricase-specific ADAs in nonhuman primates. As depicted in Figure 15 below, during the study we either:

- administered pegsiticase alone, referred to as the Empty Nanoparticle Group and indicated in blue; or
- co-administered pegsiticase with one of two dose levels of SVP-Rapamycin, referred to as the SVP-Rapamycin 0.1X and SVP-Rapamycin 1X Groups and indicated in purple and green, respectively. The SVP-Rapamycin 0.1X Group received a dose level of SVP-Rapamycin of 0.3 mg/kg and the SVP-Rapamycin 1X Group received a dose level of SVP-Rapamycin of 3 mg/kg.

The Empty Nanoparticle Group received three monthly doses of pegsiticase and each of the SVP-Rapamycin 0.1X Group and SVP-Rapamycin 1X Group received three monthly doses of pegsiticase co-administered with SVP-Rapamycin. All groups then received two monthly doses of

pegsiticase alone. The SVP-Rapamycin 0.1X Group received one-tenth of the dose administered in the SVP-Rapamycin 1X Group.

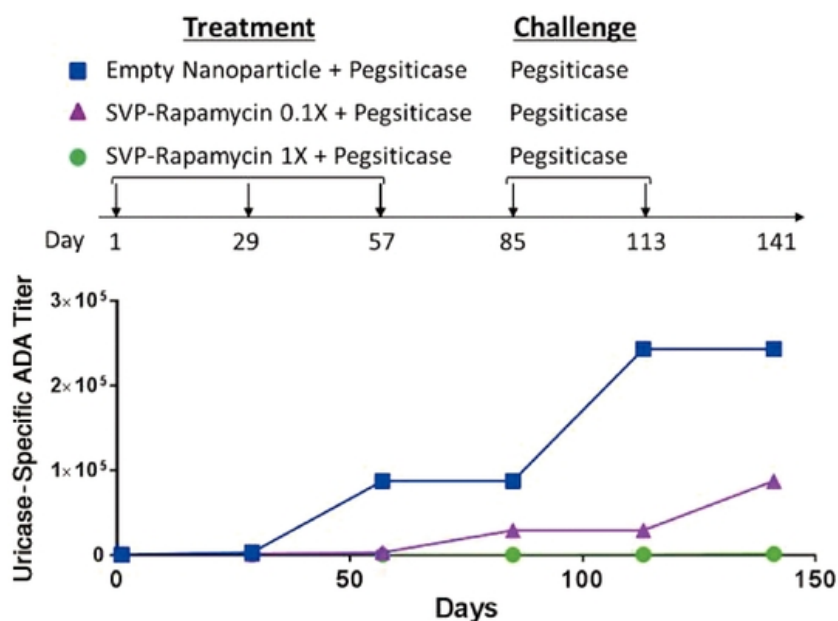


Figure 15. Preclinical Study: Proof-of-Concept in Nonhuman Primates

Antibody formation. We observed that the Empty Nanoparticle Group produced high levels of uricase-specific ADAs by the end of the study. The SVP-Rapamycin 0.1X Group and SVP-Rapamycin 1X Group were able to reduce the levels of uricase-specific ADAs significantly compared to the Empty Nanoparticle Group and, in the case of the SVP-Rapamycin 1X Group, inhibited the formation of antibodies. Our observations in this study confirmed in non-human primates the mitigation of uricase-specific ADAs we observed in mice.

Uric acid levels. As expected, we could not determine the effect that pegsiticase alone or pegsiticase co-administered with SVP-Rapamycin had on uric acid levels in nonhuman primates due to the activity of naturally occurring uricase in these animals.

Based on these preclinical studies, as well as toxicology studies conducted to conform to regulatory guidelines, referred to as current good laboratory practice, or GLP, we believe that SEL-212 demonstrated sufficient efficacy and safety in the preclinical animal models to justify movement into clinical development, and the FDA indicated that our Phase 1b clinical trial for SEL-212 was safe to proceed.

Clinical development

For chronic refractory gout, we are executing a clinical development program in which we expect to conduct five clinical studies in a total of approximately 400 subjects with gout or elevated levels of uric acid. We initiated our clinical program in the second quarter of 2015 with a Phase 1a trial of pegsiticase in subjects with elevated serum uric acid levels. We completed the patient treatment portion

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of our Phase 1a trial was completed in November 2015, initiated a Phase 1b trial in December 2015 and expect final data from both Phase 1 clinical trials in the second half of 2016. We plan to follow this Phase 1b clinical trial with an open label multi-dose Phase 2 clinical trial of SEL-212 in patients with symptomatic gout and elevated uric acid levels. After an end-of-Phase 2 meeting with the FDA, we expect that we will be required to conduct two Phase 3 clinical trials in patients with refractory gout. We plan to leverage our experience in chronic refractory gout for separate but similar clinical trials for the indication of chronic tophaceous gout.

Phase 1 and Phase 2 clinical trials

SEL-212 is currently being evaluated in a comprehensive Phase 1/2 clinical program that includes a Phase 1a and Phase 1b clinical trial in subjects with high uric acid levels as well as a Phase 2 clinical trial in patients with symptomatic gout and high uric acid levels. Each Phase 1 clinical trial was designed with the primary objective to evaluate the safety and tolerability of SEL-212 and its individual components. Additional objectives of the Phase 1 clinical trials include identifying a pegsiticase dose that is capable of lowering serum uric acid levels, evaluating the immunogenicity of pegsiticase after a single dose and demonstrating that SVP-Rapamycin co-administered with pegsiticase reduces uric acid levels and mitigates the formation of uricase-specific ADAs. The Phase 2 clinical trial will evaluate the effect of multiple doses over an extended period of time on serum uric acid and the formation of uricase-specific ADAs in approximately 36 patients with symptomatic gout and elevated serum uric acid levels. We expect to receive final data from both Phase 1 clinical trials in the second half of 2016. We expect to initiate the Phase 2 clinical trial in the second half of 2016 and receive data in the first half of 2017.

Phase 1a clinical trial

The Phase 1a clinical trial for SEL-212 was an ascending dose trial of pegsiticase alone in 22 subjects with elevated serum uric acid levels greater than 6 mg/dl who were separated into five cohorts. At the outset of the trial, each cohort received a single intravenous infusion of pegsiticase at ascending dose levels of 0.1 mg/kg for Cohort #1, 0.2 mg/kg for Cohort #2, 0.4 mg/kg for Cohort #3, 0.8 mg/kg for Cohort #4 and 1.2 mg/kg for Cohort #5. We monitored the subjects during a 30-day period post-infusion. We commenced enrollment of the clinical trial in the second quarter of 2015 and completed the treatment portion of the trial in November 2015. We observed that pegsiticase demonstrated no serious adverse events and was well tolerated at the five dose levels tested. Additionally, we observed that pegsiticase rapidly reduced and sustained average serum uric acid levels below 6 mg/dl for each cohort for 14 to 30 days, depending on the dose level. Consistent with our preclinical studies in animals, pegsiticase induced uricase-specific ADAs in all subjects with varying levels in this Phase 1a trial.

Figure 16 below depicts average serum uric acid levels of the Phase 1a clinical trial's five cohorts tested at different measurement intervals during the course of the 30-day period following the single intravenous infusion of pegsiticase at the outset of the trial.

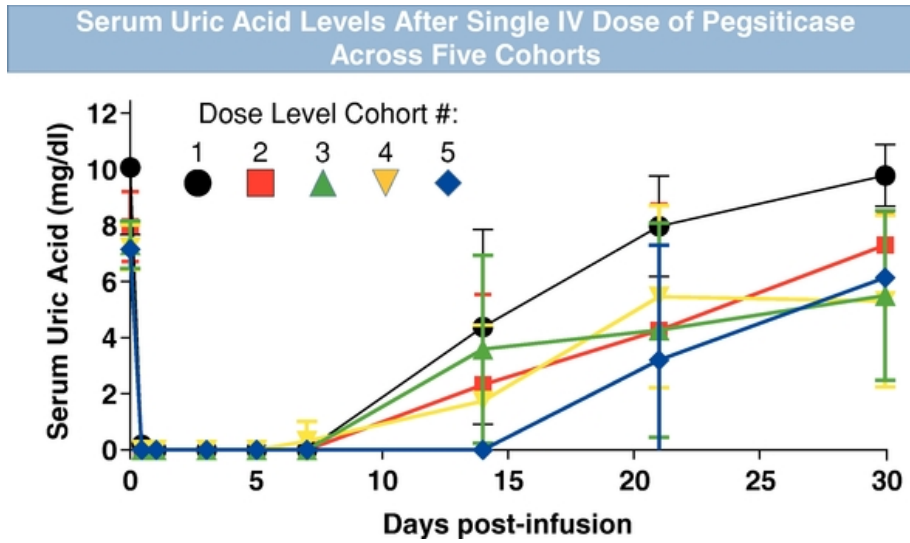


Figure 16. Phase 1a Clinical Trial: Serum Uric Acid Levels Across Five Cohorts

Figure 17 below indicates the serum uric acid and uricase-specific ADA levels for each subject in Cohort #3 of the Phase 1a clinical trial. The serum uric acid levels were measured at baseline and days seven, 14, 21 and 30 and uricase-specific ADA levels at baseline and days seven, 14 and 30 following a single intravenous injection of pegsiticase. We did not measure uricase-specific ADA levels at day 21 in the Phase 1a clinical trial. One subject in this cohort, subject number two, developed a relatively low level uricase-specific ADA titer of 40 and maintained uric acid levels below 0.5 mg/dl through the thirtieth day after dosing. By contrast, the remaining four subjects in the cohort developed levels of uricase-specific ADAs greater than 1,000 titer and uric acid levels above 5 mg/dl by the thirtieth day after dosing. Based on the results from our Phase 1a clinical trial, we observed that pegsiticase at a

tolerated dose is capable of achieving and maintaining a reduction of serum uric acid below the target of 6 mg/dl for a 30-day period in the absence of inhibitory uricase-specific ADAs.

Uricase - Specific ADA Titer and Serum Uric Acid Levels from Cohort #3 of Phase 1a Clinical Trial (0.4 mg/kg)										
Subject number	Baseline		Day 7		Day 14		Day 21		Day 30	
	Uric acid (mg/dl)	ADA (Titer)	Uric acid (mg/dl)	ADA (Titer)	Uric acid (mg/dl)	ADA (Titer)	Uric acid (mg/dl)	ADA (Titer)	Uric acid (mg/dl)	ADA (Titer)
1	7.4	Neg	<0.1	Neg	5	9720	6	N.A.	6.9	3240
2	7.5	Neg	<0.1	40	<0.1	40	<0.1	N.A.	0.4	40
3	7.3	120	<0.1	120	6.9	9720	7.6	N.A.	7.6	3240
4	7.6	Neg	<0.1	Neg	6.1	3240	7.5	N.A.	7.6	1080
5	4.9	Neg	<0.1	Neg	<0.1	1080	0.3	N.A.	5.1	1080

(Neg = Negative; N.A. = Sample not available)

Figure 17. Phase 1a Clinical Trial: Serum Uric Acid and Uricase-Specific ADA Levels of the Third Cohort

Based on our analysis of the Phase 1a clinical trial data, we selected the pegsiticase dose of 0.4 mg/kg from Cohort #3 of the Phase 1a clinical trial for further study in the Phase 1b clinical trial.

Phase 1b clinical trial

In December 2015, we initiated our Phase 1b clinical trial. We anticipate that this clinical trial will have approximately 53 subjects with serum uric acid levels greater than 6 mg/dl separated into nine cohorts. We plan to co-administer a single intravenous infusion of SVP-Rapamycin at ascending dose levels with a fixed dose of pegsiticase of 0.4 mg/kg for four of the cohorts, which will be Cohort #2, Cohort #4, Cohort #6 and Cohort #8 of the Phase 1b clinical trial, or collectively the SEL-212 Cohorts. In addition to a fixed 0.4 mg/kg dose of pegsiticase, subjects in the SEL-212 Cohorts will receive SVP-Rapamycin in the following dose levels: Cohort #2 (0.03 mg/kg), Cohort #4 (0.1 mg/kg), Cohort #6 (0.3 mg/kg) and Cohort #8 (0.5 mg/kg). We also plan to administer to Cohort #9 a fixed amount of pegsiticase alone at a dose level of 0.4 mg/kg, which we refer to as the Pegsiticase Cohort. Additionally, we intend to administer a single intravenous infusion of SVP-Rapamycin alone at the following ascending dose levels to the remaining cohorts, which will be Cohort #1 (0.03 mg/kg), Cohort #3 (0.1 mg/kg), Cohort #5 (0.3 mg/kg) and Cohort #7 (0.5 mg/kg) of the Phase 1b clinical trial, or collectively the SVP-Rapamycin Cohorts. All subjects will be followed for 30 days after their initial dose. The primary objective of the Phase 1b clinical trial is to evaluate the safety and tolerability of SVP-Rapamycin alone and in combination with a fixed dose of pegsiticase. A secondary clinical objective is to evaluate the ability of SVP-Rapamycin co-administered with pegsiticase to reduce serum uric acid levels and mitigate the formation of uricase-specific ADAs when compared to administration of pegsiticase alone. We expect that complete data from the Phase 1b clinical trial will be available in the second half of 2016.

Although the Phase 1b clinical trial is currently ongoing, as of June 3, 2016, we had completed the dosing of:

- all four SVP-Rapamycin Cohorts;
- the three SEL-212 Cohorts, Cohort #2, Cohort #4 and Cohort #6, receiving the lowest three (out of the four projected) SVP-Rapamycin ascending dose levels; and
- the Pegsiticase Cohort, Cohort #9.

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We have received 30-day observation period data for Cohort #1 (SVP-Rapamycin Cohort), Cohort #2 (SEL-212 Cohort), Cohort #3 (SVP-Rapamycin Cohort), Cohort #4 (SEL-212 Cohort), Cohort #5 (SVP-Rapamycin Cohort), Cohort #6 (SEL-212 Cohort) and Cohort #9 (Pegsiticase Cohort) of the Phase 1b clinical trial.

Figure 18 below indicates the serum uric acid levels of Cohort #3 from the Phase 1a clinical trial, in which subjects received a fixed amount of pegsiticase alone (at the same 0.4 mg/kg pegsiticase dose level as Cohort #9, the Pegsiticase Cohort, of the Phase 1b clinical trial). Figure 18 below also indicates the serum uric acid levels of Cohort #9 (Pegsiticase Cohort), Cohort #1 (SVP-Rapamycin Cohort), Cohort #2 (SEL-212 Cohort), Cohort #3 (SVP-Rapamycin Cohort), Cohort #4 (SEL-212 Cohort), Cohort #5 (SVP-Rapamycin Cohort) and Cohort #6 (SEL-212 Cohort) from the Phase 1b clinical trial. In Figure 18 below, observational data is presented for all cohorts in which subjects have reached the end of the 30-day observation period. In these subjects, serum uric acid levels were measured at baseline and days seven, 14, 21 and 30. As expected, SVP-Rapamycin alone had no relevant effect on reducing serum uric acid levels across the SVP-Rapamycin Cohorts, as such levels remained relatively constant during the 30-day period. In Cohort #2 from the Phase 1b clinical trial, which received the lowest dose of SVP-Rapamycin co-administered with pegsiticase, we observed that four out of five subjects tested maintained serum uric acid levels below 6 mg/dl through day 21 of the trial. We also observed that four out of five subjects in Cohort #4 from the Phase 1b clinical trial, which received the second lowest dose of SVP-Rapamycin co-administered with pegsiticase, maintained levels of serum uric acid of less than 0.1 mg/dl through day 30. For Cohort #6 (SEL-212 Cohort), we observed that each of the five subjects maintained levels of serum uric acid of less than 0.1 mg/dl through day 30. By comparison, for Cohort #9 (Pegsiticase Cohort), four of the five subjects returned to baseline serum uric acid levels by day 30.

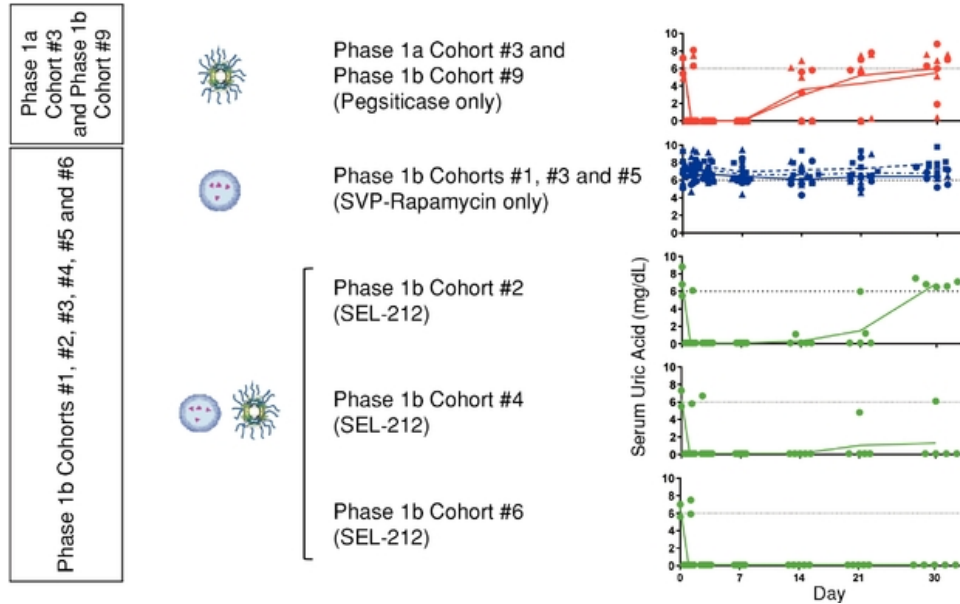


Figure 18. Phase 1b Clinical Trial: Uric Acid Levels Across Seven Phase 1b Cohorts (and Cohort #3 from the Phase 1a Clinical Trial)

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Figure 19 below shows the serum uric acid levels and uricase-specific ADA levels for each subject in Cohort #3 of the Phase 1a clinical trial and Cohort #9 (Pegsiticase Cohort) of the Phase 1b clinical trial for comparison to the serum uric acid levels and uricase-specific ADA levels for each subject in Cohort # 4 (SEL-212 Cohort) and Cohort #6 (SEL-212 Cohort) in the Phase 1b clinical trial. Cohort #3 from the Phase 1a clinical trial is depicted in Figure 19 along with Cohort #9 from the Phase 1b clinical trial for purposes of comparison against Cohort #4 and Cohort #6 from the Phase 1b clinical trial because the subjects in these cohorts received the same fixed dose of pegsiticase. In addition, Cohort #4 from the Phase 1b clinical trial is depicted below in Figure 19 because the subjects in Cohort #4 from the Phase 1b clinical trial received a higher dose of SVP-Rapamycin than did the subjects in Cohort #2 in the Phase 1b clinical trial. We have also included Cohort #6 from the Phase 1b clinical trial because these subjects received the highest dose of SVP-Rapamycin tested to date—higher than both Cohorts #2 and #4.

As depicted in Figure 19 below, in Cohort #3 from the Phase 1a clinical trial and Cohort #9 from the Phase 1b clinical trial, we observed uricase-specific ADA formation at day 14 resulting in a return to baseline levels of serum uric acid. In comparison, for Cohort #4 from the Phase 1b clinical trial, we observed minimal uricase-specific ADA formation in four of the five subjects tested with corresponding maintenance of control of serum uric acid levels through day 30. In Cohort #6 of the Phase 1b clinical trial, we observed minimal to no uricase-specific ADA formation in each of the five subjects, with corresponding maintenance of control of serum uric acid levels through day 30. In the Phase 1a clinical trial, we did not measure uricase-specific ADA levels at day 21. However, in the course of conducting the Phase 1a clinical trial, we learned that it would be useful to measure uricase-specific ADA levels at day 21 to more fully understand any variations in such levels between day 14 and day 30. As a result, for the Phase 1b clinical trial, we monitor uricase-specific ADA levels at day 21.

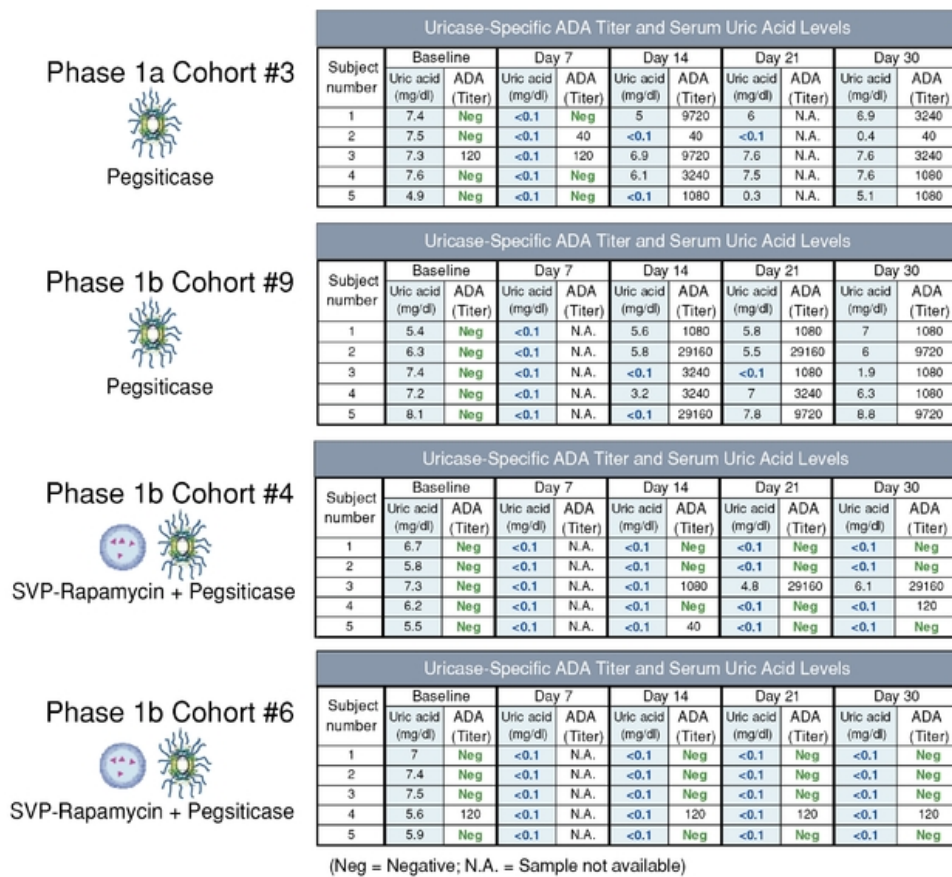


Figure 19. Comparison of Phase 1a Cohort #3, Phase 1b Cohort #9, Phase 1b Cohort #4 and Phase 1b Cohort #6: Uric Acid and Uricase-Specific ADA Levels

Figure 20 below presents a non-head-to-head comparison of the efficacy of SEL-212 in Cohort #6 of the Phase 1b clinical trial with data from two replicate, randomized, double-blind, placebo-controlled clinical trials of Krystexxa as reported in the Journal of the American Medical Association in 2011. These two Krystexxa clinical trials included 85 patients who received biweekly doses of Krystexxa, 84 patients who received monthly doses of Krystexxa and 43 patients who received a placebo. Of the Krystexxa-treated patients that were considered responders, as defined by the maintenance of uric acid levels below 6 mg/dl for 80% of the time at months three and six, the mean uric acid levels in patients on the biweekly dose regimen were more meaningfully and consistently improved than patients on the monthly dose regimen. Krystexxa has been approved for the treatment of refractory gout on a biweekly dose regimen whereas the monthly dose regimen of Krystexxa has not been approved for marketing. The graph on the left in Figure 20 below depicts the data for the four-week period after the first dose of Krystexxa from the cohorts of subjects in the Krystexxa clinical trials who received monthly doses.

The placebo control subjects, indicated in open circles in Figure 20 below, had uric acid levels above 6 mg/dl for the entire four weeks. The Krystexxa-treated subjects that went on to become responders are indicated in black circles. The Krystexxa-treated subjects that went on to become non-responders, as defined by the inability to maintain uric acid levels below 6 mg/dl for 80% of the time at months three and six, are indicated in black triangles. Only 35% of Krystexxa-treated subjects in the monthly dosing cohorts were classified as responders. Of the patients that received monthly doses, it is notable that, even at four weeks, the mean uric acid levels were above 6 mg/dl in the non-responders, representing 65% of subjects, and were above 4 mg/dl in the responders. While not depicted in Figure 20 below, 89% of all Krystexxa-treated subjects developed ADAs. In comparison, the graph on the right in Figure 20 below depicts data from Cohort #5 of the Phase 1b clinical trial, which received a single dose of SVP-Rapamycin alone, and Cohort #6 of the Phase 1b clinical trial, which received a single dose of SEL-212. All five subjects in Cohort #6 of the Phase 1b clinical trial, treated with SEL-212 and indicated in green in Figure 20 below, maintained levels of serum uric acid of less than 0.1 mg/dl through day 30. Subjects in Cohort #5 of the Phase 1b clinical trial, treated with SVP-Rapamycin alone and indicated in blue, experienced no significant reduction in uric acid levels, as such levels remained relatively constant over the 30-day period.

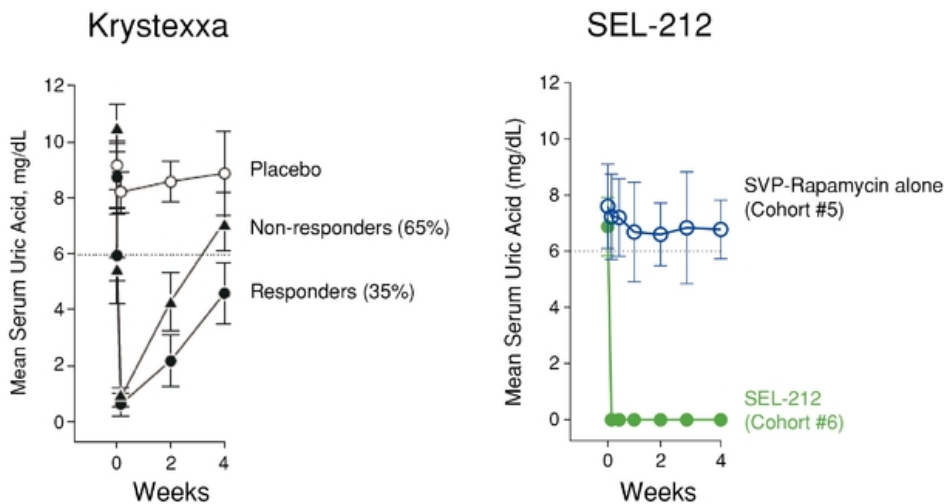


Figure 20. Comparison of the Efficacy of Krystexxa and SEL-212 After a Single Dose

While we believe the above comparison is useful in evaluating the results of Cohort #6 of the Phase 1b clinical trial, our Phase 1b clinical trial and the Krystexxa clinical trials were separate trials conducted by different investigators at different sites. In addition, there were substantial differences, including, for example, that the Krystexxa clinical trials were double-blind trials involving a substantial number of patients with refractory gout while our Phase 1b clinical trial evaluated SEL-212 in an unblinded manner in a small number of subjects with elevated uric acid levels. Moreover, we could only compare the efficacy of SEL-212 with the four-week period following the first injection of Krystexxa as SEL-212 has not yet been evaluated in a multi-dose clinical trial. In this regard, we have not conducted a head-to-head comparison of SEL-212 and Krystexxa in a clinical trial. Results of a head-to-head comparison may differ significantly from those set forth in Figure 20 above. In addition, because our Phase 1b clinical trial and the Krystexxa clinical trials were separate trials and because Cohort #6 of our Phase 1b clinical trial involved only five subjects, differences between the results of our Phase 1b

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clinical trial and the two Krystexxa clinical trials may not be statistically or clinically meaningful. For these reasons, investors should not place undue weight on the comparative information set forth above, including in Figure 20.

We collected additional serum uric acid and uricase-specific ADA data after day 30 for three of the subjects in Cohort #4 (SEL-212 Cohort) that had no or very low serum uric acid and uricase-specific ADA levels at day 30. We collected data on day 37 for all three of these subjects and again on day 42 or day 44 for two of the three subjects. Each of these three subjects had no or very low uricase-specific ADA levels on day 37, day 42 or day 44, as applicable. Serum uric acid levels remained below baseline on day 37 in all three subjects. With respect to the two subjects for which day 42 or day 44 data was available, serum uric acid levels approached or exceeded baseline by the last time point measured. We anticipated these results as we did not expect a single dose of the enzyme to be capable of clearing all of the uric acid deposits in the body. Based on our observations from the Phase 1b clinical trial data that SEL-212 was capable of controlling uric acid levels for at least 30 days in all of the subjects in Cohort #6, we believe SEL-212 has the potential to maintain low uric acid levels with monthly dosing, which we plan to test in the Phase 2 clinical trial.

As of June 3, 2016, on a combined basis, we had dosed a total of 70 subjects with either SEL-212 (SVP-Rapamycin and pegsiticase), SVP-Rapamycin alone or pegsiticase alone in connection with the Phase 1a and Phase 1b clinical trials. We have generally observed that SEL-212 and its components, SVP-Rapamycin and pegsiticase, have been well tolerated. As of June 16, 2016, there have been a total of three serious adverse events, or SAEs, in both Phase 1 clinical trials. One SAE occurred in a subject from Cohort #9 (Pegsiticase Cohort) of the Phase 1b clinical trial, a 62 year-old male, who received a dose level of pegsiticase alone of 0.4 mg/kg. This subject developed atrial fibrillation 13 days after administration of pegsiticase. The subject has been treated. The medical records from the principal investigator indicate that this subject has recovered. The principal investigator has deemed this SAE to not have been related to the study drug, pegsiticase. The second SAE occurred in a 59 year-old male from Cohort #4 (SEL-212 Cohort) of the Phase 1b clinical trial who developed a pruritic rash on his lower extremities and joint pain approximately 12 days after being dosed with SEL-212, consisting of a dose level of SVP-Rapamycin of 0.1 mg/kg and a dose level of pegsiticase of 0.4 mg/kg. This subject was treated with steroids, analgesics, anti-nausea medications and topical antihistamine cream. As a result of such treatment, the medical records from the principal investigator indicate that the rash and joint pain experienced by the subject have been resolved. This subject was the only subject in Cohort #4 (SEL-212 Cohort) that developed significant uricase-specific ADAs and whose serum uric acid levels returned to baseline by day 30. This adverse event was classified as an SAE because the subject was admitted to the emergency room instead of going directly to the investigational site for treatment. The principal investigator classified this second SAE as having been possibly related to the study drug, SEL-212. A third observation was classified by the principal investigator on June 15, 2016 as an SAE after a 59 year-old male from Cohort #7 (SVP-Rapamycin Cohort) of the Phase 1b clinical trial developed stomatitis approximately seven days after being dosed with 0.5 mg/kg of SVP-Rapamycin, the highest dose of SVP-Rapamycin in the SVP-Rapamycin Cohorts of the Phase 1b clinical trial, and experienced 4.3 kg of weight loss. Stomatitis is a form of mouth sores and inflammation of the mouth and lips that often limits food intake and, according to the label for rapamycin, is a common adverse reaction to rapamycin itself. This subject was treated with oral over-the-counter and topical antihistamines followed by a steroid gel. As of June 16, 2016, the principal investigator indicated that the subject's stomatitis was improving. The principal investigator classified this third SAE as having been possibly related to the study drug, SVP-Rapamycin.

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Phase 2 clinical trial

We are planning an open-label Phase 2 clinical trial in approximately 36 subjects with symptomatic gout and elevated serum uric acid levels. We plan to divide patients into three dose groups. Two of these groups will receive SEL-212. The other group will receive pegsiticase alone. The primary endpoints will be the safety and tolerability of multiple doses of SEL-212 and pegsiticase alone in addition to a reduction of uric acid levels from baseline. We expect that secondary endpoints for this trial will include a reduction in levels of uricase-specific ADAs and pegsiticase-specific ADAs. Additional, exploratory endpoints will include number of flares, change in tophi volume as measured by dual energy computed tomography imaging and quality of life measures.

In addition to the foregoing clinical trials, we also plan to initiate development of SEL-212 for chronic tophaceous gout.

Our SVP-Rapamycin programs for immune tolerance in gene therapy

Overview

We believe gene therapy has the potential to fundamentally change the treatment of genetic diseases in the form of replacing, augmenting or editing a gene. Gene therapy modifies the genetic content of the patient's own cells by placing corrective genetic material, or a transgene, within the nuclei of a patient's cells. The transferred genetic material enables the affected cells to become producers of a protein that is either missing or deficient in the patient. Engineered viruses that are unable to replicate themselves serve as carriers, or vectors, for the delivery of transgenes to various tissues and organs in the body. Adeno-associated viruses, or AAV, are the preferred vectors for *in vivo* gene therapy because they cannot reproduce on their own, do not cause pathogenic infections and can be produced using manufacturing practices that conform to cGMP.

Although gene therapy has made significant progress over the last several years, it faces certain limitations due to undesired immunogenicity to either the AAV vector or the encoded transgene. This undesired immunogenicity frequently exists prior to the gene therapy or is induced with the first dose. Once an antibody response to the AAV vector exists, it is likely to interfere with the efficacy of subsequent administration of the AAV vector. For naturally occurring types of AAV such as AAV1 to AAV10, patients can have prior exposure to the naturally occurring virus, which leads to the presence of pre-existing antibodies, or pre-existing immunity. The presence of pre-existing immunity is an exclusion criterion for most clinical gene therapy studies conducted with naturally occurring AAV vectors. Up to 50% of potential gene therapy patients can have pre-existing immunity, depending on the treated patient population and the AAV strain. Gene vector-specific ADAs frequently occur after the first dose and have been found to prevent the AAV vector from reaching its target cell. In addition, cellular immune responses have been found to destroy transfected cells. It is unknown exactly how long these neutralizing ADAs prevent redosing of gene therapy. However, it has been observed in studies with animals and humans that high titer AAV-specific ADAs develop and persist for more than 10 years, preventing vector readministration. Because of the induction of lasting antibodies against AAV, we believe gene therapy companies have focused on the single localized dose in diseases of the eye and central nervous system for which immunogenicity is perceived to be less of an issue. We believe that many gene therapy applications may require multiple doses, especially therapies designed to treat diseases by intravenous administration. Some of these rare genetic deficiencies are best treated when patients are infants or small children in order to prevent developmental defects. However, pediatric patients may have a higher need for repeat dosing due to higher cell turnover as the subject grows. Accordingly, we believe that a solution that enables repeat dosing for gene therapies would significantly expand the number of diseases that could be treated with these therapies.

Our solution for gene therapy

We believe SVP-Rapamycin co-administered with gene therapies has the potential to mitigate undesired immune responses and enable desired efficacy in subsequent administration of gene therapy by intravenous administration for diseases and patients where a single dose of gene therapy is unlikely to be sufficient.

In collaboration with Genethon, a not-for-profit company focusing on gene therapies, we conducted a preclinical study in mice in which we observed the ability of SVP-Rapamycin to mitigate the formation of ADAs to AAV-based gene therapy, thereby enabling repeat dosing of the AAV vector in these mice. At the outset of the study, all mice received an intravenous injection of AAV8, a commonly used AAV strain to target expression in the liver, encoding the luciferase gene, referred to as AAV8-Luciferase. On day 21 of the study, mice received a second injection of AAV8, this time encoding human coagulation Factor IX, referred to as AAV8-Factor IX. Mutations in the Factor IX gene can cause hemophilia B, a defect in blood clotting. As depicted in Figure 21 below, in addition to an injection of AAV8 encoding either the luciferase gene or Factor IX, the mice also received either:

- empty nanoparticles, with such mice referred to as the Empty Nanoparticle Group and indicated in blue; or
- SVP-Rapamycin, with such mice referred to as the SVP-Rapamycin Group and indicated in green.

We assessed AAV8-specific ADA levels to determine the formation of ADAs to the AAV8 vector. We also determined the levels of human Factor IX protein in mouse serum to determine the relative success in conveyance and expression of the Factor IX gene. We observed from our preclinical data that the SVP-Rapamycin treatment mitigated the formation of AAV8-specific ADAs in the SVP-Rapamycin Group, thereby enabling higher levels of Factor IX expression in the SVP-Rapamycin Group following the second injection on day 21 as compared to the Empty Nanoparticle Group. We believe these results indicate that the SVP-Rapamycin treatment may have the potential to mitigate undesired immune responses and enable repeat intravenous administration of gene therapies such as those utilizing the AAV8 vector.

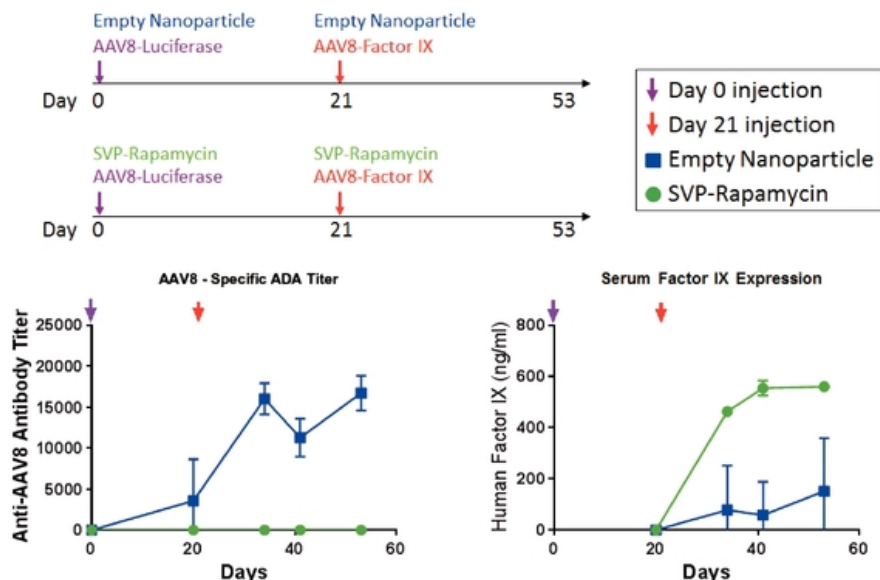


Figure 21. Preclinical Study: SVP-Rapamycin Co-Administered with AAV-Based Gene Therapy in Mice

In addition to eliciting antibody responses against the viral capsid (a protein shell that encloses the virus's genetic material), gene therapy can also induce cellular immunity mediated by cytolytic T cells, or CD8 T cells. CD8 T cells can reduce the effectiveness of gene therapy by specifically killing those cells that have taken up the AAV capsid and/or express the encoded transgene protein product. In a preclinical study, we assessed the CD8 T cell levels in the liver following the treatment of mice with an AAV8 vector alone and in combination with SVP-Rapamycin on days 0 and 21 of the study. Naïve mice that were not treated with either an AAV8 vector or SVP-Rapamycin were used as a control. On day 53, we then quantified the level of CD8 T cells in the liver by using a process known as reverse transcriptase-polymerase chain reaction, or RT-PCR, to amplify messenger ribonucleic acid, or mRNA, encoding the CD8 gene. As depicted in Figure 22 below, in this study, we observed that livers isolated from mice treated with the AAV8 vector alone showed a substantial increase in CD8 T cells compared to the naïve mice, which received neither an AAV8 vector nor SVP-Rapamycin. Based on our observations, we believe that the co-administration of SVP-Rapamycin with the AAV vector inhibited this increase in CD8 T cells.

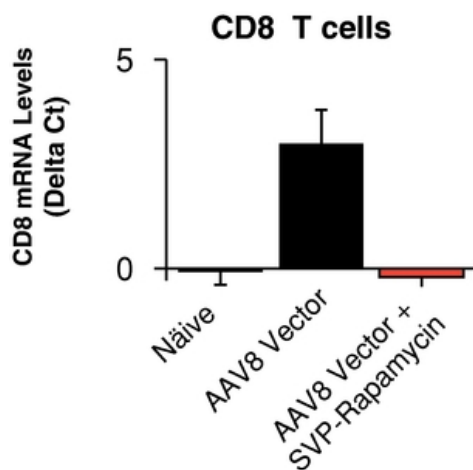


Figure 22. Preclinical Study: CD8 T Cell Levels in the Livers of Mice Treated with SVP-Rapamycin Co-Administered with AAV-Based Gene Therapy (as measured by CD8 mRNA using RT-PCR)

We also evaluated the ability of SVP-Rapamycin to mitigate the formation of ADAs to AAV capsids in nonhuman primates in a preclinical study. As depicted in Figure 23b below, nonhuman primates were screened on different dates for the presence of AAV-specific ADAs. On a later date, we drew blood from the nonhuman primates to evaluate the levels of AAV-specific ADAs again. This date is depicted in Figure 23b below as day -12 as it occurred 12 days prior to day zero of the study when the nonhuman primates received an intravenous injection of AAV8. As depicted in Figure 23a below, on day zero of the study, in addition to receiving an injection of AAV8, one nonhuman primate received empty nanoparticles, referred to as the Empty Nanoparticles Subject and indicated in purple, and two nonhuman primates received SVP-Rapamycin, referred to as SVP-Rapamycin Subject No. 1 and SVP-Rapamycin Subject No. 2 and indicated in orange and red, respectively. As depicted in Figure 23b below, on days three, 15 and 45 of the study, we again drew blood from the nonhuman primates and tested it for the presence of AAV8-specific ADAs. As depicted in Figure 23a below, on day 30 of the study, we administered to all nonhuman primates an injection of AAV-Human Factor IX together with an injection of empty nanoparticles for the Empty Nanoparticles Subject or an injection of SVP-Rapamycin for SVP-Rapamycin Subject No. 1 and SVP-Rapamycin Subject No. 2. As depicted in Figure 23c below, on day 45 of the study we tested the nonhuman primates' serum for levels of Human-Factor IX.

We assessed AAV8-specific ADA levels to determine the formation of ADAs in nonhuman primates to the AAV8 vector. We also determined the levels of human Factor IX protein in nonhuman primate serum to determine the relative success in conveyance and expression of the Factor IX gene. We observed from our preclinical data that the SVP-Rapamycin treatment mitigated the formation of AAV8-specific ADAs in SVP-Rapamycin Subject No. 1 and SVP-Rapamycin Subject No. 2, thereby enabling higher levels of Factor IX expression in the SVP-Rapamycin Subjects following the second injection on day 30 as compared to the Empty Nanoparticles Subject. We believe these results further indicate that the SVP-Rapamycin treatment may have the potential to mitigate undesired immune responses and enable repeat intravenous administration of gene therapies such as those utilizing the AAV8 vector.



Figure 23a

AAV8-Specific Neutralizing ADA Titer

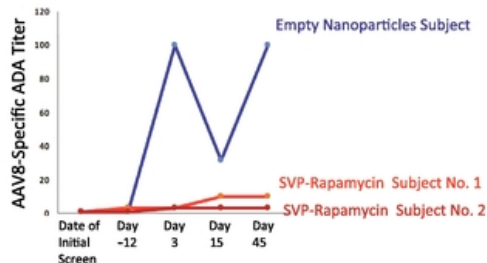


Figure 23b

Serum Factor IX Expression (Day 45)

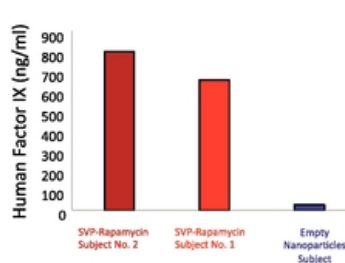


Figure 23c

Figure 23. Preclinical Study: SVP-Rapamycin Co-Administered with AAV-Based Gene Therapy in Nonhuman Primates

We believe SVP technology can be applied to induce antigen-specific immune tolerance for gene therapy involving gene augmentation, replacement or editing. Gene therapies often use a viral vector, such as an AAV vector, to place corrective genetic material into cells to treat genetic diseases. One of the key hurdles for the gene therapy field is to overcome immunogenicity against the viral vector, which can manifest itself in three ways. First, pre-existing ADAs that were induced following a natural AAV infection can neutralize the viral vector and block gene transfer. Up to 50% of patients are ineligible for gene therapy due to the presence of pre-existing ADAs. Second, ADAs form in response to a first administration of a gene therapy vector and prevent effective subsequent doses of gene therapy. Subsequent doses are particularly necessary for pediatric indications due to cellular turnover in young patients because they undergo renewal, which is the case in many pediatric indications. The ability to readminister gene therapies is also important for diseases where the goal is to transfer a high number of cells. Moreover, the third way in which immunogenicity can manifest itself against the viral vector is that the cellular immune system can respond to the transduced cells, which can reduce efficacy and pose safety concerns.

We have in-licensed the Anc80 vector from MEE. In preclinical studies, Anc80 has been observed to be a potent gene therapy vector that has demonstrated the capability of yielding superior gene expression levels in the liver compared to vectors based on naturally occurring AAV that are currently evaluated in clinical trials. As a synthetic vector, we believe Anc80 has limited cross-reactivity to naturally-occurring AAVs and therefore has the potential to treat patients with pre-existing AAV-specific ADAs. By combining SVP-Rapamycin and Anc80, we intend to develop highly differentiated gene therapies to address all three of the immunogenicity issues associated with the use of viral vectors.

In collaboration with the clinical and gene therapy laboratory at the NIH and MEE, we plan to develop a product candidate utilizing the Anc80 vector for the treatment of an ARM disorder resulting from an inborn error of metabolism. This ARM disorder can cause severe developmental defects and premature death as a result of an accumulation of toxic metabolites. Under our license agreement with

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MEE, we also have the option to develop gene therapies using Anc80 for several additional diseases including lysosomal storage, muscular and genetic metabolic diseases.

We intend to develop the combination of Anc80 and SVP-Rapamycin to increase the potential applicability of gene therapies. This would include (i) patients with pre-existing ADAs to naturally occurring AAV, a current exclusion criteria for many clinical studies, and (ii) diseases that require repeat dosing due to a young patient population or the need to reach higher levels of protein expression than can be achieved with a single dose.

We plan to develop another product candidate for the treatment of an XLM disorder, which is a metabolic disorder similar to ARM disorder. We are pursuing this second indication through collaborations with third parties with preclinical and clinical experience in this area.

Our SVP-Rapamycin programs for marketed biologics

In preclinical studies, we have observed the ability of SVP-Rapamycin to inhibit the formation of ADAs when co-administered with several marketed biologics, including Humira and Advate. Humira is an anti-inflammatory medication that is used in the treatment of rheumatoid arthritis and other autoimmune diseases. Advate is a recombinant human clotting factor VIII used in the treatment of hemophilia A.

In one such preclinical study, we co-administered SVP-Rapamycin with Humira in genetically modified mice that produce human TNF-alpha, a protein involved in systemic inflammation. Due to the constitutive expression of TNF-alpha, these mice spontaneously developed arthritis. In connection with this study:

- one group of mice, referred to as the Untreated Group, indicated in black in Figure 24c below, were left untreated;
- a second group of mice, referred to as the Humira Group, indicated in blue in Figures 24a through 24d below, were treated weekly with Humira alone from weeks 5 through 20; and
- a third group of mice, referred to as the SVP-Rapamycin Group, indicated in green in Figures 24a through 24d below, were treated weekly with SVP-Rapamycin together with Humira from weeks five through 11 and then weekly with Humira alone from weeks 12 to 20.

We evaluated Humira-specific ADA levels to determine the formation of ADAs to Humira. Levels of Humira in serum, or in the blood, were measured to determine whether the formation of ADAs increased the clearance of Humira in serum. In addition, we measured the arthritis score, based on the level of severity of the disease, each week from weeks 10 through 20, for each of the three groups.

As depicted in Figure 24a below, we observed a reduction in the formation of ADAs to Humira in the SVP-Rapamycin Group as compared to the Humira Group at week 20. Consistent with the observation of the formation of ADAs, as depicted in Figure 24b below, we observed a higher level of Humira in serum in the SVP-Rapamycin Group as compared to the Humira Group at week 19. As expected, mice in the Untreated Group did not show any Humira-specific ADAs or the presence of Humira in serum. As depicted in Figure 24c below, we observed a decrease in arthritis in the SVP-Rapamycin Group as compared to both the Humira Group and Untreated Group. Notably, the inhibition of ADAs and protection from arthritis were observed through the termination of the study at 20 weeks, even though the last treatment with SVP-Rapamycin was at 11 weeks.

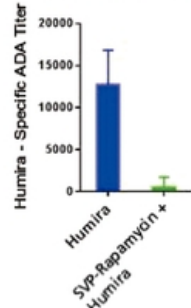
Figure 24d below depicts an x-ray at week 20 of a severely eroded ankle joint in an arthritic mouse in the Humira Group compared to the normal ankle joint of a mouse in the Humira + SVP-Rapamycin Group.

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Based on these observations, we believe the co-administration of SVP-Rapamycin with Humira results in the formation of less anti-Humira ADAs, which, in turn, increases the therapeutic levels of Humira in serum and improves the efficacy of Humira.



Humira - Specific ADA (Week 20)



Humira in Serum (Week 19)

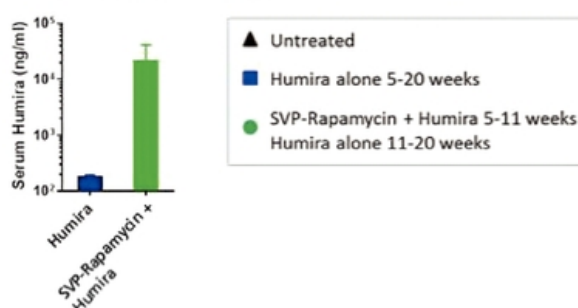


Figure 24a

Figure 24b

Arthritis Score

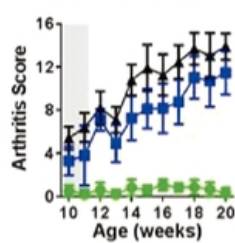


Figure 24c

X-ray images of ankle joint (Week 20)

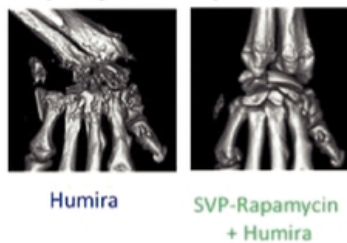


Figure 24d

Figures 24a through 24d. Preclinical Study: SVP-Rapamycin Co-Administered with Humira

We also conducted a preclinical study evaluating SVP-Rapamycin co-administered with Advate in mice with hemophilia A, a genetic disorder caused by missing or defective blood coagulation Factor VIII. As depicted in Figures 25a through 25c below, during the first 28 days of the study, or the treatment period:

- the first group of mice, referred to as the Empty Nanoparticle Group and indicated in blue, received five weekly injections of empty nanoparticle together with Advate; and
- the second group of mice, referred to as the SVP-Rapamycin Group and indicated in green, received five weekly doses of SVP-Rapamycin together with Advate.

All groups were then challenged with five injections of Advate on days 57, 81, 125, 143 and 187 of the study, referred to as the challenge period. We also administered an unrelated antigen, bacteriophage PhiX174 on days 81, 95 and 143, into all mice to evaluate whether SVP-Rapamycin caused global

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immunosuppression. We evaluated Advate-specific ADA levels to determine the formation of ADAs to Advate. We also evaluated PhiX174-specific ADA levels to determine the specificity of the SVP-Rapamycin and Advate treatment.

As depicted in Figure 25a below, we observed a reduction in the formation of ADAs to Advate in the SVP-Rapamycin Group as compared to the Empty Nanoparticle Group, which lasted over five months following the last treatment of SVP-Rapamycin. We also observed that when both groups were immunized with a different antigen, PhiX174, the SVP-Rapamycin Group and the Empty Nanoparticle Group showed relatively similar levels of PhiX174-specific ADA levels, suggesting that the SVP-Rapamycin treatment does not induce global immunosuppression, as depicted in Figure 25b below.

In a separate study, the ability of mice to control bleeding following repeated administration of Factor VIII was evaluated and expressed as the percentage of normalized hemoglobin levels, as depicted in Figure 25c below. A higher percentage of normalized hemoglobin levels indicate an increased ability of the mice to control bleeding. As depicted in Figure 25c below, we observed that mice in the SVP-Rapamycin Group were able to control bleeding at a higher rate than mice in the Empty Nanoparticle Group.

Based on our observations, we believe the co-administration of SVP-Rapamycin with Advate inhibits the formation of anti-Advate ADAs, which, in turn, increases the efficacy of Advate to treat hemophilia A, but does not trigger global immunosuppression.

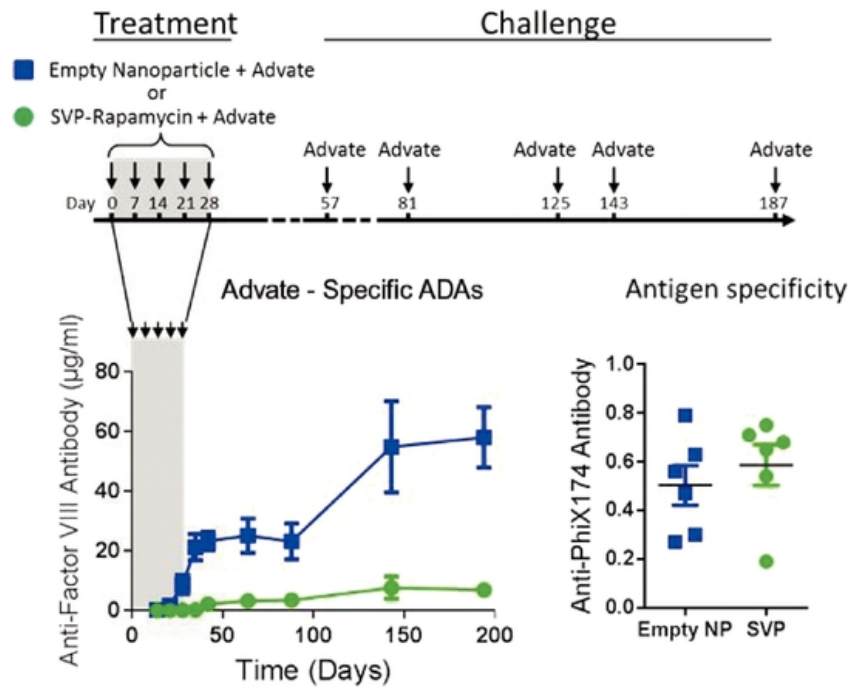


Figure 25a

Figure 25b

Control of bleeding

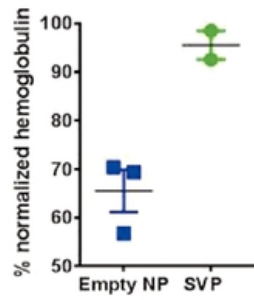


Figure 25c

Figures 25a through 25c. Preclinical Study: SVP-Rapamycin Co-Administered with Advate

Business

Our allergy and autoimmune disease programs

We are applying our SVP technology to the treatment of allergies and autoimmune diseases. Currently, many autoimmune diseases are treated with immunosuppressive therapies that indiscriminately affect the function of the entire immune system. Our SVP technology, however, is designed to reprogram the immune system to induce tolerance to a specific antigen that is causing the autoimmune disease, without impacting the rest of the immune system. We have established three collaborative programs with Sanofi to research novel SVP products for the treatment of a life-threatening food allergy, celiac disease and type 1 diabetes.

- *Life-Threatening Food Allergy.* In November 2012, we entered into an exclusive license agreement with Sanofi for the use of our SVP technology for a life-threatening food allergy. We are evaluating a SVP that encapsulates an immunomodulator together with an allergen provided by Sanofi. Our license agreement with Sanofi contemplates multiple preclinical, clinical, regulatory and sales milestones as well as a multi-tiered royalty structure.
- *Celiac Disease.* In November 2014, Sanofi exercised its option to develop a SVP-based therapy to treat celiac disease under similar financial and other terms as the food allergy program. We are evaluating a SVP that encapsulates an immunomodulator together with gluten antigens provided by Sanofi. Our license agreement with Sanofi contemplates multiple preclinical, clinical, regulatory and sales milestones as well as a multi-tiered royalty structure.
- *Type 1 Diabetes.* In September 2014, we received a grant from Sanofi, together with the Juvenile Diabetes Research Foundation, for research on SVP formulations encapsulating Rapamycin and insulin or insulin peptides.

OUR IMMUNE STIMULATION PROGRAMS

We believe our SVP technology, by encapsulating antigens and adjuvants, has the potential to be used for therapies that stimulate the immune system to treat cancer, infectious diseases and other diseases. We have early-stage programs for therapeutic treatment of HPV-associated cancers and antibody-based vaccine programs for nicotine addiction and malaria. These programs are primarily funded by grants and are the focus of our Russian operations.

Our SVP immune stimulation programs are designed to encapsulate an antigen and a toll-like receptor, or TLR, agonist as the immunomodulator. Humans possess ten TLRs, each of which recognizes distinct molecular patterns associated with pathogens. Activation of TLRs alert the immune system that a potential pathogen is present and that the immune system should mount a response. In this regard, we refer to TLR agonists as substances that activate specific TLRs. TLR agonists can be used as supplements, or adjuvants, to vaccines to increase the immune response to the vaccine by activating the TLRs in antigen-presenting cells.

Injecting TLR agonists alone can cause off-target, systemic immune stimulation, leading to the production of secreted factors called cytokines, which can effectively limit the dosage of vaccines by causing inflammation and flu-like symptoms. To address this issue, our stimulatory SVP technology is designed to limit the TLR agonists from creating a systemic immune response by encapsulating the TLR agonists within our biodegradable nanoparticle. When the TLR agonist is encapsulated with SVP, referred to as SVP-TLR agonist, it can be selectively delivered, together with the vaccine target antigen, to the antigen-presenting cells to induce antigen-specific immune stimulation.

Immune stimulation-related preclinical study

We conducted a preclinical study in mice to evaluate the ability of a SVP-TLR agonist containing an antigen to minimize the production of systemic cytokines, which are responsible for an undesired systemic immune-stimulatory response, while increasing the production of local cytokines, which are responsible for a strong and antigen-specific immune-stimulatory response.

In this study, we used a specific agonist of TLR7 and TLR8, referred to as TLR 7/8 agonist, that we either delivered in free form mixed with a nanoparticle containing an antigen or encapsulated with an antigen in a nanoparticle.

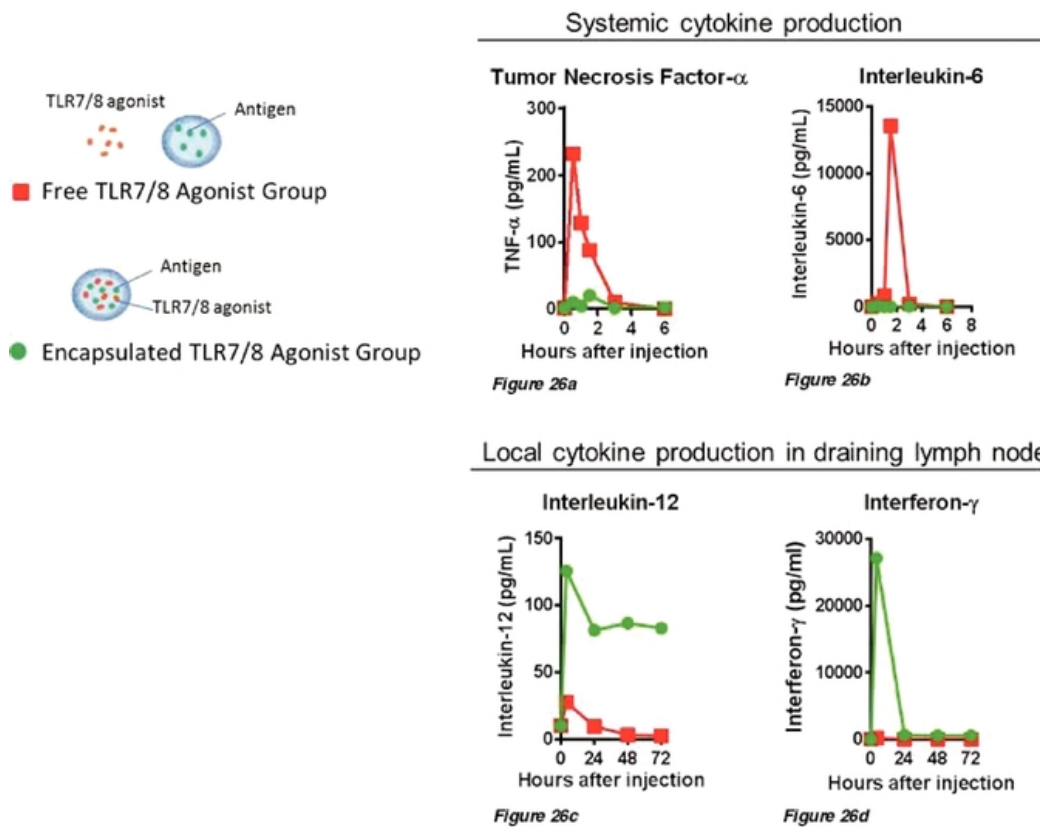
As depicted in Figures 26a through 26d below:

- the first group of mice, referred to as the Encapsulated TLR 7/8 Agonist Group and indicated in green, received a single dose of SVP encapsulating both an antigen and a TLR 7/8 agonist; and
- the second group of mice, referred to as the Free TLR 7/8 Agonist Group and indicated in red, received a single dose of SVP encapsulating antigen alone together with free TLR 7/8 agonist.

We evaluated serum levels of TNF-alpha and interleukin-6, or IL-6, two pro-inflammatory cytokines indicative of an undesired, systemic immune response and associated with flu-like symptoms, to determine the levels of systemic cytokine production, as depicted in Figures 26a and 26b below. We also evaluated the levels of interleukin-12, or IL-12, and interferon-gamma, or IFN, in the draining lymph node to determine the levels of local cytokine production involved in desired T helper cell type 1 immune responses, as depicted in Figures 26c and 26d below.

As depicted in Figures 26a and 26b below, we observed increased levels of systemic cytokine production in the Free TLR 7/8 Agonist Group in comparison to the Encapsulated TLR 7/8 Agonist Group. As depicted in Figures 26c and 26d below, we observed increased levels of local cytokine production in the draining lymph node in the Encapsulated TLR 7/8 Agonist Group as compared to the Free TLR 7/8 Agonist Group.

Based on these results, we believe that by encapsulating a TLR agonist in SVP, we are able to increase the production of local cytokines without triggering an undesired systemic immune response.



Figures 26a through 26d. Preclinical Study: Minimization of Production of Systemic Cytokines

Cancer immunotherapy

Cancer immunotherapy leverages the immune system to treat cancer. The main function of the immune system is to discriminate between "self" and "non-self" antigens. Cancer cells thrive, in part, because they are derived from the body's own cells, and thus are recognized by the immune system as self. We believe that cancer vaccines could be an important therapeutic modality to treat cancer by training the immune system to recognize cancer-associated antigens that are mutated or not expressed in normal adult tissues.

Tumors also evade the immune system by increasing the expression of certain molecules that suppress the immune response against the tumor. This mechanism may be overcome by administering products called immune checkpoint inhibitors, which are designed to block or overcome the immunosuppressive pathways and stimulate the immune system. We believe the efficacy of this approach depends on the existence of pre-existing tumor-specific cytolytic T cells, or CTL, that can be mobilized by checkpoint inhibitors. In some patients, the immune system either does not recognize the tumor or is too weak to mount a response and as a result cannot generate the CTL necessary to kill the tumor. For these patients, a vaccine therapy that stimulates the immune system and could be given in conjunction with a checkpoint inhibitor, may result in better outcomes. We believe that the combination of checkpoint inhibitors and effective cancer vaccines represents the next advance in cancer immunotherapy.

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HPV-associated cancer

HPV overview

HPV is a sexually transmitted infection, which can lead to the development of cancer. Cervical HPV infection often clears spontaneously. However, when it persists, it can lead to the development of cervical intraepithelial neoplasia, or CIN, and cervical cancer.

According to the World Health Organization, HPV infection results in an estimated 530,000 new cases of cervical cancer worldwide, with 270,000 deaths annually. The Centers for Disease Control and Prevention estimates that in the United States there are more than 26,000 cases of HPV-associated cancer per year. HPV is found in approximately 99% of cases of cervical cancer and 72% of cases of oropharyngeal head and neck cancer. The rising incidence of such cancers is thought to be related to the increasing proportion of cancers caused by HPV. In 2011, a study published in the Journal of Clinical Oncology observed that HPV prevalence in oropharyngeal cancers increased from 16.3% during 1984 to 1989 to 71.7% during 2000 to 2004. There are two HPV strains that are responsible for more than 70% of cervical cancer worldwide.

Gardasil and Cervarix are FDA-approved prophylactic vaccines for HPV-related cancers with aggregate worldwide sales reaching \$1.9 billion in 2014. While these vaccines can prevent tumor occurrence, Gardasil and Cervarix have not been approved for treatment of patients with existing HPV-related cancers.

According to the Centers for Disease Control and Prevention, in 2012, only 54% of women between the age of 13 to 17 had received at least one dose of the HPV vaccine and only 33% received a complete series of three, which may serve as a prophylactic if administered prior to exposure. This level of vaccination is well below the 80% rate set as a goal by the U.S. Department of Health and Human Services. As a result, we believe that HPV-associated cancer will be an ongoing medical condition for the foreseeable future.

Overview of our program for HPV-associated cancer

Our first CTL-activating SVP program in development is designed to treat HPV-associated cancers by stimulating the immune response to the E6 and E7 proteins, which are expressed by HPV-associated tumor cells. The HPV E6 and E7 antigens are oncogenic proteins that promote malignant transformation and tumor growth. Our SVP program for HPV-associated cancer consists of a SVP encapsulating the E6 and E7 proteins, or SVP-E6/E7, co-administered with an SVP adjuvant which contains a TLR agonist. We refer to this co-administration as SVP-HPV.

We were awarded a grant from the Skolkovo Foundation to support our program to develop an SVP immunotherapy to treat HPV-associated cancers. We believe the grant will assist us with advancing the program from preclinical to early clinical evaluation.

Preclinical development

We conducted a preclinical study in which we evaluated the ability of SVP-HPV to reverse tumor growth for HPV-associated cancers. In this study, we delivered SVP-HPV to mice using the TC-1 tumor model, which expresses the HPV E6 and E7 antigens. Mice were treated either 13 days or 14 days after the introduction (inoculation) of TC-1 tumor cells, at which time the average tumor size was approximately 200 mm³.

In this study, we administered to:

- the first group of mice, referred to as the Empty Nanoparticle Group and indicated in blue in Figures 27a and 27c below, four doses of empty nanoparticles; and

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- the second group of mice, referred to as the SVP-HPV Group and indicated in green in Figures 27b and 27c below, four doses of SVP-HPV.

As depicted in Figures 27a and 27b below, we recorded the volumes of the tumors in both the Empty Nanoparticle Group and the SVP-HPV Group to determine the efficacy of the treatment.

As depicted in Figures 27a and 27b below, we observed that the administration of SVP-HPV reduced the growth of tumors in the SVP-HPV Group in comparison to the Empty Nanoparticle Group, even when administered to mice with palpable tumors. Notably, the tumors in the mice in the SVP-HPV Group continued to grow to an average size of approximately 1,200 mm³ at day 20, before regressing back to baseline.

In a separate experiment, we re-challenged surviving mice on day 154 with a second inoculation of TC-1 tumor cells to test the durability of the immune response and the ability to prevent tumor recurrence. As depicted in Figure 27c below, we observed that immunization with SVP-HPV increases the survival rate of SVP-HPV immunized mice compared to saline treated mice, referred to as the Saline Control Group. The surviving mice withstood a second inoculation of tumors at day 154, indicating the development of long term immunological memory.

Based on these observations, we believe administration of SVP-HPV can both reduce tumor size and increase survival rate.

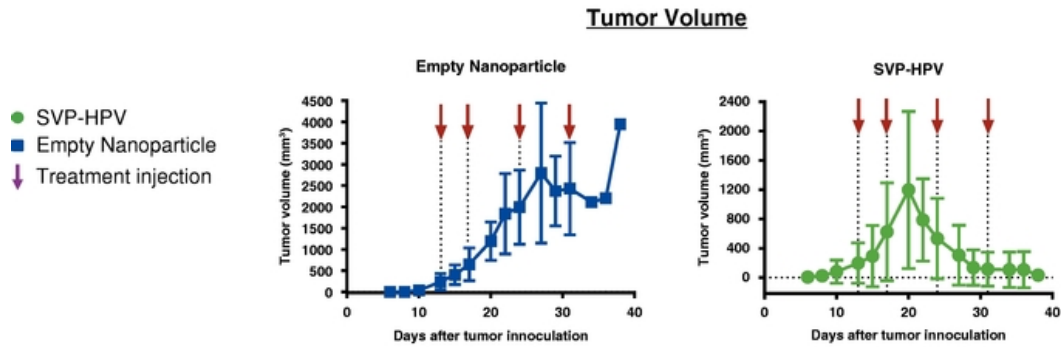


Figure 27a

Figure 27b

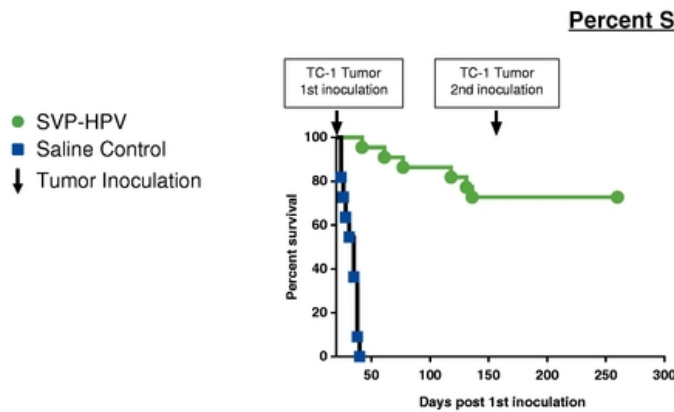


Figure 27c

Figures 27a through 27c. Preclinical Study: Administration of SVP-HPV in TC-1 Tumor Model

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We conducted a preclinical study to evaluate the synergistic effects that our SVP technology may have with certain checkpoint inhibitors such as anti-PD-L1 antibodies. In this study, mice were separated into four groups and implanted with B16F10 melanoma tumor cells, which express an endogenous tumor antigen called TRP-2.

As depicted in Figure 28 below, the:

- first group of mice, referred to as the Empty Nanoparticle + Control Antibody Group and indicated in black, received empty nanoparticles with an isotype control antibody;
- second group of mice, referred to as the Empty Nanoparticle + Anti-PD-L1 Antibody Group and indicated in blue, received empty nanoparticles with a PD-L1-specific monoclonal antibody;
- third group of mice, referred to as the SVP-TRP-2 + Control Antibody Group and indicated in green, received SVP encapsulating the TRP-2 peptide antigen and a TLR agonist with an isotype control antibody; and
- fourth group of mice, referred to as the SVP-TRP-2 + Anti-PD-L1 Antibody Group and indicated in red, received SVP encapsulating the TRP-2 peptide antigen and a TLR agonist with a PD-L1-specific monoclonal antibody.

We evaluated the presence of tumors over time in the mice to determine the efficacy of treatment. We observed that more mice in the SVP-TRP-2 + Control Antibody Group remained tumor-free and over a longer period of time than that of the Empty Nanoparticle + Control Antibody and the Empty Nanoparticle + Anti-PD-L1 Antibody Groups. The SVP-TRP-2 + Anti-PD-L1 Group showed even better efficacy, with approximately 66% of mice remaining tumor free at day 76, compared to approximately 25% of mice in the SVP-TRP-2 + Control Antibody Group and 0% of mice in each of the Empty Nanoparticle + Control Antibody and the Empty Nanoparticle + Anti-PD-L1 Antibody Groups.

Based on our observations, we believe our SVP technology may have synergistic effects with certain checkpoint inhibitors to treat cancer.

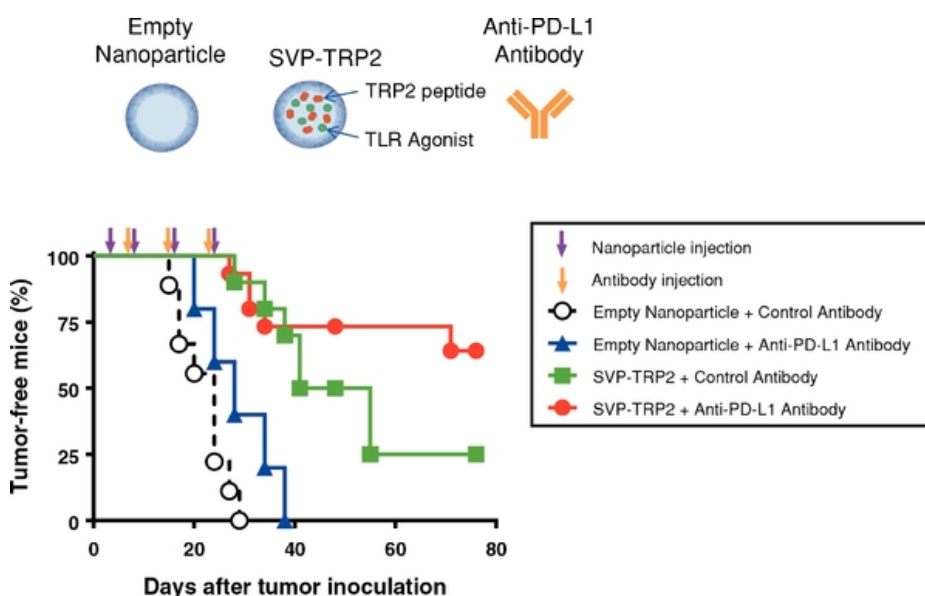


Figure 28. Preclinical Study: Administration of SVP Encapsulating the TRP-2 Peptide Antigen and TLR Agonist in B16F1-Melanoma Tumor Model

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OUR OTHER PROGRAMS

Our other immune stimulation programs are a prophylactic malaria vaccine, funded by a grant from The Bill and Melinda Gates Foundation, and a therapeutic vaccine for smoking cessation and relapse prevention, funded by a grant from the NIDA part of the National Institutes of Health.

The malaria program is designed to be a dual action, immune-stimulating SVP nanoparticle vaccine that we believe may offer the potential to protect against malaria by preventing infection and transmission. This program is in the discovery phase.

The smoking cessation and relapse prevention program aims to stimulate the immune system to produce nicotine-specific antibodies in smokers. We believe such antibodies have the potential to bind to the inhaled nicotine and prevent the inhaled nicotine from reaching the brain thereby reducing levels of nicotine in the brain to support smoking cessation and relapse prevention. The SVP-nicotine program, SEL-070, is in preclinical development. We had a prior SVP-nicotine product candidate that was partly sponsored by a grant from NIDA, which entered clinical development. Results from a Phase 1 clinical trial conducted in smokers and non-smokers with this prior product candidate showed that it was well tolerated and that nicotine-specific antibodies were induced, but at sub-therapeutic levels. On the basis of the data from this Phase 1 trial, we obtained a new grant from NIDA to further optimize our SVP-nicotine product candidate. We are currently conducting GLP toxicology studies for our optimized smoking cessation candidate.

MANUFACTURING

We manufacture SVP using a readily-scalable, self-assembly nanoemulsion process with well-defined, robust commercial pharmaceutical unit operations. This proprietary, highly specialized and precisely controlled manufacturing process enables us to reproducibly manufacture SVP across many production scales, from milligram-scale at the laboratory bench, to tens of grams to support investigational new drug application-enabling toxicology studies and early phase clinical studies, to hundreds of grams to multi-kilogram scale for commercial production. This well-defined process has been produced at multiple scales. We have also developed and executed the required detailed analytic characterization of our products. We have completed and released multiple cGMP batches of nanoparticles at the 50 gram scale for our SVP-Rapamycin program and at the 10 and 20 gram scale for our nicotine program.

For the SEL-212 program, we have scaled-up the SVP-Rapamycin production to a 50 gram scale and have initiated development at the 200 gram scale, which, at the current projected clinical dose, we believe would be suitable for commercial launch. The process is designed such that this same equipment is capable of potentially producing up to a one kilogram batch size scale. As our nanoparticle manufacturing process is compact, and therefore also portable, our strategy is to transfer our custom designed process skids to our contract manufacturing organization, or CMO, and have the CMO produce the nanoparticles, under our direction. This is the strategy we use for production of clinical supplies for clinical trials and would be the expected strategy for commercial production.

The pepsitacase enzyme is produced by fermentation in E. Coli and is sourced from 3SBio in China. 3SBio is a Chinese pharmaceutical company that produces multiple approved products in China and also has product sales in other countries around the world. 3SBio supplies the pepsitacase used in the current clinical trials of SEL-212 in the United States. Through a licensing arrangement, we own exclusive worldwide rights to pepsitacase outside of China, with co-ownership of rights in Japan and with 3SBio owning all rights in China. Under this arrangement, 3SBio has agreed to supply us with pepsitacase. We are in the process of evaluating a back-up supplier for pepsitacase in the United States.

LICENSES AND COLLABORATIONS**Massachusetts Institute of Technology**

In November 2008, we entered into a license agreement with MIT, which we refer to as the MIT License. We amended the MIT License in January 2010, November 2012 and August 2013. Under the MIT License, we acquired an exclusive worldwide license, with the right to grant sublicenses, to develop, make, sell, use and import certain licensed products that are therapeutic or prophylactic vaccines and use certain licensed processes in the exercise of rights to the licensed products, the manufacture, sale and practice of which are covered by patent rights owned or controlled by MIT, including patents jointly owned with Brigham, the President and Fellows of Harvard College, and the Children's Medical Center Corporation and its subsidiary, the Children's Hospital Corporation (formerly, the Immune Disease Institute). Our exclusivity is subject to certain retained rights of these institutions and other third parties.

Pursuant to the MIT License, we are required to use diligent efforts to develop and commercialize one or more licensed products or licensed processes, and to thereafter make such products and processes reasonably available to the public, which include annual minimum spending on research, development and commercialization by us or our sublicensees. Upon our entry into the MIT License, we paid MIT a non-refundable license issue fee, reimbursed certain of MIT's costs and issued shares of our common stock to MIT and the other institutional patent owners which were subject to certain anti-dilution, registration and other protective rights. We are obligated to pay MIT annual maintenance fees, which may be credited against the low-single-digit running royalty on annual net sales that we are also obligated to pay. Additionally, we are required to pay MIT (i) developmental milestones up to an aggregate of \$1,450,000, (ii) a mid-single digit percentage of income received in consideration of practice of patent rights or development of the products or processes in collaboration with or on behalf of a non-sublicensee corporate partner, (iii) a specified percentage of income received from sublicensees in the low thirties prior to November 25, 2009 and, after that, between 10% and 20%, and (iv) certain fees and costs. Pursuant to the MIT License, we are required to use diligent efforts to develop and commercialize one or more licensed products or licensed processes, and to thereafter make such products and processes reasonably available to the public, which include annual minimum spending of a specified amount in the low-to-mid-six figures in 2008 and 2009 and, thereafter, in the low seven figures, on research, development and commercialization by or our sublicensees.

We may terminate the MIT License at any time upon six months written notice. MIT has the right to terminate the MIT License immediately upon written notice to us if we cease to carry on our business related to the MIT License, fail to maintain insurance as required under the MIT License, file for bankruptcy, fail to pay amounts due under the MIT License, challenge or assist others in bringing a challenge to MIT's patents or fail to cure material breach within 60 days' written notice thereof. Absent early termination, the MIT License will continue until the expiration or abandonment of the last to expire patent right subject to the MIT License.

Sanofi

In November 2012, we entered into a license and research collaboration agreement with Sanofi, which we refer to as the Sanofi Agreement. Under the terms of the Sanofi Agreement, we granted Sanofi an exclusive, worldwide license to certain intellectual property rights and technologies owned by or licensed exclusively to us, including a sublicense under the MIT License, for the research, development and commercialization of one or more treatments for food allergies. The Sanofi Agreement contains an option to extend the license grant for two additional allergy indications, including celiac disease but excluding house dust mite allergies. In November 2014, Sanofi exercised the option to include celiac

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disease as an additional indication and the Sanofi Agreement was amended to add terms specific to the celiac disease indication and to terminate Sanofi's right to exercise its option for any additional indications in May 2015. Except as authorized by Sanofi or permitted under the Sanofi Agreement, during the term of the Sanofi Agreement, our exclusivity obligations prevent us from researching, developing, or commercializing products in these indications or granting third party licenses under the intellectual property rights and technologies licensed to Sanofi for use in these indications.

Under the terms of the research collaboration portion of the Sanofi Agreement, we are required to use commercially reasonable efforts to perform the activities set out for us in the research and development plans created and overseen by a joint research committee. We are responsible for manufacturing all vaccines required for research, development and commercialization of licensed products.

The research term for the first indication expired on the third anniversary of the Sanofi Agreement (November 27, 2015). We completed our research obligations within the initial three year period and are not obligated to perform any further research on the specific indication under the Sanofi Agreement. A vaccine candidate for development and commercialization was not selected by Sanofi by the end of the research plan. However, we are in discussions with Sanofi to extend the research term for the first indication by one year (until November 27, 2016).

The research term for the second indication (celiac disease) will expire upon the earlier of (a) the nomination of a development candidate for the second indication and (b) May 7, 2019. In the event that we are unable to complete our research obligations by May 7, 2019, our obligation will be limited to exercising commercially reasonable efforts to complete such research up to one year after the end of the research term. Each party is responsible for its own internal costs, as well as any third-party or out-of-pocket costs incurred in the performance of the activities laid out in the research plan. If the parties agree to expand our scope of work, such costs will be reimbursed by Sanofi based on an agreed upon budget. Once a development candidate is nominated, all development activities will be under the direction of Sanofi pursuant to a development plan to be negotiated and agreed to at that time and Sanofi will pay us for expenses incurred within certain approved limits.

Pursuant to the Sanofi Agreement, Sanofi paid us an initial payment of \$2,000,000 for the initial indication and an additional \$2,000,000 for the second indication (celiac disease). Sanofi is obligated to make additional payments to us during preclinical research totaling up to \$3,000,000 for each indication, which has been achieved for the food allergy indication. For each indication, we are also eligible for (i) a \$5,000,000 development candidate milestone payable to us at the start of preclinical development, (ii) further development milestones up to an aggregate of \$127,000,000, which includes up to an aggregate of \$57.0 million following the initiation of Phase I, Phase II and Phase III clinical trials for the indication and filing of the first biologic license application, more than two-thirds of which is attributable to the initiation of the Phase 3 clinical trial and the filing of the first biologic license application, and an aggregate of \$70.0 million upon achieving various regulatory approvals in the United States, European Union, Japan and Brazil, Russia, India or China, of which the majority is attributable to regulatory approvals in the United States, (iii) sales milestones of up to an aggregate of \$170,000,000, and (iv) tiered royalties on annual net sales of licensed products at percentages ranging from mid-single to low double-digits.

These royalty rates are subject to certain reductions. If no vaccine candidates are nominated for development for any indication by 2019, the Sanofi Agreement will expire in its entirety in 2021 and all rights granted thereunder will terminate. If licensed products have been developed pursuant to this agreement, the term will continue until the expiration of all royalty payment obligations, after which time Sanofi will have a royalty-free, perpetual license. In certain circumstances, following termination of the Sanofi Agreement, we may elect to continue developing product candidates or licensed products

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on our own, and if we choose to do so, we will be required to pay Sanofi low-single digit royalties on net sales and a percentage of licensing revenue ranging from mid-single to low-double digits.

Sanofi may terminate the Sanofi Agreement in the event of our uncured material breach, or may terminate for any reason on 6 months' written notice. In case of our uncured material breach, Sanofi may elect, instead of terminating, to continue the Sanofi Agreement and offset any damages incurred due to the default against Sanofi's payments due to us thereunder. We may terminate the Sanofi Agreement in the event of Sanofi's uncured material breach or Sanofi's challenge or assistance of others in challenging our or MIT's licensed patents.

Shenyang Sunshine Pharmaceutical Co., Ltd.

In May 2014, we entered into a license agreement with 3SBio, which we refer to as the 3SBio License. Pursuant to the 3SBio License, we were granted an exclusive license to certain pegsiticase-related patents and related "know-how" owned or in-licensed by 3SBio for the worldwide (except for Greater China and Japan) development and commercialization of products based thereupon for human therapeutic, diagnostic and prophylactic use. We are also granted a worldwide (except for Greater China) exclusive license to develop, commercialize and manufacture or have manufactured products combining our proprietary SVP technology with pegsiticase or related compounds supplied by 3SBio (or otherwise supplied if our rights to manufacture are in effect) for human therapeutic, diagnostic and prophylactic use. We were also granted a co-exclusive license to manufacture and have manufactured pegsiticase and related compounds for our preclinical and clinical use or, if the 3SBio License is terminated for 3SBio's material breach, for any use under the 3SBio License. Otherwise, we are obligated to obtain all of our supply of such compounds for Phase 3 clinical trials and commercial use from 3SBio under the terms of supply agreements to be negotiated.

Pursuant to the 3SBio License, we are required to use our commercially reasonable efforts to develop and commercialize a product containing pegsiticase or a related compound. If we do not commercialize any such product in a particular country in Asia, Africa or South America within 48 months after approval of any such product in the U.S. or a major European country, then 3SBio will have the right to do so, but only until we commercialize a product combining our SVP technology with any such compound in such country. We have paid to 3SBio an aggregate of \$1,000,000 in upfront and milestone-based payments under the 3SBio License. We are required to make future payments to 3SBio contingent upon the occurrence of events related to the achievement of clinical and regulatory approval milestones of up to an aggregate of \$21,000,000 for products containing our SVP technology, and up to an aggregate of \$41,500,000 for products without our SVP technology. We are also required to pay 3SBio tiered royalties on annual worldwide net sales (on a country-by-country and product-by-product basis) related to the pegsiticase component of products at percentages ranging from the low-to-mid single digits for products containing our SVP technology, and a range of no more than ten percentage points from the mid-single digits to low double-digits for products without our SVP technology. We will pay these royalties to 3SBio, subject to specified reductions, on a country-by-country and product-by-product basis until the later of (i) the date that all of the patent rights for that product have expired in that country, or (ii) a specified number of years from the first commercial sale of such product in such country.

The 3SBio License expires on the date of expiration of all of our royalty payment obligations unless earlier terminated by either party for an uncured material default or for the other party's bankruptcy. Any such termination by 3SBio for our material default may be on a country-by country or product-by-product basis in certain circumstances. We may also terminate the 3SBio License on a country-by-country or product-by-product basis for any reason effective upon 60 days' prior written

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notice to 3SBio or, with respect to a given product, immediately upon written notice to 3SBio if we identify a safety or efficacy concern related to such product.

BIND

In December 2008, we entered into a cross-license agreement with BIND Therapeutics, Inc. (formerly BIND Biosciences, Inc.), or BIND, which we refer to as the BIND Agreement. Pursuant to the BIND Agreement, BIND granted us a perpetual, irrevocable, royalty-free worldwide non-exclusive license under certain of BIND's existing and future patent rights to make, have made, use, sell, offer for sale and import products and services covered by such patents and patent applications in the field of certain prophylactic and therapeutic vaccines. The time period for adding new patent rights, not included in the families of previously licensed patent rights, to our license grant from BIND has expired. Pursuant to the BIND Agreement, we granted BIND a perpetual, irrevocable, royalty-free, worldwide non-exclusive license under certain of our current and future patent rights to make, have made, use, sell, offer for sale and import products and services covered by such patents and patent applications in all other fields, in each case, excluding certain future patent rights of each party related to novel targeting agents. The time period for adding new patent rights, not included in the families of previously licensed patent rights, to BIND's license grant from us has expired.

We have paid BIND an upfront license issuance fee and reimbursed certain of BIND's fees in connection with the entry into the BIND Agreement. No royalties or other payments are due to or by either party. The BIND Agreement expires upon expiration of the last patent right covered by the BIND Agreement. Neither party may unilaterally terminate the BIND Agreement for any reason. If either party materially breaches the BIND Agreement, fails to expend a specified amount in research and development activities related to the BIND Agreement, undergoes bankruptcy or insolvency, or undergoes a change of control, the future patent rights to be included in the license grant to the party breaching, failing to expend such amounts or undergoing such event under the BIND Agreement will no longer be granted to the breaching party.

Massachusetts Eye and Ear Infirmary

In May 2016, we entered into a license agreement with the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc., or, collectively, MEE, which we refer to as the MEE License. Under the MEE License, we were granted an exclusive commercial worldwide license, with the right to grant sublicenses through multiple tiers, to make, have made, use, offer to sell, sell and import certain products and to practice certain processes, the sale, use or practice of which are covered by patents and proprietary know-how owned or controlled by MEE, for use of Anc80 gene therapy vectors for gene augmentation therapies expressing certain target sequences.

MEE also granted us exclusive options to exclusively license certain of their intellectual property rights relating to several additional target sequences and variations thereof each linked to a specified disease. During a defined option period, we may exercise this right for up to a designated number of target sequences. If we exercise our options, under certain circumstances, we may substitute alternative target sequences for previously selected target sequences.

We agreed to use commercially reasonable efforts to develop and commercialize licensed products pursuant to a development plan, and to market and sell at least one product for each target sequence for which we exercised our option as soon as reasonably practicable. Subject to certain exceptions, following commercial launch we must use commercially reasonable efforts to market, sell, and maintain public availability of licensed products in a certain number of specified major markets.

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Pursuant to the MEE Agreement, we agreed to pay MEE a license fee in the low six figures, annual license maintenance fees ranging from the mid-twenty thousands to mid-seventy thousands and an option maintenance fee in the low five figures for each exercisable option. We also agreed to reimburse MEE for a specified percentage of the past patent expenses for the patents licensed to us. We also agreed to pay development milestones on a licensed product-by-licensed product basis, totaling up to an aggregate of between \$4,175,000 to \$37,025,000 and sales milestones on a licensed product-by-licensed product basis, totaling up to an aggregate of between \$50,000,000 to \$70,000,000; tiered royalties on a licensed product-by-licensed product and country-by-country basis equal to a percentage of net sales ranging from mid-single digits to mid-teens, subject to the prevalence of the targeted disease and certain reductions; and a percentage, in a range expected to be in the mid-teens depending on timing, of any sublicense income we receive from sublicensing our rights granted thereunder, subject to certain reductions and exclusions. Upon exercise of each option, we agreed to pay MEE an option exercise fee ranging from low-six figures to mid-six figures, depending on the prevalence of the targeted disease.

The MEE License will continue until the expiration of the last to expire of the patent rights licensed thereunder. We may terminate the MEE License in whole or in part upon prior written notice. MEE may terminate the MEE License on a target sequence-by-target sequence basis if we fail to make any scheduled payments in respect of such target sequence or if we materially breach a diligence obligation in respect of such target sequence, in each case if we fail to cure within a specified time period. MEE may terminate the MEE License in its entirety if we materially breach certain of our obligations related to diligence, representations and warranties, and maintenance of insurance; if we challenge the validity or enforceability of any patents licensed thereunder; if any of our executive officers are convicted of a felony relating to manufacture, use, sale or importation of licensed products; or upon our insolvency or bankruptcy.

INTELLECTUAL PROPERTY

We endeavor to protect our SVP based immunotherapy program technology, which we consider fundamental to our business, by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties, relating to our program, product candidates, their methods of use and the processes for their manufacture. Our practice is to strive to protect our intellectual property by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, programs and product candidates that are commercially important to the operation and growth of our business. We also rely on trade secrets and know-how relating to our proprietary technology, programs and product candidates, continuing innovation and in-licensing opportunities to maintain, advance and fortify our proprietary position in our SVP-based immunotherapy program and product candidates. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our program technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patents; and to operate without infringing the patents and proprietary rights of third parties.

We have developed and in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to our SVP-based immunotherapy technology, program and product candidates. Our patent portfolio contains nine issued patents in the United States and seven foreign issued patents, in all cases, owned solely by us. We also have 50 pending patent applications in

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the United States as well as 307 foreign pending patent applications, in all cases, owned solely by us. These patents and patent applications include claims directed to:

- tolerance and cancer immunotherapy programs;
- other immune stimulation programs;
- methods and compositions incorporating our proprietary SVP nanoparticle in a variety of tolerance applications, including:
 - mitigating or treating anti-drug antibodies association with protein drugs (such as SEL-212), and
 - genetic therapies (such as viral delivery of genes);
- development and commercialization of SEL-212, including both composition of matter and method of treatment claims (there are three patent families that cover the SEL-212 product, one of which is a licensed, issued U.S. patent that covers the SEL-212 product, which expires in 2021); and
- methods and compositions incorporating our proprietary SVP nanoparticle in a variety of cancer immunotherapy applications, including:
 - creating various cancer vaccines, and
 - combination treatments, including co-treatment with PD-1/PDL-1 checkpoint inhibitors.

Set forth below is a table indicating the expiration dates for our owned patent families, or expected expiration dates in the case of our owned patent application families, corresponding to each of our programs.

Program	Description	Patent Family(1)	Expiration(2)
Refractory and chronic tophaceous gout (SEL-212)	SVP-Rapamycin co-administered with pegsiticase	19	2032-2035
Gene therapy	SVP-Rapamycin co-administered with AAV vector	19	2032-2035
Food allergy	SVP-adjuvant and SVP-food allergen	13	2032-2035
Celiac disease	SVP-Rapamycin and SVP-gluten	13	2032-2035
Type 1 diabetes	SVP-Rapamycin and SVP-insulin	15	2032-2035
Smoking cessation and relapse prevention (SEL-070)	SVP-adjuvant and SVP-nicotine	6	2030-2032
HPV-associated cancer (SEL-701)	SVP-adjuvant and SVP-HPV antigen	6	2030-2032
Malaria	SVP-adjuvant and SVP-malaria antigen	6	2030-2032

(1) Reflects number of relevant patent and patent application families.

(2) Reflects expiration date and estimated expiration date ranges of issued patents and patent applications, respectively.

In addition, we have exclusively or non-exclusively licensed intellectual property, including the following patent portfolio: 18 U.S. issued patents; 16 foreign issued patents; 9 U.S. pending patent applications; and 56 foreign pending applications. The licensed patents and patent applications cover

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various aspects of the technology being developed by us, including claims directed to compositions of matter and methods of use, and have been filed in various countries worldwide including in North America, Europe and Asia, with material expiration dates varying from 2021 to, if claims are issued, 2028.

As we continue to develop the SVP-based immunotherapy program technology, we intend to pursue, when possible, patent protection for product candidates, methods of use and processes for manufacture. We continually evaluate and enhance our intellectual property strategy as we develop new program technologies and product candidates. To that end, we are prepared to file additional patent applications if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. In addition to filing and prosecuting patent applications in the United States, we often file analogous patent applications in the European Union and in additional foreign countries where we believe such filing is likely to be beneficial, including but not limited to Australia, Brazil, China, Eurasia, including the Russian Federation, Europe, South Korea, Mexico, India, Israel and Japan.

Each patent's term depends upon the laws of the countries in which they are obtained. The patent term in most countries in which we file is 20 years from the earliest date of filing of a non-provisional patent application. Notably, the term of U.S. patents may be extended due to delays incurred due to compliance with FDA or by delays encountered during prosecution that are caused by the USPTO. For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent, depending upon the length of time the drug is under regulatory review. There is a limit to the amount of time a patent may be extended in the United States; no patent extension can extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar patent term extensions are available in Europe and other jurisdictions for patents that cover regulatory-approved drugs. We intend to apply for patent term extensions on patents covering our product candidates if and when they receive FDA approval. We expect to seek patent term extensions to any of our issued patents in any jurisdiction where these are available; however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Currently, we own or license patents with material expiration dates ranging from 2021 to 2032. If patents are issued on pending patent applications that we own or license, the resulting patents are expected to have material expiration dates ranging from 2027 to 2035. However, the actual patent protection period varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Generally, the patent positions of companies similar to ours are uncertain and encompass complex legal and factual questions. There has been no consistent policy regarding the scope of claims allowable in patents in the field of immunotherapy in the United States. The foreign patent situation is even more uncertain. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the United States and other countries may lessen our ability to protect our intellectual property and enforce our proprietary rights, and more generally could affect the value of our intellectual property. Specifically, our ability to stop third parties from making, using, selling, offering to sell, or importing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining and enforcing patent claims that cover our program technology, inventions and improvements. With respect to both company-owned and in-licensed intellectual property, we cannot be certain that patents will be granted with respect to any of our pending patent

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applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially beneficial in protecting our programs and product candidates and the methods used to manufacture those programs and product candidates. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our programs or product candidates. The field of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our patented immunotherapy technology, programs and product candidates and practicing our proprietary technology. Our issued patents and those that may issue in the future may be challenged, invalidated, or circumvented, which could inhibit our ability to stop competitors from marketing related programs or product candidates or limit the length of the term of patent protection that we may have for our immunotherapy technology, programs and product candidates. Additionally, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. Consequently, we may have competition for our immunotherapy technology, programs and product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any economic advantage of the patent. For this and more comprehensive risks related to our proprietary technology, inventions, improvements, programs and product candidates, please see the section entitled "Risk factors—Risks related to our intellectual property."

We currently have three trademark registrations, one in the United States, one in Europe and one in Russia. We intend to file applications for trademark registrations in connection with our product candidates in various jurisdictions, including the United States.

We may also rely on trade secrets to protect our confidential and proprietary information. However, trade secrets are difficult to protect. Although we seek to protect our program technology and product candidates as trade secrets, in part, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators and advisors, third parties may independently discover substantially equivalent trade secrets or otherwise gain access to our trade secrets or disclose our technology. It is our policy to require our employees, contractors, consultants, collaborators and advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our confidentiality and other agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors require them to assign or grant us licenses to inventions they invent as a result the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

We also seek to protect the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach.

COMPETITION

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our SVP technology, our expertise in triggering antigen-specific immune responses, integrated research, clinical and manufacturing capabilities, development experience, scientific knowledge and portfolio strategy provide us with competitive advantages, we face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of SEL-212, and any other tolerance or immune stimulation product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products. SEL-212 may compete with others in the gout market, including Krystexxa, which contains a pegylated uricase similar to the Pegsiticase component of SEL-212 and is indicated for the treatment of refractory gout. Horizon Pharma plc, whose affiliates recently acquired Krystexxa, may find other approaches to eliminate undesired immunogenicity to Krystexxa. Long-term treatment with global immunosuppressive products may increase the susceptibility to contract infections, tumors and may lead to organ failure. Large companies with active research to prevent the formation of ADAs and treat allergies or autoimmune diseases include Sanofi, Pfizer Inc., or Pfizer, and Merck & Co., Inc., or Merck. Small, early-stage biopharmaceutical companies active in the research for new technologies to induce antigen-specific tolerance include Anokion SA, Cour Pharmaceutical Development Company, Inc., Apitepe International NV, Evotec AG and Dendright International, Inc. We believe that desensitization strategies are restricted to allergies, take more time to achieve a therapeutic effect than therapies that use an immuno-modulator and are more restricted in breadth of efficacy and applications than SVP products.

Our immunostimulatory therapies are also subject to intense competition. In cancer therapy, the most common methods of treating patients are surgery, radiation and drug therapy, including chemotherapy and immunotherapy. Large pharmaceutical companies, including AstraZeneca PLC, or AstraZeneca, Roche Holding AG, Pfizer, Merck, Bristol-Myers Squibb Company, and Amgen Inc., as well as smaller biopharmaceutical companies including Immune Design Corp. are active in the research and

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development of cancer vaccines. There are a variety of vaccine approaches to treat HPV-associated cancer including the use of DNA vaccines, novel adjuvants, novel antigens and novel delivery vectors for the antigen. Clinical-stage companies with these approaches include, among others, Inovio Pharmaceuticals, Inc., in Phase 2 clinical development with VGX3100, ISA Pharmaceuticals, B.V., in Phase 2 clinical development with ISA-101, Genticel, in Phase 2 clinical development with GTL001, and AstraZeneca, in Phase 1 clinical development with INO-3112, which it licensed from Inovio Pharmaceuticals, Inc. We believe that our approach shares the safety of approved vaccine technologies that use antigens and adjuvants and could be synergistic with the use of checkpoint inhibitors such as PD-1 and PD-L1 inhibitors.

We are also competing in the development of new prophylactic vaccines with large pharmaceutical companies such as Sanofi, Pfizer, Merck, GlaxoSmithKline Pharmaceuticals Ltd, Johnson & Johnson, and AstraZeneca and smaller biopharmaceutical companies such as Genocea Biosciences, Inc. and Novavax Inc.

GOVERNMENT REGULATION

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Our most advanced product candidate, SEL-212, is subject to regulation in the United States as a combination product. If marketed individually, each component would be subject to different regulatory pathways and would require approval of independent marketing applications by the FDA. A combination product, however, is assigned to a Center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of our SEL-212, we believe that the primary mode of action is attributable to the biologic component of the product. In the case of SEL-212, which we believe will be regulated as a therapeutic biologic, the FDA's Center for Drug Evaluation and Research, or CDER, will have primary jurisdiction over premarket development. The CDER currently has regulatory responsibility, including premarket review and continuing oversight, over certain therapeutic biologic products that were previously regulated by the Center for Biologics Evaluation and Research, or CBER. We expect to seek approval of SEL-212 through a single Biologics License Application, or BLA, reviewed by CDER, and we do not expect that the FDA will require a separate marketing authorization for each constituent of SEL-212.

Biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. SEL-212 and any other product candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries.

U.S. biological products development process

The process required by the FDA before a biologic, including a gene therapy, may be marketed in the United States generally involves the following:

- completion of extensive nonclinical testing, sometimes referred to as preclinical testing, including laboratory tests, animal trials and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLPs, and applicable requirements for humane use of laboratory animals;

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- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practice, or GCP, regulations and any additional requirements for the protection of human research subjects and their health information, to establish the safety, purity and potency of the proposed biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to expected benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

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Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase I.* The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase II.* The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase III.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labelling.

Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA or the sponsor or its data safety monitoring board may suspend a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products

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whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. review and approval processes

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

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Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than the applicant interprets the same data. If the FDA decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase IV clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of standard BLAs in 10 months from the filing date and 90% of priority BLAs in six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Orphan designation

The FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the United States. Orphan designation must be requested before submitting a BLA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application

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to market the same product for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

We have not requested orphan designation for our product candidates, but depending on the proposed indication for which we intend to develop our future products, we may in the future request such designation.

Expedited development and review programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a biological product subject to accelerated approval perform adequate and well-controlled post-marketing clinical studies. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the

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commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In addition, under the provisions of FDASIA, the FDA established a Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. Requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Even if we receive one of these designations for our product candidates, the FDA may later decide that our product candidates no longer meet the conditions for qualification. In addition, these designations may not provide us with a material commercial advantage.

Gene therapy products

With respect to any gene therapy products we may develop, the FDA works closely with the NIH and its Recombinant DNA Advisory Committee, or RAC, a federal advisory committee that discusses protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. Where a gene therapy study is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, prior to the submission of an IND to the FDA, a protocol and related documentation is submitted to and the study is registered with the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA, however many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The FDA also has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy clinical trials for delayed adverse events, potency testing, and chemistry, manufacturing and control information in gene therapy INDs.

The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public. With gene therapy protocols, if the FDA allows the IND to proceed, but the RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process.

In addition, there is a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events in these trials.

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Post-approval requirements

Maintaining substantial compliance with applicable federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include record-keeping requirements, reporting of adverse effects and reporting updated safety and efficacy information.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labelling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain GMP compliance. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Biosimilars and exclusivity

The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, only one biosimilar has been licensed under the BPCIA, although numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be

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expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for certain biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and only beginning to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

Government regulation outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the European Union, for example, a clinical trial authorization, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical study development may proceed.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

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In the European Economic Area, or EEA, which is composed of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of MAs.

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210 days review period is reduced to 150 days.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

To obtain regulatory approval of an investigational biological product under European Union regulatory systems, we must submit a marketing authorization application, which is similar to the U.S. BLA. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of

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a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if the:

- second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- applicant consents to a second orphan medicinal product application; or
- applicant cannot supply enough orphan medicinal product.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Other healthcare laws

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the biopharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security, and physician payment transparency laws.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions

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and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the ACA to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved (e.g., off-label) uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, the ACA broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that

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a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties of up to an aggregate of \$150,000 per year and up to an aggregate of \$1 million per year for "knowing failures." Covered manufacturers must submit reports by the 90th day of each calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices, and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to, as well as imposed certain other privacy obligations on, "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

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Coverage and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological products for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations.

The process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

Healthcare reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs

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coverage under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and imposed an annual excise tax of 2.3% on any entity that manufactures or imports medical devices, which was suspended from January 1, 2016, to December 31, 2017, by the Consolidated Appropriations Act of 2016, but will be reinstated starting January 1, 2018, absent further action.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

Additionally, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the fiscal years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013 and, due to the Bipartisan Budget Act of 2015, will stay in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and imaging centers.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

FACILITIES

Our headquarters are located in Watertown, Massachusetts, where we occupy 27,833 square feet of office and laboratory space. The term of the lease expires on March 31, 2017. We also lease approximately 2,500 square feet of office and laboratory space in Moscow, Russia on a month to month basis.

EMPLOYEES

As of March 31, 2016, we had 54 full-time employees, 44 of whom were primarily engaged in research and development activities. A total of 25 employees have an M.D. or Ph.D. degree. None of our employees is represented by a labor union and we consider our employee relations to be good.

Management

EXECUTIVE OFFICERS, KEY EMPLOYEE, DIRECTORS AND DIRECTOR NOMINEE

The following table sets forth the name, age and position of each of our executive officers, key employee, directors and director nominee as of June 8, 2016.

Name	Age	Position
Executive Officers		
Werner Cautreels, Ph.D.	63	President and Chief Executive Officer and Director
Lloyd Johnston, Ph.D.	48	Chief Operating Officer and Senior Vice President, Research and Development
Takashi Kei Kishimoto, Ph.D.	56	Chief Scientific Officer
Peter Keller, M.Sci.	45	Chief Business Officer
David Abraham, J.D.	50	Chief Compliance Officer, General Counsel and Corporate Secretary
Earl Sands, M.D.	58	Chief Medical Officer
David Siewers, CPA	62	Chief Financial Officer
Other Key Employee		
Dmitry Ovchinnikov, Ph.D.	38	General Director, Selecta RUS
Directors and Director Nominee		
Omid Farokhzad, M.D.(3)	47	Director
Carl Gordon, Ph.D.(1)	51	Director
Peter Barton Hutt, LL.B., LL.M.(2)	81	Director
Edwin M. Kania(1)(2)	58	Director
Robert Langer, Sc.D.(4)	67	Director
Amir Nashat, Sc.D.(1)(3)	43	Director
Aymeric Sallin, M.S.(2)	42	Director
Leysan Shaydullina, M.D.(4)	37	Director
George Siber, M.D.(4)	71	Director
Timothy A. Springer, Ph.D.(3)(5)	68	Director Nominee

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

(4) Each of Drs. Langer and Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part. Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering.

(5) Dr. Springer will be elected to our board of directors contingent upon, and effective upon, the effectiveness of the registration statement of which this prospectus forms a part.

EXECUTIVE OFFICERS AND KEY EMPLOYEES

Werner Cautreels, Ph.D. has served as our President, Chief Executive Officer and member of our board of directors since July 2010. Prior to joining Selecta, Dr. Cautreels was Chief Executive Officer of Solvay Pharmaceuticals, the pharmaceuticals division of the Solvay Group, in Brussels, Belgium, from 2005 until Solvay Pharmaceuticals was acquired by Abbott Laboratories in February 2010.

Management

Before becoming the CEO of Solvay Pharmaceuticals, Dr. Cautreels was their Global Head of R&D from 1998. Prior to joining Solvay, he was employed by Sanofi, Sterling-Winthrop from 1979 to 1994, and Nycomed-Amersham from 1994 to 1998 in a variety of R&D management positions in Europe and in the United States. Dr. Cautreels was a director of Innogenetics NV in Gent, Belgium and ArQule Inc., in Woburn, Massachusetts from 1999 to 2006. He currently serves as a director of Seres Therapeutics, Inc. and Galapagos NV, in Mechelen, Belgium. He was the President of the Belgian-Luxemburg Chamber of Commerce for Russia and Belarus until June 2010. Dr. Cautreels received his Ph.D. in Chemistry, specializing in Mass Spectrometry, from the University of Antwerp (Antwerp, Belgium), and his financial and business training from the Advanced Management Program at Harvard Business School.

Lloyd Johnston, Ph.D. has served as our Chief Operating Officer and Senior Vice President, Research and Development since January 2014. Dr. Johnston served as Selecta's Senior Vice President of Pharmaceutical Research, Development and Operations from 2011 to 2013 and Vice President of Pharmaceutical Research from July 2008 to 2011. Prior to joining Selecta, Dr. Johnston was Vice President of Operations for Alkermes, Inc. from 2004 to 2008, and served in several roles, including Director of Manufacturing, from 1999 to 2004, with responsibility for process development, scale-up, and clinical manufacturing for pulmonary and sustained release injectable products, as well as leadership of Alkermes' manufacturing facility in Chelsea, MA. At Alkermes, Dr. Johnston was also a project leader and member of Steering Committees for numerous products through various stages of development from Phase 1 through registration. Dr. Johnston was an original member of Advanced Inhalation Research Inc., or AIR, a private company formed in 1998 and acquired by Alkermes in 1999. Prior to joining AIR, Dr. Johnston was a lecturer in the Department of Chemical Engineering at the University of New South Wales in Sydney, Australia. He received his B.Sc. in Chemical Engineering from Queen's University in Ontario, Canada, and his M.S. and Ph.D. in Chemical Engineering from MIT.

Takashi Kei Kishimoto, Ph.D. has served as our Chief Scientific Officer since June 2011. Prior to joining Selecta, Dr. Kishimoto was Vice President of Discovery Research at Momenta Pharmaceuticals, Inc., where he served in several leadership positions from March 2006 to June 2011 and led a multidisciplinary team in advancing both novel and complex generic products for inflammation, oncology, and cardiovascular disease. He served as Senior Director of Inflammation Research at Millennium Pharmaceuticals, Inc. from 1999 to 2006, where he provided the scientific leadership for four programs in clinical development, and as an Associate Director of Research at Boehringer Ingelheim Pharmaceuticals. Dr. Kishimoto has published over 50 peer-reviewed articles in scientific journals, including Nature, Science, Cell and the New England Journal of Medicine. Dr. Kishimoto received his B.A. from New College of the University of South Florida and his Ph.D. in Immunology from Harvard University.

Peter Keller, M.Sci. has served as our Chief Business Officer since he joined Selecta from Abbott Laboratories in February 2011. After the acquisition of Solvay Pharmaceuticals in February 2010 by Abbott Laboratories, he led the integration process for five R&D and manufacturing facilities in Europe. Before the acquisition, Mr. Keller was Vice President, Head of Mergers & Acquisitions and Alliance Management at Solvay Pharmaceuticals from March 2007 to February 2010, where he negotiated license and acquisition agreements in various therapeutic areas such as vaccines, neurology, and cardiology. He was the lead negotiator for the \$1.5 billion fenofibrate alliance between Solvay Pharmaceuticals and Abbott Laboratories and instrumental in the \$6.2 billion acquisition of Solvay Pharmaceuticals by Abbott Laboratories. Mr. Keller previously worked in management consulting at McKinsey & Company from October 2000 to February 2007 and Simon Kucher & Partners from July

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1998 to September 2000. Mr. Keller received his M.Sci. in Industrial Engineering and Management from the Technical University of Karlsruhe in Karlsruhe, Germany.

David Abraham, J.D. has served as our General Counsel and Corporate Secretary since he joined Selecta in May 2011. From January 2009 to April 2011, Mr. Abraham was a member of Innovation Legal Group, a boutique intellectual property law firm. From August 2006 to December 2008, Mr. Abraham was Executive Director for Patents at Durect Corporation, a small-cap specialty pharmaceutical company. From February 2004 to August 2006, he was Senior Patent Counsel for ALZA Corporation, or ALZA, a Johnson & Johnson company. Prior to working at Durect and ALZA, Mr. Abraham was employed by the law firms of Wilson Sonsini Goodrich and Rosati, and Finnegan Henderson Farabow Garrett and Dunner. Mr. Abraham also was a Patent Examiner at the USPTO. Mr. Abraham received his B.S. in Chemical Engineering from the University of Rochester and his J.D. from the George Washington School of Law.

Earl Sands, M.D. has served as our Chief Medical Officer since July 2015. From July 2014 to May 2015, Dr. Sands served as the Chief Medical Officer of Targacept, Inc., now part of Catalyst Biosciences, a biopharmaceutical company focused on protease therapeutic agents, where he was responsible for providing strategic and scientific input on intellectual property matters and in-licensing opportunities. From 2013 to 2014, Dr. Sands was the Chief Medical Officer of Plasma Surgical, Inc., a developer of surgical and therapeutic applications, where he was responsible for strategic integrated clinical development plans and execution. From 2011 to 2013, Dr. Sands served as President of Alpha Med Solutions, LLC, a consulting firm. From 2003 to 2011, Dr. Sands served in various capacities at Solvay Pharmaceuticals, both prior to and following the acquisition by Abbott Laboratories, including Executive Vice President, Market Access, from 2008 to 2011, Senior Vice President of R&D and acting Chief Medical Officer from 2006 to 2008, and Director of Women's Health from 2003 to 2006. Previously, Dr. Sands served as Senior Regional Medical Director, Professional and Scientific Relations, at Procter & Gamble Pharmaceuticals, was a founding partner and medical director at Innovation in Medical Education and Training, was a Managing Partner of Women's Health Care, PC and was Chairman of the OB/GYN department at Pottstown Memorial Medical Center in Pottstown, Pennsylvania. Dr. Sands received his B.A. in Premedical Sciences from Lehigh University and his M.D. from Hahnemann University School of Medicine.

David Siewers has served as our Chief Financial Officer since September 2009. Mr. Siewers has 30 years of experience in financial management, financial systems design and implementation, equity and debt financing and mergers and acquisitions. Prior to joining Selecta, Mr. Siewers was an independent consultant from 2002 to 2009, providing strategic guidance and tactical implementation of accounting systems, management and regulatory reporting, internal controls, profitability and cost analysis to an array of clients ranging from startups to mid-level companies. Previously, Mr. Siewers held various positions in the financial services industry, including Senior Vice President and Divisional Chief Financial Officer roles within Fleet Financial Group and Senior Vice President of Putnam Investments. Mr. Siewers received his B.S. in Accounting from Marietta College and received his CPA in 1978 while working at KPMG.

OTHER KEY EMPLOYEES

Dmitry Ovchinnikov, Ph.D. has served as the General Director of our Russian operations since August 2013, and served as General Deputy Director from May 2012 to August 2013. Prior to joining Selecta, Dr. Ovchinnikov was a medical director for ZAO Sandoz (Russia), a Novartis company, from December 2010 to May 2012, and was responsible for medical support and compliance, clinical trials and pharmacovigilance. Dr. Ovchinnikov was also a member of the Russia executive committee at Sandoz and took part in the elaboration of development strategy for the Russian branch. From

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November 2006 to December 2010, Dr. Ovchinnikov worked at Janssen-Cilag, a Johnson & Johnson company, as a medical manager for Russia and the Commonwealth of Independent States, and from December 2004 to November 2006 he served as a clinical research associate for PAREXEL RUS LLC, a life sciences consulting firm and a division of PAREXEL International. Dr. Ovchinnikov received his M.S. and Ph.D. in Biochemistry/Oncology/Virology from Lomonosov Moscow State University in Moscow, Russia.

DIRECTORS

Omid Farokhzad, M.D. is one of our co-founders and has served as a member of our board of directors since 2007. Dr. Farokhzad is an Associate Professor at Harvard Medical School, or HMS and a physician-scientist in the Department of Anesthesiology at Brigham and Women's Hospital, or BWH, positions he has held since 2004. Dr. Farokhzad directs the Laboratory of Nanomedicine and Biomaterials at BWH. Prior to joining the HMS faculty, Dr. Farokhzad completed his postgraduate clinical and postdoctoral research trainings, respectively, at BWH/HMS and MIT in the laboratory of Dr. Langer. He is the recipient of the 2013 RUSNANOPRIZE. Dr. Farokhzad has been directly involved in the launch and development of four biotechnology companies and, on occasion, has assumed additional roles in support of management. From 2006 to 2014, Dr. Farokhzad served on the Board of Directors of BIND Therapeutics, Inc. He received his M.D. and M.A. from Boston University School of Medicine, and his M.B.A. from MIT. Dr. Farokhzad's extensive knowledge of our business and the nanomedicine field and his medical training contributed to our board of directors' conclusion that he should serve as a director of our company.

Carl Gordon, Ph.D. has served as a member of our board of directors since 2010. Dr. Gordon serves as General Partner and Co-Head of Private Equity of OrbiMed Advisors LLC, which he co-founded in 1998. From 1995 to 1997 he was a senior biotechnology analyst at Mehta and Isaly, and from 1993 to 1995 he was a Fellow at The Rockefeller University. Dr. Gordon currently serves on the board of directors of numerous private companies. Previously, Dr. Gordon had served on the board of directors of Acceleron Pharma Inc., Amarin Corporation plc and Pacira Pharmaceuticals, Inc. Dr. Gordon received his B.S. in Chemistry from Harvard College and his Ph.D. in Molecular Biology from MIT. Dr. Gordon's venture capital experience, expertise in the scientific field of molecular biology and financial credentials contributed to our board of directors' conclusion that he should serve as a director of our company.

Peter Barton Hutt, LL.B., LL.M. has served as a member of our board of directors since 2010. Mr. Hutt is a senior counsel in the Washington, D.C. law firm of Covington & Burling specializing in food and drug law. Mr. Hutt began his law practice with the firm in 1960 and, except for his four years in the government, has continued at the firm ever since. Mr. Hutt served as Chief Counsel for the FDA during 1971 to 1975. Since 1994 he has taught a course on Food and Drug Law at Harvard Law School. Mr. Hutt serves on the board of directors of Seres Therapeutics, Inc., Xoma Corp., BIND Therapeutics, Inc., Concert Pharmaceuticals, Inc., Flex Pharma, Inc. and Q Therapeutics, Inc. From 2009 to 2015, Mr. Hutt served on the board of directors of DBV Technologies, from 2001 to 2014 he served on the board of Momenta Pharmaceuticals, Inc., from 2008 to 2011, he served on the board of Celera Corp and from 2002 to 2012 he served on the board of ISTA Pharmaceuticals, Inc. Mr. Hutt received his B.A. from Yale University, his LL.B. from Harvard Law School and his LL.M. from New York University. Mr. Hutt's extensive knowledge of and experience with food and drug law and his service on numerous boards of directors in the biotechnology and pharmaceutical industries contributed to our board of directors' conclusion that he should serve as a director of our company.

Edwin M. Kania has served as a member of our board of directors since 2013. Mr. Kania is Co-Founder of Flagship Ventures, a Boston-based venture capital firm, and serves as a Managing

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Partner for several of its funds. He served as Chairman of Flagship Ventures between 2001 and 2014. Prior to co-founding Flagship Ventures in 2000, Mr. Kania was a General Partner at OneLiberty Ventures and its predecessor firm, Morgan Holland Ventures. His direct investment experience covers over 100 companies. Since 2004, he has served on the board of directors of Acceleron Pharma Inc., a clinical stage biopharmaceutical company that focuses on regulating cellular growth. Mr. Kania has also served on the boards of Aspect Medical, EXACT Sciences and other public and private companies. Mr. Kania received his B.S. in Physics from Dartmouth College and his M.B.A. from Harvard Business School. Mr. Kania's extensive investment experience in the biotechnology sector contributed to our board of directors' conclusion that he should serve as a director of our company.

Robert Langer, Sc.D. is one of our co-founders and has served as a member of our board of directors since 2007. Dr. Langer also serves as Chairman of our scientific advisory board. Dr. Langer has been an Institute Professor at MIT since 2005, and prior to that was an Assistant Professor, Associate Professor and then Professor at MIT starting in 1977. Dr. Langer has received the National Medal of Science, National Medal of Technology and Innovation, Wolf Prize in Chemistry, Charles Stark Draper Prize, Albany Medical Center Prize in Medicine and Biomedical Research and the Lemelson-MIT Prize for Invention and Innovation. Dr. Langer is one of the very few individuals ever elected to the American Institute of Medical and Biological Engineering, the National Academy of Engineering and the National Academy of Sciences. He currently serves on the board of directors of Ocata Therapeutics, BIND Therapeutics, Inc. and PureTech Health PLC, and previously served as a director of Momenta Pharmaceuticals from 2001 to 2009, Wyeth from 2004 to 2009, Fibrocell Science, Inc. from 2010 to 2012 and Millipore Corp from 2009 to 2010. Dr. Langer received his B.S. from Cornell University and his Sc.D. from MIT, both in Chemical Engineering. Dr. Langer's pioneering academic work in nanotechnology and drug delivery contributed to our board of directors' conclusion that he should serve as a director of our company. Dr. Langer will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part.

Amir Nashat, Sc.D. has served as a member of our board of directors since 2008. Dr. Nashat has been a Managing General Partner at Polaris Venture Partners, a venture capital firm, since 2009 and focuses on investments in the life sciences. He currently serves on the board of directors of Fate Therapeutics, Inc., BIND Therapeutics, Inc., aTyr Pharma, Inc. and several private companies. Dr. Nashat has also served as a director of Receptos, Inc., Adnexus Therapeutics, Inc. (acquired by Bristol-Myers Squibb Company) and other private companies. Dr. Nashat completed his Sc.D. as a Hertz Fellow in Chemical Engineering at MIT with a minor in biology under the guidance of Dr. Langer. Dr. Nashat earned both his M.S. and B.S. in materials science and mechanical engineering at the University of California, Berkeley. Dr. Nashat's extensive experience as a venture capitalist and board member to numerous companies in the biotechnology industry contributed to our board of directors' conclusion that he should serve as a director of our company.

Aymeric Sallin, M.S. has served as a member of our board of directors since 2008. Mr. Sallin has served as the Chief Executive Officer of NanoDimension, a venture capital firm, since 2002 and is the founder of that firm. Since 2014, Mr. Sallin has served as a strategic advisory board member of the École Polytechnique Fédérale de Lausanne, or EPFL. Since 2002, Mr. Sallin has worked to promote nanotechnology around the world, and has received the NSTI Fellow Award and 2012 EPFL Alumni award for his contribution to the field of nanotechnology. Mr. Sallin has worked to generate and close investments of hundreds of millions of dollars into several of NanoDimension's portfolio companies. He currently serves as a board member of View, Inc., CROCUS Technology and Tarveda Therapeutics. Mr. Sallin is also a member of the Swiss Academy of Technical Sciences. Mr. Sallin received his Masters in Physical Engineering from EPFL in Lausanne, Switzerland. Mr. Sallin's extensive knowledge

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of our business and the nanomedicine field contributed to our board of directors' conclusion that he should serve as a director of our company.

Leysan Shaydullina, M.D. has served as a member of our board of directors since April 2015. Since October 2014, Dr. Shaydullina has served as Managing Director of management company RUSNANO LLC. From April 2009 to October 2014, she served as Investment Director of JSC RUSNANO Management Company and then of RUSNANO management company. She also served as an associate at JSC RUSNANO from 2008 to 2009. In 2008, Dr. Shaydullina served as a senior consultant with Regionatistica LLC, a Russian-based consulting company. From 2004 to 2008, she was head of the investment department and manager of innovative projects at Innovative Technopark IDEA, or Technopark, a Russian-based business incubator. Prior to Technopark, in 2004, Dr. Shaydullina served as a senior health insurance expert at ROSNO, now part of Allianz Insurance, a Russian insurance provider, and served as a surgeon for the Children's Republican Clinical Hospital of the Ministry of Health in Russia from 2001 to 2003. Dr. Shaydullina received her M.B.A. from the Academy of National Economy under the Government of the Russian Federation, and her M.D. from Kazan State Medical University in Kazan, Russia. Dr. Shaydullina's experience in business strategy, managing investments and the life sciences industry contributed to our board of directors' conclusion that she should serve as a director of our company. Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering.

George Siber, M.D. has served as a member of our board of directors since 2009. Since 2008, Dr. Siber has served as an Adjunct Professor at John Hopkins University in the School of Public Health. From 1996 to 2006, Dr. Siber served in various capacities at Wyeth Lederle Vaccines and Wyeth Vaccines Research, including Executive Vice President and Chief Scientific Officer. While at Wyeth, Dr. Siber oversaw the development and approval of multiple widely-used childhood vaccines, including Prevnar, a pneumococcal vaccine which has achieved multibillion dollar revenues, Acel-Imune, an acellular pertussis vaccine, and Meningitec, a meningococcal meningitis vaccine. Prior to Wyeth, Dr. Siber was Director of the Massachusetts Public Health Biologic Laboratories and a Harvard Medical School Associate Professor of Medicine at Dana Farber Cancer Institute. During this time, Dr. Siber led the research and manufacturing of multiple vaccines and immune globulins including Respigam, a human immune globulin against respiratory syncytial virus. Dr. Siber has served as executive director and scientific advisory board chairman of Genocea Biosciences, Inc. since 2013, and served as executive chairman from 2007 to 2013. Dr. Siber received his B.Sc. from Bishop's University in Quebec, Canada, and received his M.D.C.M. from McGill University in Quebec, Canada. He completed his post-doctoral training in internal medicine at Rush-Presbyterian-St. Luke's Medical Center in Chicago and Beth Israel Deaconess Medical Center in Boston, and his post-doctoral training in infectious disease and vaccinology at Children's Hospital and Beth Israel, in affiliation with Harvard Medical School in Boston. We believe that Dr. Siber's experience in life sciences and vaccine industries and his experience overseeing the development of multiple vaccines qualified him to serve as a member of our board of directors. Dr. Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part.

Timothy A. Springer, Ph.D. will serve as a member of our board of directors contingent upon, and effective upon, the effectiveness of the registration statement of which this prospectus forms a part. Dr. Springer has served as a scientific advisor to us since December 2008. Since 1989, Dr. Springer has served as the Latham Family Professor at Harvard Medical School. He has also served as Senior Investigator in the Program in Cellular and Molecular Medicine at Boston Children's Hospital since 2012, and as Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School and Professor of Medicine at Boston Children's Hospital since 2011. Dr. Springer was the

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Founder of LeukoSite, a biotechnology company acquired by Millennium Pharmaceuticals in 1999. Dr. Springer received a B.A. from the University of California, Berkeley, and a Ph.D. from Harvard University. Dr. Springer's extensive knowledge of our business and the nanomedicine field contributed to our board of directors' conclusion that he should serve as a director of our company.

BOARD COMPOSITION AND ELECTION OF DIRECTORS

Director independence

Our board of directors currently consists of ten members. However, Drs. Langer and Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part. Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering. In addition, Dr. Springer will be elected to our board of directors contingent upon, and effective upon, the effectiveness of the registration statement of which this prospectus forms a part. Accordingly, upon the completion of this offering, our board of directors will consist of eight members. Our board of directors has determined that, of these eight directors, Carl Gordon, Peter Barton Hutt, Edwin Kania, Amir Nashat, Aymeric Sallin and Timothy Springer do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of The NASDAQ Stock Market LLC, or NASDAQ. There are no family relationships among any of our directors or executive officers.

Classified board of directors

In accordance with our restated certificate of incorporation that will go into effect upon the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the closing of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Carl Gordon, Edwin Kania and Timothy Springer, and their terms will expire at our first annual meeting of stockholders following this offering;
- the Class II directors will be Omid Farokhzad, Amir Nashat and Aymeric Sallin, and their terms will expire at our second annual meeting of stockholders following this offering; and
- the Class III directors will be Werner Cautreels and Peter Barton Hutt, and their terms will expire at the third annual meeting of stockholders following this offering.

Our restated certificate of incorporation, which will become effective upon the closing of this offering, will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company. Our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of our outstanding voting stock entitled to vote in the election of directors.

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BOARD LEADERSHIP STRUCTURE

Our board of directors is currently chaired by our President and Chief Executive Officer, Werner Cautreels. Our corporate governance guidelines provide that, if the chairman of the board is a member of management or does not otherwise qualify as independent, the independent directors of the board may or may not elect a lead director. Amir Nashat currently serves as our lead director. The lead director's responsibilities include, but are not limited to: presiding over all meetings of the board of directors at which the chairman is not present, including any executive sessions of the independent directors; approving board meeting schedules and agendas; and acting as the liaison between the independent directors and the chief executive officer and chairman of the board. Our corporate governance guidelines further provide the flexibility for our board of directors to modify our leadership structure in the future as it deems appropriate.

ROLE OF THE BOARD IN RISK OVERSIGHT

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

BOARD COMMITTEES

Our board of directors has established three standing committees—audit, compensation and nominating and corporate governance—each of which operates under a charter that has been approved by our board of directors. Upon the closing of this offering, each committee's charter will be available under the Corporate Governance section of our website at www.selectabio.com. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Audit committee

The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;

Management

- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- discussing our risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities Exchange Commission, or SEC, rules.

Effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part, the members of our audit committee will be Carl Gordon, Edwin Kania and Amir Nashat. Edwin Kania will serve as chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and The NASDAQ Global Market. Our board of directors has determined that Carl Gordon, Edwin Kania and Amir Nashat meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable listing standards of NASDAQ. Our board of directors has determined that Edwin Kania is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable NASDAQ rules and regulations.

Compensation committee

The compensation committee's responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to CEO compensation;
- determining our CEO's compensation;
- reviewing and approving, or making recommendations to our board with respect to, the compensation of our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis"; and
- preparing the annual compensation committee report required by SEC rules.

Effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part, the members of our compensation committee will be Peter Barton Hutt, Edwin Kania and Aymeric Sallin. Peter Barton Hutt will serve as chairperson of the committee. Our board of directors has determined that each of Peter Barton Hutt, Edwin Kania and Aymeric Sallin is independent under the applicable NASDAQ rules and regulations, is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act and is an "outside director" as that term is defined in Section 162(m) of the Code.

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Nominating and corporate governance committee

The nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become board members;
- recommending to our board of directors the persons to be nominated for election as directors and to each board committee;
- reviewing and making recommendations to our board of directors with respect to management succession planning;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors.

Effective upon the effectiveness of the registration statement of which this prospectus forms a part, the members of our nominating and corporate governance committee will be Omid Farokhzad, Amir Nashat and Timothy Springer. Amir Nashat will serve as the chairperson of the committee. Our board of directors has determined that Amir Nashat and Timothy Springer are independent under the applicable NASDAQ rules and regulations. Under the applicable NASDAQ rules, we are permitted to phase-in our compliance with the independent nominating and corporate governance committee requirements of NASDAQ as follows: (1) one independent member at the time of listing, (2) a majority of independent members within 90 days of listing and (3) all independent members within one year of listing. Within one year of our listing on The NASDAQ Global Market, we expect that Dr. Farokhzad will have resigned from our nominating and corporate governance committee and that any new director added to the nominating and corporate governance committee will be independent under the applicable NASDAQ rules.

Compensation committee interlocks and insider participation

No member of our compensation committee is or has been our current or former officer or employee. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2015.

Code of ethics and code of conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon the closing of this offering, our code of business conduct and ethics will be available under the Corporate Governance section of our website at www.selectabio.com. In addition, we intend to post on our website all disclosures that are required by law or the listing standards of NASDAQ concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Executive and director compensation

EXECUTIVE COMPENSATION

This section discusses the material components of the executive compensation program offered to our named executive officers identified below. For 2015, our named executive officers were:

- Werner Cautreels, Ph.D., President and Chief Executive Officer;
- Earl Sands, M.D., Chief Medical Officer; and
- Takashi Kishimoto, Ph.D., Chief Scientific Officer.

We are an "emerging growth company," within the meaning of the JOBS Act, and have elected to comply with the reduced compensation disclosure requirements available to emerging growth companies under the JOBS Act.

2015 SUMMARY COMPENSATION TABLE

Name and principal position	Year	Salary (\$)	Option awards \$(1)	Non-equity incentive plan compensation \$(2)	All other compensation \$(3)	Total
Werner Cautreels, Ph.D. President and Chief Executive Officer	2015	400,000	568,798	130,000	—	1,098,798
	2014	447,545	374,504	140,000	38,130	1,000,179
Earl Sands, M.D. Chief Medical Officer	2015	143,231(4)	388,147	40,000(4)	22,847	594,225
Takashi Kishimoto, Ph.D. Chief Scientific Officer	2015	290,000	92,266	85,000	3,400	470,666
	2014	275,000	90,101	80,000	3,400	448,501

- (1) Represents the aggregate grant date fair value of stock options computed in accordance with ASC Topic 718, excluding the effect of estimated forfeitures. For a description of the assumptions used in valuing these awards, see Note 11 to our audited financial statements included elsewhere in this prospectus.
- (2) Represents amounts earned under our annual performance based bonus program. For additional information, see "Performance Bonuses" below.
- (3) For Dr. Kishimoto, the 2015 amount represents our company's matching contributions to 401(k) plan accounts. For Dr. Sands, the amount represents \$3,400 in our company's matching contributions to his 401(k) plan account and \$19,447 in reimbursements for expenses incurred in 2015 for travel between his home in Georgia and our offices in Massachusetts.
- (4) Dr. Sands commenced employment with us in July 2015 and amounts shown reflect his partial year of employment with our company.

NARRATIVE DISCLOSURE TO SUMMARY COMPENSATION TABLE

The primary elements of compensation for our named executive officers are base salary, annual performance bonuses and equity-based compensation awards. The named executive officers also participate in employee benefit plans and programs that we offer to our other full-time employees on the same basis.

Base salaries

We pay our named executive officers a base salary to compensate them for the satisfactory performance of services rendered to our company. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. Base salaries for our named executive officers have generally been

Executive and director compensation

set at levels deemed necessary to attract and retain individuals with superior talent and were originally established in each named executive officer's employment agreement.

In early 2015, the compensation committee of our board of directors, or the Compensation Committee, approved an increase in Dr. Kishimoto's annual base salary from \$275,000 to \$290,000, effective January 1, 2015. Dr. Sands commenced employment with us in July 2015 and, pursuant to the terms of his employment agreement, was entitled to an initial annual base salary of \$280,000. Dr. Cautreels did not receive a base salary increase in 2015.

Our named executive officers' base salaries for 2015 were \$400,000 for Dr. Cautreels, \$280,000 for Dr. Sands and \$290,000 for Dr. Kishimoto.

In early 2016, our board of directors approved increases in the annual base salaries of our named executive officers. Following this increase, Dr. Cautreel's annual base salary is \$425,000, Dr. Sands' annual base salary is \$300,000 and Dr. Kishimoto's annual base salary is \$315,000.

Performance bonuses

We offer our named executive officers the opportunity to earn annual cash bonuses to compensate them for attaining short-term company and individual performance goals. Each named executive officer has an annual target bonus that is expressed as a percentage of his annual base salary. The 2015 target bonus percentage for our named executive officers was 25% of their respective base salaries. Dr. Sands' 2015 cash bonus was pro-rated for his partial year of employment with our company.

Our Compensation Committee, based upon the recommendation of our chief executive officer, establishes company performance goals each year and, at the completion of the year, determines actual bonus payouts after assessing company performance against these goals and each named executive officer's individual performance and contributions to the company's achievements. The 2015 company performance goals were based on attaining financing and business development milestones and the expansion of our business portfolio.

The actual cash bonuses earned by our named executive officers for 2015 are reported under the "Non-equity incentive award" column of the 2015 and 2014 Summary Compensation Table above.

Equity compensation

We grant stock options to our named executive officers as the long-term incentive component of their compensation. We have historically granted stock options to named executive officers when they commenced employment with us and have from time to time thereafter made additional grants as, and when, our board of directors determined appropriate to reward, retain or encourage particular named executive officers.

Our stock options have an exercise price at least equal to the fair market value of our common stock on the date of grant, as determined by our board of directors, and vest as to 25% of the underlying shares on the first anniversary of the date of grant and in equal monthly installments over the following 36 months, subject to the holder's continued employment with us and potential accelerated vesting in certain circumstances, including as described below for our named executive officers in the section titled "Potential payments upon a change in control." From time to time, our board of directors may also construct alternate vesting schedules as it determines are appropriate to motivate particular employees. Our stock options may be intended to qualify as incentive stock options under the Code and generally permit "early exercise" of any unvested portion in exchange for shares of restricted stock subject to the same vesting schedule as the stock option.

Executive and director compensation

We granted stock options in the following amounts to our named executive officers during 2015:

Named executive officer	2015 options granted (#)
Werner Cautreels, Ph.D.	123,076
Earl Sands, M.D.	102,564
Takashi Kishimoto, Ph.D.	12,820

These options were granted under our 2008 Equity Incentive Plan, or the 2008 Plan, with exercise prices equal to the fair market value on the date of grant, as determined by our board of directors, and are subject to our standard vesting schedule described above, except in the case of Dr. Cautreels' option, which vests in 48 equal monthly installments.

In connection with this offering, we adopted a 2016 Incentive Award Plan, or the 2016 Plan, to facilitate the grant of cash and equity incentives to our directors, employees (including our named executive officers) and consultants and to enable our company to obtain and retain the services of these individuals, which we believe is essential to our long-term success. Following the effective date of our 2016 Plan, we will not make any further grants under our 2008 Plan. However, the 2008 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. For additional information about the 2016 Plan, please see the section titled "2016 Incentive Award Plan" below.

Retirement, health, welfare and additional benefits

Our named executive officers are eligible to participate in our employee benefit plans and programs, including medical and dental benefits, flexible spending accounts, long-term care benefits, and short- and long-term disability and life insurance, to the same extent as our other full-time employees, subject to the terms and eligibility requirements of those plans. Dr. Sands is entitled to be reimbursed up to \$6,100 per month for expenses incurred for lodging and travel between his home in Georgia and our offices in Massachusetts while performing duties for us.

We sponsor a 401(k) defined contribution plan in which our named executive officers may participate, subject to limits imposed by the Code, to the same extent as our other full-time employees. Currently, we match 50% of contributions made by participants in the 401(k) plan up to a maximum company match of \$3,400 per year. All matching contributions are subject to vesting at the rate of 25% per year of service.

Executive and director compensation

OUTSTANDING EQUITY AWARDS AT 2015 FISCAL YEAR-END

Name	Vesting commencement date	Option awards			Stock awards		
		Number of securities underlying unexercised options (#) exercisable ⁽¹⁾	Number of securities underlying unexercised options (#) unexercisable	Option exercise price (\$)	Option expiration date	Number of securities that have not vested (#)	Market value of securities that have not vested (\$)
Werner Cautreels, Ph.D.	12/4/2015	123,076(2)	—	6.40	12/4/2025	—	—
	1/1/2014	57,692(3)	—	8.97	4/7/2024	—	—
	1/1/2013	16,613(3)	—	2.77	6/13/2023	—	—
	1/1/2013	—	—	—	—	5,895(5)	40,010
	1/1/2012	41,025(4)	—	3.44	3/29/2022	—	—
Earl Sands, M.D.	9/8/2015	102,563(3)	—	9.36	9/8/2025	—	—
Takashi Kishimoto, Ph.D.	1/1/2015	12,819(3)	—	9.36	2/21/2025	—	—
	1/1/2014	12,820(3)	—	8.97	4/7/2024	—	—
	1/1/2013	6,410(3)	—	2.77	6/13/2023	—	—
	7/11/2011	89,743(4)	—	2.77	9/7/2021	—	—

- (1) All stock options held by our named executive officers, whether vested or unvested, are immediately exercisable on the date of grant. Shares purchased upon exercise of an unvested option become restricted stock and are subject to our right of repurchase in the event the option holder's service with us terminates prior to the date the shares vest for a purchase price equal to the exercise price paid for the shares.
- (2) The option vests in 48 equal monthly installments, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting in the event of a termination without cause or resignation for good reason within 12 months following a change in control. As of December 31, 2015, all shares underlying the option were unvested.
- (3) The option vests as to 25% of the total shares underlying the option on the first anniversary of the vesting commencement date and in equal monthly installments over the ensuing 36 months, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting in the event of a termination without cause or resignation for good reason within 12 months following a change in control. As of December 31, 2015, (i) for Dr. Cautreels, 30,048 shares underlying the option with a January 1, 2014 vesting commencement date were unvested, and 4,153 shares underlying the option with a January 1, 2013 vesting commencement date were unvested; (ii) for Dr. Sands, 102,564 shares underlying the option with a September 8, 2015 vesting commencement date were unvested; and (iii) for Dr. Kishimoto, 12,819 shares underlying the option with a January 1, 2015 vesting commencement date were unvested, 6,677 shares underlying the option with a January 1, 2014 vesting commencement date were unvested, and 1,736 shares underlying the option with a January 1, 2013 vesting commencement date were unvested.
- (4) All shares underlying the option are fully vested.
- (5) Represents shares of restricted stock obtained upon early exercise of an option on November 30, 2013. The shares vest as to 25% of the total shares on the one year anniversary of the vesting commencement date and in equal monthly installments over the ensuing 36 months, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting in the event of a termination without cause or resignation for good reason within 12 months following a change in control.

EMPLOYMENT ARRANGEMENTS

We have entered into employment agreements with each of our named executive officers. Certain key terms of these agreements and letters are described below.

Dr. Cautreels, Dr. Kishimoto and Dr. Sands

We entered into an employment agreement with Dr. Cautreels in July 2010, with Dr. Kishimoto in June 2011 and with Dr. Sands in July 2015. The employment agreements are for unspecified terms and entitle Dr. Cautreels, Dr. Kishimoto and Dr. Sands to annual target bonus opportunities of 25% of their respective annual base salaries. Their current base salaries are discussed in more detail above in the section titled "Base salaries."

Executive and director compensation

In the event either of Dr. Cautreels, Dr. Kishimoto or Dr. Sands is terminated by us without "cause" or he resigns for "good reason," subject to his timely executing a release of claims in our favor, he is entitled to receive base salary continuation for a period of 9 months for Dr. Cautreels or 6 months for Dr. Kishimoto and Dr. Sands, payment of all bonuses earned but unpaid as of the date of termination and continued health coverage for a period of 9 months for Dr. Cautreels or 6 months for Dr. Kishimoto and Dr. Sands. If, however, any of Dr. Cautreels, Dr. Kishimoto or Dr. Sands begins a subsequent consulting or employment arrangement during the period in which he is otherwise entitled to receive these payments and benefits, then any cash compensation paid to him in connection with the subsequent arrangement will be credited towards any severance amounts owed by us and we will not be required to provide or pay for any benefits that are provided to him through the subsequent arrangement.

The employment agreements contain restrictive covenants pursuant to which each of Dr. Cautreels, Dr. Kishimoto and Dr. Sands has agreed to refrain from competing with us or soliciting our employees or consultants following his termination of employment for a period of one year. However, the restricted period will be extended to two years in the event the named executive officer is terminated by the company for "cause."

For purposes of the employment agreements, "cause" generally means Dr. Cautreels', Dr. Kishimoto's or Dr. Sands' commission of, or indictment or conviction of, any felony or any crime involving dishonesty, participation in any fraud against the company, intentional damage to any company property, misconduct which materially and adversely reflects upon the business, operations or reputation of the company, which misconduct has not been cured (or cannot be cured) within 10 days after the company gives written notice regarding such misconduct, or breach of any material provision of the employment agreement or any agreement between him and the company, which breach has not been cured (or cannot be cured) within 10 days after the company gives written notice regarding such breach.

For purposes of the employment agreements, "good reason" generally means, subject to certain cure rights, Dr. Cautreels', Dr. Kishimoto's or Dr. Sands' termination of his employment due to the company's breach of any one or more of the material provisions of the employment agreement, a material reduction by the company of his responsibilities or base salary, or, with respect to Dr. Cautreels and Dr. Kishimoto only, a relocation by the company of his place of employment by more than 40 miles.

POTENTIAL PAYMENTS UPON A CHANGE IN CONTROL

The agreements governing the named executive officers' unvested stock options provide for full accelerated vesting if the named executive officers' employment is terminated by us without cause or if they resign for good reason, in either case, within 12 months following a change in control.

RECENT DEVELOPMENTS REGARDING EXECUTIVE COMPENSATION

In May 2016, in anticipation of and subject to the consummation of this offering, our board of directors approved certain changes to our named executive officers' compensation arrangements. These included adjusting our named executive officers' target bonus opportunities, granting equity incentive awards and entering into new employment agreements, each as described in more detail below.

Target bonuses

Our board of directors approved increases to the target bonus amounts for our named executive officers to 45% of his base salary for Dr. Cautreels and 35% of his base salary for each of Drs. Sands and Kishimoto. The target bonus increases will become effective upon the closing of this offering.

Executive and director compensation

Equity incentive awards

Effective on the effectiveness of the registration statement of which this prospectus forms a part, our board of directors approved stock option grants under the 2016 Plan to our named executive officers in the following amounts: Dr. Cautreels: 115,384 shares, Dr. Sands: 53,999 shares and Dr. Kishimoto: 24,512 shares. The shares will have a per share exercise price equal to the initial public offering price of our common stock and will vest as to 25% of the total number of shares on the first anniversary of the grant date and in 36 substantially equal monthly installments thereafter.

Employment agreements

We have entered into new employment agreements with each of our named executive officers, effective on the closing of this offering.

The agreements entitle our named executives officers to continue to receive their current annual base salaries set forth above and to receive the new target bonus opportunities described above under the heading "Target Bonuses."

If we terminate Dr. Cautreels, Dr. Sands or Dr. Kishimoto without "cause" or he resigns for "good reason," subject to his timely executing a release of claims in our favor and continued compliance with a separate restrictive covenant agreement, he is entitled to receive (i) base salary continuation for a period of 12 months, (ii) a prorated portion of the annual bonus he would otherwise have earned for the year of termination, based on actual performance for the full year (or based on his target bonus if such termination occurs during the first quarter of the calendar year), and (iii) direct payment of or reimbursement for continued medical, dental or vision coverage pursuant to COBRA for up to 12 months. If such termination occurs within the 12 months following or the 60 days preceding a change in control, each named executive officer would be entitled to receive, in addition to the foregoing payments and benefits, accelerated vesting of such named executive officer's outstanding unvested company equity awards that vest solely based on the passage of time. The company must provide a named executive officer 30 days' notice, or pay in lieu of notice, in the event we terminate such named executive officer for any reason other than "cause".

For purposes of the new employment agreements, "cause" generally means, subject to applicable cure rights, the named executive officer's (i) commission of, or indictment or conviction of, any felony or any crime involving dishonesty; (ii) participation in any fraud against the company; (iii) intentional damage to any company property; (iv) misconduct which materially and adversely reflects upon the business, operations, or reputation of the company; or (v) breach of any material provision of the employment agreement or any other written agreement with the company. "Good reason" generally means, subject to the company's cure rights, the occurrence of any of the following, without the named executive officer's written consent (i) a material reduction in his base salary or target bonus opportunity; (ii) a material diminution in his authority, title, duties or areas of responsibility; (iii) the requirement that he report to someone other than the board of directors with respect to Dr. Cautreels or the chief executive officer with respect to Drs. Sands and Kishimoto; (iv) the relocation of his primary office to a location more than 40 miles from the Boston metropolitan area; or (v) a material breach by the company of the employment agreement or any other written agreement with the named executive officer.

We also expect to enter into non-disclosure, non-competition and assignment of intellectual property agreements with the named executive officers pursuant to which each of Drs. Cautreels, Sands and Kishimoto will agree to refrain from engaging in direct competition with us or soliciting our employees, in each case, while employed and following his termination of employment for any reason for a period of 12 months.

Executive and director compensation

INCENTIVE PLANS

The following summarizes the material terms of the incentive plans in which our employees, including the named executive officers, participate.

2016 Incentive Award Plan

Effective the day prior to the first public trading date of our common stock, we adopted and our stockholders approved the 2016 Incentive Award Plan, or the 2016 Plan, under which we may grant cash and equity-based incentive awards to eligible service providers in order to attract, retain and motivate the persons who make important contributions to our company. The material terms of the 2016 Plan are summarized below.

Eligibility and administration. Our employees, consultants and directors, and employees and consultants of our subsidiaries, will be eligible to receive awards under the 2016 Plan. The 2016 Plan will be administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under the 2016 Plan, Section 16 of the Exchange Act, stock exchange rules and other applicable laws. The plan administrator will have the authority to take all actions and make all determinations under the 2016 Plan, to interpret the 2016 Plan and award agreements and to adopt, amend and repeal rules for the administration of the 2016 Plan as it deems advisable. The plan administrator will also have the authority to determine which eligible service providers receive awards, grant awards and set the terms and conditions of all awards under the 2016 Plan, including any vesting and vesting acceleration provisions, subject to the conditions and limitations in the 2016 Plan.

Shares available for awards. An aggregate of 1,210,256 shares of our common stock will initially be available for issuance under the 2016 Plan. The number of shares initially available for issuance will be increased by an annual increase on January 1 of each calendar year beginning in 2017 and ending in and including 2026, equal to the least of (A) 4% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (B) a smaller number of shares determined by our board of directors. No more than 8,133,333 shares of common stock may be issued under the 2016 Plan upon the exercise of incentive stock options. Shares issued under the 2016 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under the 2016 Plan or the 2008 Plan expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2016 Plan. Awards granted under the 2016 Plan in substitution for any options or other stock or stock-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2016 Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive stock options.

Awards. The 2016 Plan provides for the grant of stock options, including incentive stock options, or ISOs, and nonqualified stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, dividend equivalents, restricted stock units, or RSUs, and other stock or cash based awards. Certain awards under the 2016 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under the 2016 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

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- *Stock options and SARs.* Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, in contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of a stock option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date (or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of a stock option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders). The maximum aggregate number of shares of common stock with respect to one or more options or SARs that may be granted to any one person during any fiscal year of the company will be .
- *Restricted stock and RSUs.* Restricted stock is an award of nontransferable shares of our common stock that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver shares of our common stock in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on shares of our common stock prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted stock and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2016 Plan.
- *Other stock or cash based awards.* Other stock or cash based awards are awards of cash, fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock or other property. Other stock or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other stock or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance criteria. The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the 2016 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on stockholders' equity; total stockholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value

Executive and director compensation

added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

Certain transactions. In connection with certain corporate transactions and events affecting our common stock, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2016 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2016 Plan and replacing or terminating awards under the 2016 Plan. In addition, in the event of certain non-reciprocal transactions with our stockholders, the plan administrator will make equitable adjustments to the 2016 Plan and outstanding awards as it deems appropriate to reflect the transaction.

Provisions of the 2016 Plan Relating to Director Compensation. The 2016 Plan provides that the plan administrator may establish compensation for non-employee directors from time to time subject to the 2016 Plan's limitations. Prior to commencing this offering, our stockholders approved the initial terms of our non-employee director compensation program, which is described below under the heading "Director Compensation." Our board of directors or its authorized committee may modify the non-employee director compensation program from time to time in the exercise of its business judgment, taking into account such factors, circumstances and considerations as it shall deem relevant from time to time, provided that the sum of any cash compensation or other compensation and the grant date fair value of any equity awards granted under the 2016 Plan as compensation for services as a non-employee director during any fiscal year may not exceed \$1,000,000 in the fiscal year of a non-employee director's initial service as a non-employee director or \$750,000 in any subsequent fiscal year. The plan administrator may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the plan administrator may determine in its discretion, subject to the limitations in the 2016 Plan.

Plan amendment and termination. Our board of directors may amend or terminate the 2016 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2016 Plan, may materially and adversely affect an award outstanding under the 2016 Plan without the consent of the affected participant and stockholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator can, without the approval of our stockholders, amend any outstanding stock option or SAR to reduce its price per share. The 2016 Plan will remain in effect until the tenth anniversary of its

Executive and director compensation

effective date, unless earlier terminated by our board of directors. No awards may be granted under the 2016 Plan after its termination.

Foreign participants, claw-back provisions, transferability and participant payments. The plan administrator may modify awards granted to participants who are foreign nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the 2016 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2016 Plan, and exercise price obligations arising in connection with the exercise of stock options under the 2016 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, shares of our common stock that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

2016 Employee Stock Purchase Plan

Effective the day prior to the first public trading date of our common stock, we adopted and our stockholders approved the 2016 Employee Stock Purchase Plan, or the 2016 ESPP. The material terms of the 2016 ESPP are summarized below.

Shares available for awards; administration. A total of 173,076 shares of our common stock will initially be reserved for issuance under the 2016 ESPP. In addition, the number of shares available for issuance under the 2016 ESPP will be annually increased on January 1 of each calendar year beginning in 2017 and ending in and including 2026, by an amount equal to the least of (A) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares as is determined by our board of directors, provided that no more than 1,903,846 shares of our common stock may be issued under the 2016 ESPP. The foregoing numbers are subject to adjustment in certain events, as described below.

Our board of directors or a committee of our board of directors will have authority to interpret the terms of the 2016 ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of the 2016 ESPP.

Eligibility. Our employees are eligible to participate in the 2016 ESPP if they are customarily employed by us or a participating subsidiary for more than 20 hours per week and more than five months in any calendar year. However, an employee may not be granted rights to purchase stock under our 2016 ESPP if such employee, immediately after the grant, would own (directly or through attribution) stock possessing 5% or more of the total combined voting power or value of all classes of our common or other class of stock.

Grant of rights. The 2016 ESPP is intended to qualify under Section 423 of the Code and stock will be offered under the 2016 ESPP during offering periods. The length of the offering periods under the 2016 ESPP will be determined by the plan administrator and may be up to 27 months long. Employee payroll deductions will be used to purchase shares on each purchase date during an offering period. The purchase dates for each offering period will be the final trading day in the offering period. Offering periods under the 2016 ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

The 2016 ESPP permits participants to purchase common stock through payroll deductions of up to 25% of their eligible compensation, which includes a participant's gross base compensation for services

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to us, including overtime payments and excluding sales commissions, incentive compensation, bonuses, expense reimbursements, fringe benefits and other special payments. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period, which, in the absence of a contrary designation, will be 6,410 shares. In addition, no employee will be permitted to accrue the right to purchase stock under the 2016 ESPP at a rate in excess of \$25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our common stock as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of our common stock. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the purchase date, which will be the final trading day of the offering period. Participants may voluntarily end their participation in the 2016 ESPP at any time at least one week prior to the end of the applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under the 2016 ESPP other than by will or the laws of descent and distribution.

Certain transactions. In the event of certain non-reciprocal transactions or events affecting our common stock known as "equity restructurings," the plan administrator will make equitable adjustments to the 2016 ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares of stock subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase stock on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

Plan amendment. The plan administrator may amend, suspend or terminate the 2016 ESPP at any time. However, stockholder approval of any amendment to the 2016 ESPP will be obtained for any amendment which increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the 2016 ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the 2016 ESPP or changes the 2016 ESPP in any manner that would cause the 2016 ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

2008 Plan

Our board of directors and stockholders have approved the 2008 Plan, under which we may grant stock options and restricted stock awards to employees, directors and consultants or advisors of our company or its affiliates. We had reserved a total of 2,213,412 shares of our common stock for issuance under the 2008 Plan as of June 8, 2016.

Following the effectiveness of the 2016 Plan, we will not make any further grants under the 2008 Plan. However, the 2008 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. Shares of our common stock subject to awards granted under the 2008 Plan

Executive and director compensation

that are forfeited, lapse unexercised or are settled in cash and which following the effective date of the 2016 Plan are not issued under the 2008 Plan will be available for issuance under the 2016 Plan.

Administration. Our board of directors administers the 2008 Plan and has the authority to issue awards under the 2008 Plan, to interpret the 2008 Plan and awards outstanding thereunder, to prescribe, amend and rescind rules and regulations relating to the 2008 Plan, to determine the terms and provisions of award agreements under the 2008 Plan, to correct any defect, omission or inconsistency in the 2008 Plan or in any award agreement, and to make all other determinations in the judgment of the board of directors that are necessary and desirable for the administration of the 2008 Plan. The board of directors may delegate its authority under the 2008 Plan to a committee of the board. Following the effectiveness of this offering, we expect that the board of directors will delegate its general administrative authority under the 2008 Plan to its Compensation Committee.

Types of awards. The 2008 Plan provides for the grant of non-qualified and incentive stock options and restricted stock awards to employees, directors and consultants or advisors of the company or its affiliates, except that stock options intended to qualify as incentive stock options under the Code may only be granted to employees. As of the date of this prospectus, awards of stock options and restricted stock are outstanding under the 2008 Plan.

Certain transactions. If certain changes are made in, or events occur with respect to, our common stock, the 2008 Plan and outstanding awards will be appropriately adjusted in the class, number and, as applicable, exercise price of securities as determined by the board of directors. In the event of certain corporate transactions, including a consolidation, merger, sale of all or substantially all of our assets or a liquidation, our board or the board of directors of any corporation assuming the obligations under the 2008 Plan, may, in its discretion, take any one or more of the following actions, as to some or all options outstanding under the 2008 Plan (and need not take the same action as to each such option): (i) provide for the assumption or substitution of the option; (ii) upon written notice to the optionee, provide for the termination of all unexercised options unless exercised within a specified period; (iii) in the event of a merger in which stockholders receive cash payment for shares surrendered, make or provide for a cash payment to optionees based on the difference between (A) the merger consideration times the number of shares subject to outstanding options and (B) the aggregate exercise price of the outstanding options, in exchange for termination of such options; and (iv) provide that all outstanding options shall become exercisable in part or in full immediately prior to such event. With respect to shares of restricted stock, any securities, cash or other property received in exchange for such shares shall continue to be governed by the provisions of any restricted stock agreement pursuant to which they were issued.

Amendment and termination. The board of directors may terminate, modify or amend the 2008 Plan from time to time, provided that any amendment or modification may not adversely affect the rights of a holder of an outstanding award without such holder's consent. The board of directors may amend or modify the 2008 Plan and any outstanding incentive stock options to the extent necessary to qualify any or all such options for favorable federal income tax treatment.

DIRECTOR COMPENSATION

While certain of our non-employee directors receive consulting fees under the terms of consulting agreements with our company, we have not historically paid cash fees to our non-employee directors for their service on our board but have, from time to time, granted stock options to non-employee directors and founders to compensate them for their board service. Dr. Cautreels, our President and Chief Executive Officer, also serves on our board of directors but receives no additional compensation for this service.

Executive and director compensation

Other than as set forth in the table below with respect to amounts earned under consulting agreements with certain directors, our non-employee directors did not receive any compensation for their service on our board of directors during 2015.

2015 DIRECTOR COMPENSATION TABLE

Name	Fees earned or paid in cash (\$)	Option awards (\$)	All other compensation (\$)(1)	Total (\$)
Omid Farokhzad, M.D.	—	—	147,000	147,000
Carl Gordon, Ph.D.	—	—	—	—
Peter Barton Hutt J.D., L.L.B., L.L.M	—	—	—	—
Edwin M. Kania	—	—	—	—
Robert Langer, Sc.D.(2)	—	—	75,000	75,000
Amir Nashat, Sc.D.	—	—	—	—
Aymeric Sallin, M.S.	—	—	—	—
Leysan Shaydullina, M.D.(2)(4)	—	—	—	—
George Siber, M.D.(2)	—	—	36,000	36,000
Yurii Udaltsov, Cand. Sc.(3)	—	—	—	—

- (1) Represents compensation earned in 2015 under the consulting agreements with the company and, with respect to Dr. Farokhzad, an additional \$72,000 pursuant to an unwritten arrangement. For additional information regarding these agreements, see "Certain relationships and related party transactions."
- (2) Drs. Langer and Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part. Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering.
- (3) Yurii Udaltsov resigned from our board of directors effective in April 2015.
- (4) Dr. Shaydullina joined our board of directors in April 2015.

The table below shows the aggregate number of option awards (exercisable and unexercisable) held by each non-employee director as of December 31, 2015. None of our non-employee directors held stock awards in our company as of that date.

Name	Options outstanding at fiscal year end
Omid Farokhzad, M.D.	61,913
Carl Gordon, Ph.D.	—
Peter Barton Hutt J.D., L.L.B., L.L.M	44,871
Edwin M. Kania	—
Robert Langer, Sc.D.(1)	73,451
Amir Nashat, Sc.D.	—
Aymeric Sallin, M.S.	—
Leysan Shaydullina, M.D.(1)	—
George Siber, M.D.(1)	31,574
Yurii Udaltsov, Cand. Sc.	—

- (1) Drs. Langer and Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part. Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering.

Effective upon the effectiveness of the registration statement of which this prospectus forms a part, we adopted and our stockholders approved a compensation program for our non-employee directors

Executive and director compensation

under which each non-employee director will receive the following amounts for their services on our board of directors:

- an option to purchase 12,820 shares of our common stock upon the director's initial election or appointment to our board of directors that occurs after our initial public offering,
- if the director has served on our board of directors for at least six months as of the date of an annual meeting of stockholders, an option to purchase 6,410 shares of our common stock on the date of the annual meeting;
- an annual director fee of \$35,000, and
- if the director serves on a committee of our board of directors, an additional annual fee as follows:
 - chairman of the board or lead independent director, \$15,000,
 - chairman of the audit committee, \$15,000,
 - audit committee member other than the chairman, \$7,500,
 - chairman of the compensation committee, \$10,000,
 - compensation committee member other than the chairman, \$5,000,
 - chairman of the nominating and corporate governance committee, \$7,500, and
 - nominating and corporate governance committee member other than the chairman, \$3,500.

Stock options granted to our non-employee directors under the program will have an exercise price equal to the fair market value of our common stock on the date of grant and will expire not later than ten years after the date of grant. The stock options granted upon a director's initial election or appointment will vest in substantially equal monthly installments over three years following the date of grant. The stock options granted annually to directors will vest in a single installment on the earlier of the day before the next annual meeting or the first anniversary of the date of grant. In addition, all unvested stock options will vest in full upon the occurrence of a change in control.

Director fees under the program will be payable in arrears in four equal quarterly installments not later than the fifteenth day following the final day of each calendar quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board and no fee will be payable in respect of any period prior to the effective date of the registration statement of which this prospectus is a part.

Each member of our board of directors is entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors and any committee of the board of directors on which he or she serves.

Certain relationships and related person transactions

The following includes a summary of transactions since January 1, 2013 to which we have been a party in which the amount involved exceeded or will exceed \$120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and director compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

PREFERRED STOCK FINANCINGS AND CONVERTIBLE NOTES FINANCING

Series D Preferred Stock Financing. Between April 7, 2014 and August 14, 2014, we sold to investors in private placements an aggregate of 3,211,105 shares of series D preferred stock at a purchase price of \$4.50 per share, for net aggregate consideration of approximately \$14.3 million.

Convertible Notes Financing. On April 10, 2015 and June 23, 2015, we sold to investors in private placements an aggregate of \$7.1 million of convertible promissory notes, or the 2015 notes. The 2015 notes accrued at an interest rate of 8%, compounding monthly. In connection with the series E preferred stock financing described below, the principal amount of the 2015 notes and accrued interest thereon was automatically converted into an aggregate of 1,619,550 shares of our series E preferred stock in August 2015.

Series E Preferred Stock Financing. On August 27, 2015, September 3, 2015 and September 17, 2015, we issued and sold to investors in private placements an aggregate 8,888,888 shares of our series E preferred stock at a purchase price of \$4.50 per share, for aggregate consideration of approximately \$40 million, including approximately \$7.3 million in principal and accrued interest under the 2015 notes that converted into shares of series E preferred stock.

The following table sets forth the aggregate number of shares of our capital stock acquired by beneficial owners of more than 5% of our capital stock in the financing transactions described above. Each share of our series D preferred stock identified in the following table will convert into 0.2683 shares of common stock upon the closing of this offering. Upon the closing of this offering, (i) our series E preferred stock will automatically convert into a number of shares of common stock and (ii) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. See "Prospectus summary—The offering" for a related offering price per share sensitivity analysis.

Participants	Series D preferred stock	Series E preferred stock
5% or Greater Stockholders(1)		
Entities affiliated with Polaris Venture Partners(2)	472,276	638,420(4)
Flagship Ventures Fund 2007, L.P.	461,922	487,532(5)
RUSNANO	314,353	781,322(6)
Entities affiliated with OrbiMed Advisors LLC(3)	149,894	1,798,762(7)
NanoDimension L.P.	159,752	363,006(8)
TAS Partners LLC and Leukon Partners, LP, as affiliated entities	219,580	637,952(9)

(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the caption "Principal stockholders."

Certain relationships and related person transactions

- (2) Represents securities acquired by Polaris Venture Partners V, L.P., Polaris Venture Partners Entrepreneurs' Fund V, L.P., Polaris Venture Partners Founders' Fund V, L.P. and Polaris Venture Partners Special Founders' Fund V, L.P.
- (3) Represents securities acquired by OrbiMed Private Investments III, LP and OrbiMed Associates III, LP.
- (4) Includes 416,198 shares of series E preferred stock issued upon conversion of an aggregate amount of \$1.9 million in principal and accrued interest of the 2015 notes.
- (5) Includes 407,076 shares of series E preferred stock issued upon conversion of an aggregate amount of \$1.8 million in principal and accrued interest of the 2015 notes.
- (6) Includes 259,100 shares of series E preferred stock issued upon conversion of an aggregate amount of \$1.2 million in principal and accrued interest of the 2015 notes.
- (7) Includes 132,096 shares of series E preferred stock issued upon conversion of an aggregate amount of \$0.6 million in principal and accrued interest of the 2015 notes.
- (8) Includes 140,784 shares of series E preferred stock issued upon conversion of an aggregate amount of \$0.6 million in principal and accrued interest of the 2015 notes.
- (9) Includes 193,509 shares of series E preferred stock issued upon conversion of an aggregate amount of \$0.9 million in principal and accrued interest of the 2015 notes.

Some of our directors and our director nominee are associated with our principal stockholders as indicated in the table below:

Director or director nominee	Principal stockholder
Amir Nashat, Sc.D.	Entities affiliated with Polaris Venture Partners
Edwin M. Kania	Flagship Ventures Fund 2007, L.P.
Leysan Shaydullina, M.D.(1)	RUSNANO
Carl Gordon, Ph.D.	Entities affiliated with OrbiMed Advisors LLC
Aymeric Sallin, M.S.	NanoDimension L.P.
Timothy A. Springer, Ph.D.(2)	TAS Partners LLC and Leukon Partners, LP, as affiliated entities

- (1) Dr. Shaydullina will resign from our board of directors contingent upon, and effective immediately prior to, the closing of this offering.
- (2) Dr. Springer will be elected to our board of directors contingent upon, and effective upon, the effectiveness of the registration statement of which this prospectus forms a part.

INVESTORS' RIGHTS AGREEMENT

We entered into an amended and restated investors' rights agreement in April 2014, which was further amended in July 2014, August 2015 and June 2016 with our directors Omid Farokhzad and Robert S. Langer, the holders of our preferred stock, including entities in which certain other of our directors are related, Ulrich von Andrian, a prior beneficial owner of 5% of our capital stock, and certain other stockholders. The agreement provides for certain rights relating to the registration of such holders' common stock, including shares issuable upon conversion of preferred stock, and a right of first refusal to purchase future securities sold by us. See "Description of capital stock—Registration rights" for additional information.

VOTING AGREEMENT

We entered into an amended and restated voting agreement in August 2015, by and among us and certain of our stockholders, pursuant to which the following directors were elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve: Amir Nashat Sc.D.; Edwin M. Kania Jr.; Aymeric Sallin; Carl L. Gordon, Ph.D.; Leysan Shaydullina; Robert S. Langer, Jr., Sc.D.; Omid Farokhzad, M.D.; Werner Cautreels, Ph.D.; Peter Barton Hutt; and George Siber, M.D. Pursuant to the voting agreement, Drs. Farokhzad, and Langer were initially

Certain relationships and related person transactions

selected to serve on our board of directors as representatives of holders of our common stock, as designated by a majority of our founders. Dr. Cautreels was initially selected to serve on our board of directors in his capacity as our Chief Executive Officer. Drs. Nashat and Gordon, Messrs. Kania and Sallin, and Dr. Shaydullina were initially selected to serve on our board of directors as representatives of holders of our preferred stock, as designated by Polaris Venture Partners IV, L.P., OrbiMed Private Investments III, LP, Flagship Ventures, NanoDimension L.P. and RUSNANO, respectively. Mr. Hutt and Dr. Siber were initially selected to serve on our board of directors as independent directors, as designated by a majority of the other directors.

In addition, pursuant to the voting agreement, we, as the sole equity holder of our Russian subsidiary, Selecta RUS, elected the following directors of Selecta RUS who, as of the date of this prospectus, continue to so serve: Leysan Shaydullina, M.D., Alexander Korchevskiy, Werner Cautreels, Ph.D., Lloyd Johnston, Ph.D. and Dmitry Ovchinnokov, Ph.D. Pursuant to the voting agreement, Drs. Werner Cautreels, Lloyd Johnston and Dmitry Ovchinnokov were selected to serve on the Selecta RUS board of directors, as designated by our board of directors. Mr. Korchevskiy was selected to serve on the Selecta RUS board of directors, as designated by VTB Capital I2BF Netherlands B.V., a Dutch limited company, and Selecta RKFN Ltd., a Russian limited liability company, or collectively I2BF. Dr. Shaydullina was selected to serve on the Selecta RUS board of directors, as designated by RUSNANO.

The voting agreement will terminate in its entirety in connection with this offering. The composition of our board of directors after this offering is described in more detail under "Management—Board composition and election of directors."

EMPLOYMENT AGREEMENTS

We have entered into employment agreements or offer letters with our named executive officers. For more information regarding the agreements with our named executive officers, see "Executive and director compensation—Executive compensation arrangements."

CONSULTING AGREEMENTS

We entered into consulting agreements with directors Omid Farokhzad, Robert Langer and George Siber, and Ulrich von Andrian. Each of Drs. Langer and Siber will resign from our board of directors contingent upon, and effective immediately prior to, the effectiveness of the registration statement of which this prospectus forms a part.

The consulting agreements provide for annual payments of \$75,000 for each of Drs. Farokhzad, Langer and von Andrian and \$36,000 for Dr. Siber. Dr. Siber also received stock options to purchase up to 123,140 shares of common stock at an exercise price equal to fair market value on the date of grant. We also pay Dr. Farokhzad \$72,000 per year in addition to the annual \$75,000 payment under his consulting agreement, but have agreed with Dr. Farokhzad to discontinue this additional \$72,000 per year payment upon the closing of this offering.

The consulting agreements for each of Drs. Farokhzad, Langer and von Andrian provide that we may terminate the agreements at any time, but must deposit with an escrow agent the consulting fees for the prior 90 days which would then be payable to the consulting party post-termination. The agreements may also be terminated without penalty by both parties upon mutual consent or by the consulting party with 30 days' prior written notice. The consulting agreement for Dr. Siber provides that the agreement may be terminated by mutual consent of the parties or by either party upon 30 days' prior written notice. Each agreement contains provisions regarding intellectual property assignment, confidentiality, noncompetition and nonsolicitation. Our existing consulting agreement with Dr. Siber will terminate upon the closing of this offering. We expect to enter into a consulting

Certain relationships and related person transactions

agreement with Dr. Siber after this offering regarding his continued service on our scientific advisory board.

For more information regarding compensation that we have paid to each of Drs. Farokhzad, Langer and Siber, see "Executive and director compensation—Director compensation."

INDEMNIFICATION AGREEMENTS

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

STOCK OPTION GRANTS TO EXECUTIVE OFFICERS AND DIRECTORS

We have granted stock options to our executive officers and certain of our directors as more fully described in the section entitled "Executive and director compensation."

PARTICIPATION IN THIS OFFERING

Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

POLICIES AND PROCEDURES FOR RELATED PERSON TRANSACTIONS

Our board of directors has adopted a written related person transaction policy, to be effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act of 1933, as amended, or the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds \$120,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

Principal stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock, as of May 31, 2016, and as adjusted to reflect the sale of shares of common stock in this offering, by:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors and our director nominee; and
- all of our executive officers, directors and our director nominee as a group.

The number of shares beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Applicable percentage ownership information is based on 12,664,048 shares of common stock outstanding as of May 31, 2016, which assumes the conversion of the 8,888,888 outstanding shares of our series E preferred stock as of May 31, 2016 into an aggregate of 3,297,480 shares of our common stock, which will automatically occur upon completion of this offering. Upon the closing of this offering, (i) our series E preferred stock will automatically convert into a number of shares of common stock and (ii) outstanding warrants to purchase shares of our series E preferred stock will become warrants to purchase a number of shares of our common stock, in each case, determined, in part, by the initial public offering price for this offering, which we have assumed to be \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. Accordingly, the number of shares of our common stock issuable upon conversion of all of our preferred stock and exercise of our warrants outstanding would correspondingly increase or decrease, as applicable, in the event of any change in the initial public offering price per share. See "Prospectus summary—The offering."

In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of May 31, 2016 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed stockholders is 480 Arsenal Street, Building One, Watertown, Massachusetts 02472. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on

Principal stockholders

any other shares sold to the public in this offering. The information set forth in the table below does not reflect any potential purchase of any shares in this offering by such parties.

Name of beneficial owner	Shares beneficially owned prior to offering		Shares beneficially owned after offering	
	Number	Percentage	Number	Percentage
5% or Greater Stockholders				
Entities affiliated with Polaris Venture Partners(1)	1,757,234	13.9%	1,757,234	10.4%
Flagship Ventures Fund 2007, L.P.(2)	1,659,205	13.1%	1,659,205	9.8%
RUSNANO(3)	1,361,434	10.7%	1,361,434	8.0%
Entities affiliated with OrbiMed Advisors LLC(4)	1,251,707	9.9%	1,251,707	7.4%
TAS Partners LLC and Leukon Partners, LP, as affiliated entities(5)	965,330	7.6%	965,330	5.7%
NanoDimension L.P.(6)	658,345	5.2%	658,345	3.9%
Named Executive Officers, Directors and Director Nominee				
Werner Cautreels, Ph.D.(7)	412,097	3.2%	412,097	2.4%
Takashi Kei Kishimoto, Ph.D.(8)	108,172	*	108,172	*
Earl Sands, M.D.	25,640	*	25,640	*
Omid Farokhzad, M.D.(9)	419,861	3.3%	419,861	2.5%
Carl Gordon, Ph.D.(4)	1,251,707	9.9%	1,251,707	7.4%
Peter Barton Hutt(10)	36,324	*	36,324	*
Edwin M. Kania, Jr.(2)	1,659,205	13.1%	1,659,205	9.8%
Robert Langer, Jr., Sc. D.(11)	534,793	4.2%	534,793	3.1%
Amir Nashat, Sc.D.(1)	1,757,234	13.9%	1,757,234	10.4%
Aymeric Sallin, M.S.(6)	—	—	—	—
Leysan Shaydullina(3)	—	—	—	—
George Siber, M.D.(12)	31,574	*	31,574	*
Timothy A. Springer, Ph.D.(5)	965,330	7.6%	965,330	5.7%
All executive officers, directors and director nominee as a group (17 persons)(13)	7,596,270	60.0%	7,596,270	44.9%

* Less than 1%.

- (1) Consists of (i) 1,675,639 shares of common stock held by Polaris Venture Partners V, L.P., or Polaris V, (ii) 19,990 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by Polaris V, (iii) 32,654 shares of common stock held by Polaris Venture Partners Entrepreneurs' Fund V, L.P., or Polaris EFund V, (iv) 389 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by Polaris EFund V, (v) 11,474 shares of common stock held by Polaris Venture Partners Founders' Fund V, L.P., or Polaris FFund V, (vi) 136 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by Polaris FFund V, (vii) 16,753 shares of common stock held by Polaris Venture Partners Special Founders' Fund V, L.P., or Polaris SFFund V, and (viii) 199 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by Polaris SFFund V. The general partner of each of the Funds is Polaris Venture Management Co., V, L.L.C., or the General Partner. The General Partner may be deemed to have sole voting and investment power with respect to the shares held by the Funds, and disclaims beneficial ownership of all the shares held by the Funds except to the extent of its proportionate pecuniary interest therein. The members of North Star Venture Management 2000, LLC are also members of the General Partner. As members of North Star Venture Management 2000, LLC and the General Partner, such members, or the Management Members, may be deemed to share voting and investment powers for the shares held by the Funds. The Management Members disclaim beneficial ownership of all such shares held by the funds except to the extent of their proportionate pecuniary interests therein. Dr. Amir Nashat, our director, is a member of the General Partner. To the extent that he is deemed to share voting and investment powers with respect to the shares held by the Funds, Dr. Nashat disclaims beneficial ownership of his proportionate pecuniary interest therein. The address of the beneficial owner is c/o Polaris Venture Partners, 1000 Winter Street, Suite 3350, Waltham, MA 02451.
- (2) Consists of (i) 1,638,943 shares of common stock held of record by Flagship Ventures Fund 2007, L.P., or Flagship Ventures 2007, and (ii) 20,262 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held of record by Flagship Ventures 2007. Flagship Ventures 2007 General Partner, LLC, or Flagship 2007 LLC, is the

Principal stockholders

general partner of Flagship Ventures 2007 and Noubar B. Afeyan Ph.D. and Edwin M. Kania, Jr. are the managers of Flagship 2007 LLC. Flagship 2007 LLC, Dr. Afeyan and Mr. Kania may be deemed to share voting and investment power with respect to all shares held by Flagship Ventures 2007. Flagship 2007 LLC, Dr. Afeyan and Mr. Kania expressly disclaim beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address for Flagship Ventures 2007 is One Memorial Drive, 7th Floor, Cambridge, MA 02142.

- (3) Consists of (i) 1,348,331 shares of common stock held by RUSNANO and (ii) 13,103 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by RUSNANO. RUSNANO is a joint stock company organized under the laws of the Russian Federation. The Russian Federation owns 100% of RUSNANO. RUSNANO is managed by RUSNANO Management Company LLC, the Executive Board of which has the power to vote and dispose of the securities held directly by RUSNANO below a certain amount, and is supervised by the Board of Directors of RUSNANO, which, along with the Executive Board of RUSNANO Management Company LLC, has the power to dispose of the securities held directly by RUSNANO above a certain amount. Anatoly Chubais, Vladimir Avetissian, German Pikhoya, Oleg Kiselev, Boris Podolsky and Yury Udaltsov, as the members of the Executive Board of RUSNANO Management Company LLC, and Arkadiy Dvorkovich, Anatoly Chubais, Igor Agamirzyan, Mikhail Alfimov, Oleg Fomichev, Andrey Ivanov, Denis Manturov, Vladislav Putilin, Pavel Teplukhin, Viktor Vekselberg and Ilya Yuzhanov, as the members of the Board of Directors of RUSNANO, may be deemed to have or share beneficial ownership of these securities. Each of them disclaims any such beneficial ownership. The address of each of RUSNANO and RUSNANO Management Company LLC is 10A prospect 60-letiya Oktyabrya, Moscow, Russia 117036.
- (4) Consists of (i) 1,233,390 shares of common stock held by OrbiMed Private Investments III, LP, or OrbiMed Private, (ii) 6,513 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by OrbiMed Private, (iii) 11,743 shares of common stock held by OrbiMed Associates III, LP, or OrbiMed Associates and, together with OrbiMed Private, the OrbiMed Funds, and (iv) 61 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by OrbiMed Associates, OrbiMed Capital GP III LLC, or GP III, is the general partner of OrbiMed Private and OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of GP III and the general partner of OrbiMed Associates. Mr. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed Advisors. By virtue of such relationships, GP III, OrbiMed Advisors and Mr. Isaly may be deemed to have voting and investment power over the securities held by the OrbiMed Funds and as a result may be deemed to have beneficial ownership over such securities. Dr. Carl Gordon, one of our directors, is a member of OrbiMed Advisors. Each of GP III, OrbiMed Advisors, Mr. Isaly and Dr. Gordon disclaims beneficial ownership of all the shares held by the OrbiMed Funds except to the extent of its or his proportionate pecuniary interest therein. The mailing address of the beneficial owner is 601 Lexington Avenue, New York, NY 10022.
- (5) Consists of (i) 437,396 shares of common stock held by TAS Partners, LLC, or TAS, (ii) 4,304 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by TAS, (iii) 518,304 shares of common stock held by Leukon Investments LP, or Leukon, and (iv) 5,326 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016. LKST, Inc. is the general partner of Leukon. Timothy Springer, our director nominee, is the president of LKST, Inc. and is also the manager of TAS. Mr. Springer disclaims beneficial ownership of the shares held by TAS and Leukon except to the extent of his pecuniary interest therein. Each of TAS and Leukon disclaim beneficial ownership of the shares held by the other except to the extent of their pecuniary interest therein. The address of TAS and Leukon is 36 Woodman Road, Chestnut Hill, MA 02467.
- (6) Consists of (i) 651,338 shares of common stock held by NanoDimension L.P., or ND LP, and (ii) 7,007 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016 held by ND LP. NanoDimension Management Ltd., or ND GP, serves as the general partner of ND LP and possesses power to direct the voting and disposition of the shares owned by ND LP and may be deemed to have indirect beneficial ownership of the shares held by ND LP. ND GP disclaims beneficial ownership of such shares, except to the extent of its pecuniary interest therein. The ND GP owns no securities of the issuer directly. Jonathan Nicholson and Richard Coles are the members of the board of directors of ND GP and share voting and dispositive power over the shares held by ND LP. Aymeric Sallin is a member of the investment advisory committee of NDGP that provide investment recommendation to NDGP. Each such person disclaims beneficial ownership of the shares reported herein, except to the extent of his respective pecuniary interest therein. The address for NanoDimension Limited Partnership is Governor's Square, Unit 3-213-6, 23 Lime Tree Bay Ave, Grand Cayman, Cayman Islands KY1-1302.
- (7) Includes 110,894 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016.
- (8) Includes 108,172 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016.
- (9) Includes (i) 65,652 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016; (ii) 202,051 shares of common stock held by a family trust for which Dr. Farokhzad's wife serves as trustee; and (iii) 20,609 shares of common stock held by BioDynamics Core, L.P., which is managed by BioDynamics, LLC, of which Dr. Farokhzad is a member. Dr. Farokhzad disclaims beneficial ownership over the shares held by the family trust and BioDynamics Core, L.P. except to the extent of any pecuniary interest therein.
- (10) Includes 36,324 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016.
- (11) Includes 77,190 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016.
- (12) Includes 31,574 shares of common stock underlying outstanding stock options exercisable within 60 days of May 31, 2016.
- (13) Includes (i) 833,588 shares of common stock underlying outstanding stock options and (ii) 57,180 shares of common stock underlying warrants exercisable within 60 days of May 31, 2016.

Description of capital stock

GENERAL

The following description summarizes some of the terms of our restated certificate of incorporation and restated bylaws that will become effective upon the closing of this offering, our outstanding warrants, the investors' rights agreement and of the General Corporation Law of the State of Delaware. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation, restated bylaws, warrants and investors' rights agreement, copies of which have been or will be filed as exhibits to the registration statement of which this prospectus is a part, as well as the relevant provisions of the General Corporation Law of the State of Delaware. The description of our common stock and preferred stock reflects changes to our capital structure that will occur upon the closing of this offering.

Following the closing of this offering, our authorized capital stock will consist of 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share.

On May 31, 2016, there were 2,773,468 shares of common stock outstanding, including 4,415 shares of unvested restricted common stock subject to repurchase by us, held of record by 80 stockholders. This amount does not include shares of common stock to be issued upon the conversion of outstanding shares of preferred stock that will convert automatically upon the closing of this offering.

COMMON STOCK

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our restated certificate of incorporation and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our restated certificate of incorporation. See below under "—Anti-takeover effects of Delaware law and our certificate of incorporation and bylaws" and "—Amendment of charter provisions." Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Description of capital stock

PREFERRED STOCK

Under the terms of our restated certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

OPTIONS

As of May 31, 2016, options to purchase 1,723,704 shares of our common stock were outstanding under our 2008 plan, of which 677,324 had not vested and 1,046,380 had vested as of that date, excluding 390,796 shares of common stock issuable upon the exercise of options to be granted in connection with this offering under our 2016 Plan, which will become effective in connection with this offering, to some of our executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering.

WARRANTS

In connection with our credit facility, on August 9, 2013 and July 25 2014, we issued warrants to Oxford and Pacific Western Bank exercisable for an aggregate of 66,668 shares of our series D preferred stock. Upon conversion of the series D preferred stock into common stock in connection with this offering, the warrants will become exercisable for 17,888 shares of common stock at a weighted average exercise price of \$16.77. If unexercised, the warrants will expire on August 9, 2023 and July 25, 2024.

On July 24, 2015, we issued warrants to investors in a previous convertible note financing exercisable for an aggregate of 80,813 shares of common stock at an exercise price of \$17.55 per share. If unexercised, the warrants will expire on July 24, 2018.

On August 27, 2015, September 3, 2015 and September 17, 2015, we issued series E common warrants to the investors in our series E preferred stock financing exercisable for an aggregate of 569,791 shares of common stock at an exercise price of \$0.04 per share. Upon the filing of the registration statement of which this prospectus forms a part, the warrants were automatically exercised on a cashless basis for an aggregate of 567,306 shares of common stock.

In connection with our credit facility, on December 31, 2015, we issued warrants to Oxford and Pacific Western Bank exercisable for an aggregate of 37,978 shares of our series E preferred stock. Upon conversion of the series E preferred stock into common stock in connection with this offering, the warrants will become exercisable for 14,088 shares of common stock at a weighted average exercise price of \$17.55 per share of common stock based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus (see "Prospectus summary—The offering"). If unexercised, the warrants will expire on December 31, 2025.

Description of capital stock

REGISTRATION RIGHTS

As of May 31, 2016, upon the closing of this offering, holders of approximately 12,016,162 shares of our common stock, including shares issuable upon the exercise of warrants, or their transferees will be entitled to the following rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to an amended and restated investors' rights agreement by and among us and certain of our stockholders, until such shares can otherwise be sold without restriction under Rule 144, or until the rights otherwise terminate pursuant to the terms of the investors' rights agreement. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Demand registration rights

If at any time beginning 180 days after the closing date of this offering the holders of at least 50% of the registrable securities request in writing that we effect a registration with respect to all or part of such registrable securities then outstanding, we may be required to register their shares. We are obligated to effect at most two registrations in response to these demand registration rights. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback registration rights

If at any time after this offering we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 registration rights

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of the registrable securities request in writing that we effect a registration with respect to registrable securities at an aggregate price to the public in the offering of at least \$2,000,000, we will be required to effect such registration; provided, however, that we will not be required to effect such a registration if, within a given calendar year, we have already effected two registrations on Form S-3 for the holders of registrable securities.

Expenses

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders and blue sky fees and expenses.

Termination of registration rights

The registration rights terminate upon the earlier of five years after the effective date of the registration statement of which this prospectus is a part, or, with respect to the registration rights of an individual holder, when the holder can sell all of such holder's registrable securities in a 90-day period without restriction under Rule 144 under the Securities Act.

Description of capital stock

ANTI-TAKEOVER EFFECTS OF DELAWARE LAW AND OUR CERTIFICATE OF INCORPORATION AND BYLAWS

Some provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated preferred stock

The ability of our board of directors, without action by the stockholders, to issue shares of undesignated preferred stock under our restated certificate of incorporation with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder meetings

Our restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for advance notification of stockholder nominations and proposals

Our restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of stockholder action by written consent

Our restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. For more information on the classified board, see "Management—Board composition and election of directors." This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Description of capital stock

Removal of directors

Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders not entitled to cumulative voting

Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware anti-takeover statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of forum

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of charter provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result

Description of capital stock

from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests

TRANSFER AGENT AND REGISTRAR

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

STOCK EXCHANGE LISTING

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "SELB."

Shares eligible for future sale

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock.

Upon the closing of this offering, we will have outstanding an aggregate of 16,914,048 shares of common stock, assuming the issuance of 4,250,000 shares of common stock offered by us in this offering, after giving effect to the assumptions described under "Prospectus summary—The offering," and assuming no exercise of options or warrants after May 31, 2016. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 12,664,048 shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below. Additionally, any shares purchased in this offering by participants in our directed share program who purchase more than \$1,000,000 of shares will be subject to a 25-day lock-up period and any shares purchased in this offering by our existing stockholders that are required to file reports pursuant to Section 16 of the Exchange Act will be subject to a 180-day lock-up period, in each case, unless the lock-up period is waived by UBS Securities LLC and Stifel, Nicolaus & Company, Incorporated on behalf of the underwriters. Upon expiration of the lock-up period, we estimate that approximately 12,664,048 shares will be available for sale in the public market, subject in some cases to applicable volume limitations under Rule 144.

In addition, of the 1,723,704 shares of our common stock that were subject to stock options outstanding as of May 31, 2016, options to purchase 1,046,380 shares of common stock were vested as of May 31, 2016 and, upon exercise, these shares will be eligible for sale subject to the lock-up agreements described below and Rules 144 and 701 under the Securities Act.

LOCK-UP AGREEMENTS

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, have agreed that, without the prior written consent of UBS Securities LLC and Stifel, Nicolaus & Company, Incorporated on behalf of the underwriters, we and they will not, subject to certain exceptions, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock,

whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

Shares eligible for future sale

Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above. For a further description of these lock-up agreements, please see "Underwriting."

RULE 144

Affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 169,140 shares immediately after this offering; or
- the average weekly trading volume in our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of \$50,000, the seller must file a notice on Form 144 with the SEC and The NASDAQ Global Market concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

RULE 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

Shares eligible for future sale

The SEC has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

EQUITY PLANS

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by nonaffiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

REGISTRATION RIGHTS

Holders of shares of our common stock, including shares issuable upon the exercise of warrants, or their transferees will be entitled to registration rights with respect to such shares for public resale under the Securities Act. See "Description of capital stock—Registration rights" for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

Material U.S. federal income tax consequences to non-U.S. holders

The following discussion is a summary of certain material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax consequences. The consequences of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local, or non-U.S. tax laws are not discussed. This discussion is based on the United States Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the United States Internal Revenue Service, or the IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and do not intend to seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership, and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences that may be relevant to a non-U.S. holder in light of such non-U.S. holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to non-U.S. holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle, or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers, or traders in securities or currencies;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships, or other entities or arrangements treated as partnerships for U.S. federal income tax purposes, or investors in any such entities;
- tax-exempt or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons for whom our stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code; and
- tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the

Material U.S. federal income tax consequences to non-U.S. holders

partner, the activities of the partnership, and certain determinations made at the partner level. Partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them of the purchase, ownership, and disposition of our common stock.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS, LEGAL OR TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER OTHER U.S. FEDERAL TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, OR NON-U.S. TAXING JURISDICTION, OR UNDER ANY APPLICABLE INCOME TAX TREATY.

DEFINITION OF A NON-U.S. HOLDER

For purposes of this discussion, a "non-U.S. holder" is any beneficial owner of our common stock that is not a "U.S. person," a partnership, or an entity disregarded as separate from its owner, each for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a U.S. person for U.S. federal income tax purposes.

DISTRIBUTIONS

As described in the section entitled "Dividend policy," we do not expect to declare or pay dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "Sale or other taxable disposition."

Subject to the discussion below on effectively connected income, dividends paid to a non-U.S. holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the non-U.S. holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate. A non-U.S. holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

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If dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), the non-U.S. holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the non-U.S. holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net basis at regular graduated rates. A non-U.S. holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

SALE OR OTHER TAXABLE DISPOSITION

A non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at regular graduated U.S. federal income tax rates. A non-U.S. holder that is taxed as a corporation for U.S. federal income tax purposes also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not expect to become a USRPHC. Because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, however, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if (i) such class of stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and (ii) such non-U.S. holder owned, actually or constructively, 5% or less of such class of our stock throughout the shorter of the five-year period ending on the date of the sale or other disposition or the non-U.S. holder's holding period for such stock. If the foregoing exception does not apply, and if we are or were to become a USRPHC, a

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purchaser may be required to withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock and such non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code).

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

INFORMATION REPORTING AND BACKUP WITHHOLDING

Payments of dividends on our common stock will not generally be subject to backup withholding provided the applicable withholding agent does not have actual knowledge or reason to know such holder is a U.S. person and the holder either certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN, W-8BEN-E, or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the non-U.S. holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a U.S. person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of these information returns that are filed with the IRS may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

ADDITIONAL WITHHOLDING TAX ON PAYMENTS MADE TO FOREIGN ACCOUNTS

Withholding taxes may be imposed under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the IRS requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock, and will apply to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2019. Prospective investors should consult their tax advisors regarding the potential application of these withholding provisions.

Underwriting

We are offering the shares of our common stock described in this prospectus through the underwriters named below. UBS Securities LLC and Stifel, Nicolaus & Company, Incorporated are acting as joint book-running managers of this offering and as representatives of the underwriters. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, each of the underwriters has severally agreed to purchase, and we have agreed to sell to the underwriters, the number of shares of common stock listed next to its name in the following table.

Underwriters	Number of shares
UBS Securities LLC	
Stifel, Nicolaus & Company, Incorporated	
Canaccord Genuity Inc.	
Needham & Company, LLC	
Total	<u>4,250,000</u>

The underwriting agreement provides that the underwriters must buy all of the shares of common stock if they buy any of them. However, the underwriters are not required to pay for the shares covered by the underwriters' option to purchase additional shares as described below.

Our common stock is offered subject to a number of conditions, including:

- receipt and acceptance of our common stock by the underwriters; and
- the underwriters' right to reject orders in whole or in part.

We have been advised by the representatives that the underwriters intend to make a market in our common stock but that they are not obligated to do so and may discontinue making a market at any time without notice.

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses electronically.

OPTION TO PURCHASE ADDITIONAL SHARES

We have granted the underwriters an option to buy up to an aggregate of 637,500 additional shares of our common stock. The underwriters have 30 days from the date of this prospectus to exercise this option. If the underwriters exercise this option, they will each purchase additional shares of common stock approximately in proportion to the amounts specified in the table above.

UNDERWRITING DISCOUNT

Shares sold by the underwriters to the public will initially be offered at the initial offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$ _____ per share from the initial public offering price. Sales of shares made outside of the United States may be made by affiliates of the underwriters. If all the shares are not sold at the initial public offering price, the representatives may change the offering price and the other selling terms. Upon execution of the underwriting agreement, the underwriters will be obligated to purchase the shares at the prices and upon the terms stated therein.

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The following table shows the per share and total underwriting discount we will pay to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase up to 637,500 additional shares.

	No exercise	Full exercise
Per share	\$	\$
Total	\$	\$

We estimate that the total expenses of the offering payable by us, not including the underwriting discount, will be approximately \$3.9 million. We have agreed with the underwriters to pay certain fees and expenses related to the review and qualification of this offering by the Financial Industry Regulatory Authority, Inc. and "blue sky" expenses in an amount not to exceed \$35,000.

NO SALES OF SIMILAR SECURITIES

We, our executive officers and directors, and holders of substantially all of our common stock have entered into lock-up agreements with the underwriters. Under the lock-up agreements, subject to certain exceptions, we and each of these persons may not, without the prior written approval of UBS Securities LLC and Stifel, Nicolaus & Company, Incorporated, offer, sell, contract to sell, pledge, or otherwise dispose of, directly or indirectly, or hedge our common stock or securities convertible into or exchangeable or exercisable for our common stock. These restrictions will be in effect for a period ending on and including the date that is 180 days after the date of this prospectus.

UBS Securities LLC and Stifel, Nicolaus & Company, Incorporated may, at any time and in their sole discretion, release some or all the securities from these lock-up agreements. If the restrictions under the lock-up agreements are waived, shares of our common stock may become available for resale into the market, subject to applicable law, which could reduce the market price of our common stock.

INDEMNIFICATION

We have agreed to indemnify the several underwriters against certain liabilities, including certain liabilities under the Securities Act. If we are unable to provide this indemnification, we have agreed to contribute to payments the underwriters may be required to make in respect of those liabilities.

NASDAQ LISTING

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "SELB."

PRICE STABILIZATION, SHORT POSITIONS

In connection with this offering, the underwriters may engage in activities that stabilize, maintain or otherwise affect the price of our common stock during and after this offering, including:

- stabilizing transactions;
- short sales;
- purchases to cover positions created by short sales;
- imposition of penalty bids; and
- syndicate covering transactions.

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Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of our common stock while this offering is in progress. Stabilization transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. These transactions may also include making short sales of our common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering and purchasing shares of common stock on the open market to cover short positions created by short sales. Short sales may be "covered short sales," which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be "naked short sales," which are short positions in excess of that amount.

The underwriters may close out any covered short position by either exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option.

Naked short sales are short sales made in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchased in this offering.

The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of that underwriter in stabilizing or short covering transactions.

These stabilizing transactions, short sales, purchases to cover positions created by short sales, the imposition of penalty bids and syndicate covering transactions may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result of these activities, the price of our common stock may be higher than the price that otherwise might exist in the open market. The underwriters may carry out these transactions on NASDAQ, in the over-the-counter market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. Neither we, nor any of the underwriters make any representation that the underwriters will engage in these stabilization transactions or that any transaction, once commenced, will not be discontinued without notice.

DETERMINATION OF OFFERING PRICE

Prior to this offering, there was no public market for our common stock. The initial public offering price will be determined by negotiation among us and the representatives of the underwriters. The principal factors to be considered in determining the initial public offering price include:

- the information set forth in this prospectus and otherwise available to the representatives;
- our history and prospects and the history and prospects for the industry in which we compete;
- our past and present financial performance;
- our prospects for future earnings and the present state of our development;
- the general condition of the securities market at the time of this offering;

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- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

The estimated public offering price range set forth on the cover page of this preliminary prospectus is subject to change as a result of market conditions and other factors. Neither we nor the underwriters can assure investors that an active trading market will develop for our common stock or that the common stock will trade in the public market at or above the initial public offering price.

DIRECTED SHARE PROGRAM

At our request, the underwriters have reserved up to 5% of the common stock being offered by this prospectus for sale at the initial public offering price to our directors, officers, employees and other individuals associated with us and members of their families. The sales will be made by UBS Financial Services Inc., a selected dealer affiliated with UBS Securities LLC, an underwriter of this offering, through a directed share program. We do not know if these persons will choose to purchase all or any portion of these reserved shares, but any purchases they do make will reduce the number of shares available to the general public. Any reserved shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares of common stock. Participants in the directed share program who purchase more than \$1,000,000 of shares shall be subject to a 25-day lock-up with respect to any shares sold to them pursuant to that program. This lock-up will have similar restrictions to the lock-up agreements described in "Shares eligible for future sale—Lock-up agreements." Any shares sold in the directed share program to our directors or executive officers shall be subject to the lock-up agreements described above.

AFFILIATIONS

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and their affiliates may from time to time in the future engage with us and perform services for us or in the ordinary course of their business for which they will receive customary fees and expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities or instruments of us. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of these securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in these securities and instruments.

ELECTRONIC DISTRIBUTION

A prospectus in electronic format may be made available on the internet or through other online services maintained by one or more of the underwriters participating in this offering, or by their affiliates. In those cases, prospective investors may view offering terms online and, depending upon the particular underwriter, prospective investors may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on any underwriter's

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website and any information contained in any other website maintained by an underwriter is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter and should not be relied upon by investors.

NOTICE TO PROSPECTIVE INVESTORS

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any shares of common stock which are the subject of the offering contemplated by this prospectus (the "Shares") may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Directive;
- (b) by the underwriters to fewer than 100, or, if the Relevant Member State has implemented the relevant provisions of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of Shares shall result in a requirement us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State. The expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in each Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

The EEA selling restriction is in addition to any other selling restrictions set out in this prospectus.

United Kingdom

This prospectus is only being distributed to and is only directed at: (1) persons who are outside the United Kingdom; (2) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order"); or (3) high net worth companies, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons falling within (1)-(3) together being referred to as "relevant persons"). The shares are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such shares will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this prospectus or any of its contents.

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Australia

This prospectus is not a formal disclosure document and has not been, nor will be, lodged with the Australian Securities and Investments Commission. It does not purport to contain all information that an investor or their professional advisers would expect to find in a prospectus or other disclosure document (as defined in the Corporations Act 2001 (Australia)) for the purposes of Part 6D.2 of the Corporations Act 2001 (Australia) or in a product disclosure statement for the purposes of Part 7.9 of the Corporations Act 2001 (Australia), in either case, in relation to the securities.

The securities are not being offered in Australia to "retail clients" as defined in sections 761G and 761GA of the Corporations Act 2001 (Australia). This offering is being made in Australia solely to "wholesale clients" for the purposes of section 761G of the Corporations Act 2001 (Australia) and, as such, no prospectus, product disclosure statement or other disclosure document in relation to the securities has been, or will be, prepared.

This prospectus does not constitute an offer in Australia other than to persons who do not require disclosure under Part 6D.2 of the Corporations Act 2001 (Australia) and who are wholesale clients for the purposes of section 761G of the Corporations Act 2001 (Australia). By submitting an application for our securities, you represent and warrant to us that you are a person who does not require disclosure under Part 6D.2 and who is a wholesale client for the purposes of section 761G of the Corporations Act 2001 (Australia). If any recipient of this prospectus is not a wholesale client, no offer of, or invitation to apply for, our securities shall be deemed to be made to such recipient and no applications for our securities will be accepted from such recipient. Any offer to a recipient in Australia, and any agreement arising from acceptance of such offer, is personal and may only be accepted by the recipient. In addition, by applying for our securities you undertake to us that, for a period of 12 months from the date of issue of the securities, you will not transfer any interest in the securities to any person in Australia other than to a person who does not require disclosure under Part 6D.2 and who is a wholesale client.

Hong Kong

The contents of this prospectus have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this prospectus, you should obtain independent professional advice. Please note that (i) our securities may not be offered or sold in Hong Kong, by means of this prospectus or any document other than to "professional investors" within the meaning of Part I of Schedule 1 of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) (SFO) and any rules made thereunder, or in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong) (CO) or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO, and (ii) no advertisement, invitation or document relating to our securities may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere) which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the SFO and any rules made thereunder.

Japan

Our securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and our securities will not be offered or

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sold, directly or indirectly, in Japan, or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan, or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of our securities may not be circulated or distributed, nor may our securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where our securities are subscribed or purchased under Section 275 by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired our securities pursuant to an offer made under Section 275 except:
 - (1) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (2) where no consideration is or will be given for the transfer;
 - (3) where the transfer is by operation of law; or
 - (4) as specified in Section 276(7) of the SFA.

Switzerland

This Prospectus does not constitute an issue prospectus pursuant to Article 652a or Article 1156 of the Swiss Code of Obligations (CO) and the shares will not be listed on the SIX Swiss Exchange. Therefore, the Prospectus may not comply with the disclosure standards of the CO and/or the listing rules (including any prospectus schemes) of the SIX Swiss Exchange. Accordingly, the shares may not be offered to the public in or from Switzerland, but only to a selected and limited circle of investors, which do not subscribe to the shares with a view to distribution.

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Greece

The securities have not been approved by the Hellenic Capital Markets Commission for distribution and marketing in Greece. This document and the information contained therein do not and shall not be deemed to constitute an invitation to the public in Greece to purchase the securities. The securities may not be advertised, distributed, offered or in any way sold in Greece except as permitted by Greek law.

Dubai International Finance Centre

This prospectus relates to an Exempt Offer in accordance with the Markets Rules of the Dubai Financial Services Authority. This prospectus is intended for distribution only to Professional Clients who are not natural persons. It must not be delivered to, or relied on by, any other person. The Dubai Financial Services Authority has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The Dubai Financial Services Authority has not approved this document nor taken steps to verify the information set out in it, and has no responsibility for it. The securities to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial adviser.

Legal matters

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP. Certain legal matters will be passed upon for the underwriters by Cooley LLP.

Experts

Our consolidated financial statements as of December 31, 2014 and December 31, 2015, and for the years then ended, appearing in this prospectus and the related registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to the consolidated financial statements) appearing elsewhere herein, and are included in reliance on such report given on the authority of such firm as experts in accounting and auditing.

Where you can find more information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the SEC pursuant to the Exchange Act. You may read and copy this information at the Public Reference Room of the SEC, 100 F Street, N.E., Room 1580, Washington, District of Columbia 20549. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is www.sec.gov.

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Report of independent registered public accounting firm

To the Board of Directors and Stockholders
Selecta Biosciences, Inc. and Subsidiaries

We have audited the accompanying consolidated balance sheets of Selecta Biosciences, Inc. and subsidiaries ("the Company") as of December 31, 2015 and 2014, and the related consolidated statements of comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for each of the two years in the period ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Selecta Biosciences, Inc. and subsidiaries at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has recurring losses from operations and negative cash flows from operations and will require additional capital to fund planned operations. These conditions raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 30, 2016, except for Note 17(b), as to which the date is June 8, 2016

CONSOLIDATED BALANCE SHEETS

	December 31,		March 31,		Pro forma
	2014	2015	2016	2016	March 31,
	(in thousands, except share and per share data)				(unaudited)
					(unaudited)
Assets					
Current assets:					
Cash and cash equivalents	\$ 16,592	\$ 32,337	\$ 17,051	\$ 17,051	
Short term investments	—	4,125	8,928	8,928	
Restricted cash	1,244	133	682	682	
Accounts receivable	674	824	1,627	1,627	
Prepaid expenses and other current assets	602	1,494	1,598	1,598	
Total current assets	19,112	38,913	29,886	29,886	
Property and equipment, net	1,983	2,029	2,040	2,040	
Restricted cash and other deposits	1,106	316	316	316	
Other assets	27	1,566	2,481	2,481	
Total assets	<u>\$ 22,228</u>	<u>\$ 42,824</u>	<u>\$ 34,723</u>	<u>\$ 34,723</u>	
Liabilities, redeemable convertible preferred stock, and stockholders' deficit					
Current liabilities:					
Accounts payable	\$ 351	\$ 2,179	\$ 788	\$ 788	
Accrued expenses	1,853	3,378	3,185	3,185	
Loans payable, current portion	2,578	—	673	673	
Deferred revenue, current portion	3,018	1,313	1,219	1,219	
Contingently repayable grant funding	1,431	420	452	452	
Total current liabilities	9,231	7,290	6,317	6,317	
Non-current liabilities:					
Deferred rent and lease incentive	274	105	—	—	
Contingently repayable grant funding long-term	—	—	—	—	
Loans payable, net of current portion	4,824	11,855	11,169	11,169	
Deferred revenue, net of current portion	1,364	2,295	2,895	2,895	
Other long-term liabilities	257	290	310	—	
Total liabilities	15,950	21,835	20,691	20,381	
Commitments and contingencies (Notes 7 and 12)					
Redeemable convertible preferred stock:					
Series A redeemable convertible preferred stock, \$0.0001 par value; 2,589,868 shares authorized, issued, and outstanding (liquidation preference of \$3,500,151 at December 31, 2014, \$3,650,104 at December 31, 2015 and \$3,687,592 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	3,493	3,644	3,682	—	
Series B redeemable convertible preferred stock, \$0.0001 par value; 7,437,325 shares authorized, issued, and outstanding (liquidation preference of \$20,568,097 at December 31, 2014, \$21,473,963 at December 31, 2015 and \$21,700,429 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	20,533	21,448	21,676	—	
Series C redeemable convertible preferred stock, \$0.0001 par value; 5,000,002 shares authorized, issued, and outstanding (liquidation preference of \$19,300,282 at December 31, 2014, \$20,200,282 at December 31, 2015 and \$20,425,282 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	19,270	20,178	20,404	—	
Series D redeemable convertible preferred stock, \$0.0001 par value; 8,166,662 shares authorized at December 31, 2014 and 2015 and March 31, 2016 (unaudited); 8,099,994 shares issued and outstanding at December 31, 2014 and 2015 and March 31, 2016 (unaudited) (liquidation preference of \$41,125,871 at December 31, 2014, \$43,312,869 at December 31, 2015 and \$43,859,619 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	40,570	42,902	43,477	—	
Series SRN redeemable convertible preferred stock, \$0.0001 par value; 5,611,112 shares authorized at December 31, 2014 and 2015 and March 31, 2016 (unaudited); 2,111,109 shares issued and outstanding at December 31, 2014 and 2015 and March 31, 2016 (unaudited) (liquidation preference of \$9,499,991 at December 31, 2014, \$9,499,991 at December 31, 2015 and \$9,499,991 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	10,167	12,082	12,541	—	
Series E redeemable convertible preferred stock, \$0.0001 par value; 9,030,654 shares authorized at December 31, 2015 and March 31, 2016 (unaudited); 8,888,888 shares issued and outstanding at December 31, 2015 and at March 31, 2016 (unaudited) (liquidation preference of \$40,802,658 at December 31, 2015 and \$41,402,659 at March 31, 2016 (unaudited); none issued and outstanding pro forma)	—	37,228	38,057	—	
Total redeemable convertible preferred stock	94,033	137,482	139,837	—	
Stockholders' equity (deficit):					
Common stock, \$0.0001 par value; 46,000,000, 62,164,377 and 62,164,377 shares authorized at December 31, 2014 and 2015 and March 31, 2016 (unaudited) respectively; 2,139,262, 2,180,976 and 2,183,541 shares issued, 2,123,997, 2,173,399, 2,177,858 shares outstanding as of December 31, 2014 and 2015 and March 31, 2016 (unaudited), respectively. 12,641,402 issued and 12,635,719 outstanding pro forma (unaudited)	—	—	—	—	1
Additional paid in capital	1	1	1	140,147	
Accumulated deficit	(83,880)	(111,508)	(121,051)	(121,051)	
Accumulated other comprehensive loss	(3,876)	(4,986)	(4,755)	(4,755)	
Total stockholders' equity (deficit)	(87,755)	(116,493)	(125,805)	14,342	
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	<u>\$ 22,228</u>	<u>\$ 42,824</u>	<u>\$ 34,723</u>	<u>\$ 34,723</u>	

See accompanying notes.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year ended December 31,		Three months ended March 31,	
	2014	2015	2015	2016
	(in thousands, except share and per share data)			
			(unaudited)	(unaudited)
Grant and collaboration revenue	\$ 3,040	\$ 6,011	\$ 1,034	\$ 2,088
Operating expenses:				
Research and development	10,486	22,980	4,972	6,648
General and administrative	7,953	8,335	1,872	2,381
Total operating expenses	<u>18,439</u>	<u>31,315</u>	<u>6,844</u>	<u>9,029</u>
Loss from operations	(15,399)	(25,304)	(5,810)	(6,941)
Investment income	111	171	62	13
Foreign currency transaction gain (loss), net	3,004	933	194	(220)
Interest expense	(552)	(948)	(179)	(310)
Other expense, net	(44)	(26)	—	(18)
Net loss	<u>(12,880)</u>	<u>(25,174)</u>	<u>(5,733)</u>	<u>(7,476)</u>
Other comprehensive loss:				
Foreign currency translation adjustment	(3,281)	(1,110)	(208)	231
Comprehensive loss	<u>\$ (16,161)</u>	<u>\$ (26,284)</u>	<u>\$ (5,941)</u>	<u>\$ (7,245)</u>
Net loss	(12,880)	(25,174)	(5,733)	(7,476)
Accretion of redeemable convertible preferred stock	(4,951)	(7,335)	(1,561)	(2,356)
Net effect of extinguishment of Series SRN redeemable convertible preferred stock	1,459	—	—	—
Net loss attributable to common stockholders	<u>\$ (16,372)</u>	<u>\$ (32,509)</u>	<u>\$ (7,294)</u>	<u>\$ (9,832)</u>
Net loss per share attributable to common stockholders				
Basic and diluted	<u>\$ (7.84)</u>	<u>\$ (15.13)</u>	<u>\$ (3.43)</u>	<u>\$ (4.52)</u>
Weighted average common shares outstanding				
Basic and diluted	<u>2,090,677</u>	<u>2,150,422</u>	<u>2,126,878</u>	<u>2,175,037</u>
Pro forma net loss per share attributable to common stockholders (unaudited)				
Basic and diluted		<u>\$ (2.53)</u>		<u>\$ (0.59)</u>
Pro forma weighted average common shares of common stock outstanding (unaudited)				
Basic and diluted		<u>9,980,469</u>		<u>12,632,923</u>

See accompanying notes.

Selecta Biosciences, Inc. and Subsidiaries

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT

(in thousands, except share data)	Series A redeemable convertible preferred stock		Series B redeemable convertible preferred stock		Series C redeemable convertible preferred stock		Series D redeemable convertible preferred stock		Series SRN redeemable convertible preferred stock		Series E redeemable convertible preferred stock		Common stock		Additional paid-in Capital	Accumulated deficit	Accumulated comprehensive loss	Stockholders' deficit
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
	(in thousands, except share data)																	
Balance at December 31, 2013	2,589,868	3,350	7,437,325	19,662	5,000,002	18,381	4,888,889	24,366	777,777	4,643	—	—	2,027,254	—	1	(68,869)	(595)	(69,463)
Issuance of Series D redeemable convertible preferred stock, net of issuance costs of \$100,734	—	—	—	—	—	—	3,211,105	14,349	—	—	—	—	—	—	—	—	—	—
Net effect of extinguishment of Series SRN redeemable preferred stock (see Note 8)	—	—	—	—	—	—	—	—	—	(1,459)	—	—	—	—	1,459	—	—	1,459
Issuance of Series SRN redeemable convertible preferred stock, net of issuance costs of \$209,587	—	—	—	—	—	—	—	—	1,333,332	5,790	—	—	—	—	—	—	—	—
Vesting of restricted common stock	—	—	—	—	—	—	—	—	—	—	—	—	58,104	—	69	—	—	69
Issuance of common stock upon exercise of options	—	—	—	—	—	—	—	—	—	—	—	—	38,639	—	68	—	—	68
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,224	—	—	1,224
Accretion of preferred stock to redemption value	—	143	—	871	—	889	—	1,855	—	1,193	—	—	—	—	(2,820)	(2,131)	—	(4,951)
Currency translation adjustment	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(3,281)	(3,281)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(12,880)	—	(12,880)
Balance at December 31, 2014	2,589,868	\$ 3,493	7,437,325	\$ 20,533	5,000,002	\$ 19,270	8,099,994	\$ 40,570	2,111,109	\$ 10,167	—	\$ —	2,123,997	\$ 0	\$ 1	\$(83,880)	\$(3,876)	\$(87,755)
Issuance of Series E redeemable convertible preferred stock, net of issuance costs of \$213,469	—	—	—	—	—	—	—	—	—	—	8,888,888	36,114	—	—	—	—	—	—
Allocation of Issuance Cost to Common Warrants	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of common stock warrants	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3,647	—	—	3,647
Vesting of restricted common stock	—	—	—	—	—	—	—	—	—	—	—	—	7,688	—	23	—	—	23
Issuance of common stock upon exercise of options	—	—	—	—	—	—	—	—	—	—	—	—	41,714	—	86	—	—	86
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1,125	—	—	1,125
Accretion of preferred stock to redemption value	—	151	—	915	—	908	—	2,332	—	1,915	—	1,114	—	—	(4,881)	(2,454)	—	(7,335)
Currency translation adjustment	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(1,110)	(1,110)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(25,174)	—	(25,174)
Balance at December 31, 2015	2,589,868	\$ 3,644	7,437,325	\$ 21,448	5,000,002	\$ 20,178	8,099,994	\$ 42,902	2,111,109	\$ 12,082	8,888,888	\$ 37,228	2,173,399	\$ 0	\$ 1	\$(111,508)	\$(4,986)	\$(116,493)
Vesting of restricted common stock	—	—	—	—	—	—	—	—	—	—	—	—	1,895	—	5	—	—	5
Issuance of common stock upon exercise of options	—	—	—	—	—	—	—	—	—	—	—	—	2,564	—	2	—	—	2
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	—	—	282	—	—	282
Accretion of preferred stock to redemption value	—	38	—	228	—	226	—	575	—	459	—	829	—	—	(289)	(2,067)	—	(2,356)
Currency translation adjustment	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	231	231
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(7,476)	—	(7,476)
Balance at March 31, 2016 (unaudited)	2,589,868	\$ 3,682	7,437,325	\$ 21,676	5,000,002	\$ 20,404	8,099,994	\$ 43,477	2,111,109	\$ 12,541	8,888,888	\$ 38,057	2,177,858	\$ 0	\$ 1	\$(121,051)	\$(4,755)	\$(125,805)

See accompanying notes.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		Three months ended March 31,	
	2014	2015	2015	2016
	(in thousands)		(unaudited)	(unaudited)
Operating activities				
Net loss	\$ (12,880)	\$ (25,174)	\$ (5,733)	\$ (7,476)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation	864	1,044	193	178
Stock-based compensation expense	1,224	1,125	302	282
Non-cash interest expense	155	198	27	41
Change in fair value of redeemable convertible preferred stock warrant	38	(83)	—	20
Changes in operating assets and liabilities:				
Accounts receivable	(514)	(153)	180	(805)
Prepaid expenses and other assets	(404)	(1,011)	(379)	(35)
Restricted cash and other deposits	(1,779)	977	282	(1,752)
Accounts payable	(90)	667	975	(424)
Deferred revenue	(20)	(507)	(537)	386
Contingently repayable grant funding	305	(805)	(426)	—
Accrued expenses and other liabilities	415	1,259	218	(581)
Net cash used in operating activities	(12,686)	(22,463)	(4,898)	(10,166)
Investing activities				
Purchase of short term government obligations	—	(3,516)	—	(3,412)
Purchases of property and equipment	(227)	(1,163)	(123)	(143)
Net cash provided by (used in) investing activities	(227)	(4,679)	(123)	(3,555)
Financing activities				
Net proceeds from issuance of preferred stock and warrants	20,140	32,669	—	—
Proceeds from issuance convertible note, net of issuance costs	—	7,092	—	—
Principle payments on loan payable	—	(2,336)	(227)	—
Deferred IPO costs	—	(302)	—	(1,684)
Proceeds from loans payable, net of issuance costs	4,494	6,674	—	—
Issuance of common stock	137	109	20	7
Net cash provided by financing activities	24,771	43,906	(207)	(1,677)
Effect of exchange rate changes on cash	(3,323)	(1,019)	(230)	112
Net (decrease) increase in cash and cash equivalents	8,535	15,745	(5,458)	(15,286)
Cash and cash equivalents at beginning of period	8,057	16,592	16,592	32,337
Cash and cash equivalents at end of period	<u>\$ 16,592</u>	<u>\$ 32,337</u>	<u>\$ 11,134</u>	<u>\$ 17,051</u>
Cash paid during the year for:				
Interest	<u>\$ 366</u>	<u>\$ 531</u>	<u>\$ 150</u>	<u>\$ 243</u>
Supplemental Noncash Financing Activities:				
Venture debt termination fee liability	<u>\$ 270</u>	<u>\$ 270</u>	<u>\$ —</u>	<u>\$ —</u>
Issuance of preferred warrants in connection with venture loans	<u>\$ 121</u>	<u>\$ 137</u>	<u>\$ —</u>	<u>\$ —</u>
Accrued dividends and accretion of preferred stock to redemption value	<u>\$ 4,951</u>	<u>\$ 7,335</u>	<u>\$ 1,561</u>	<u>\$ 2,356</u>
Conversion of bridge loans into Series E preferred	<u>\$ —</u>	<u>\$ 7,288</u>	<u>\$ —</u>	<u>\$ —</u>

See accompanying notes.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

1. Nature of business and basis of presentation

Selecta Biosciences, Inc. (the "Company") was incorporated in Delaware on December 10, 2007, and is based in Watertown, Massachusetts. The Company is a biopharmaceutical company dedicated to developing nanoparticle immunomodulatory drugs for the treatment and prevention of human diseases. Since inception, the Company has devoted its efforts principally to research and development of its technology and product candidates, recruiting management and technical staff, acquiring operating assets, and raising capital.

The Company is subject to a number of risks similar to other early life science companies including, but not limited to, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology, and market acceptance of its products.

Unless otherwise indicated, all amounts are in millions except share and per share amounts.

Basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP"). The consolidated financial statements and accompanying notes are stated in U.S. dollars. Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The accompanying unaudited consolidated financial statements and the related notes as of March 31, 2016 and for the three months ended March 31, 2015 and 2016 are condensed and are prepared pursuant to the rules and regulations of the U.S. Securities and Exchange Commission regarding interim financial reporting. Accordingly, they do not include all of the information and disclosures required by U.S. GAAP for complete financial statements and should be read in conjunction with the Company's audited financial statements for the years ended December 31, 2014 and 2015. In the opinion of management, the Company has prepared the accompanying unaudited condensed consolidated financial statements for the three months ended March 31, 2015 and 2016 on the same basis as its audited financial statements, and these condensed consolidated financial statements include all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the results of the interim periods presented. The operating results for the interim periods presented are not necessarily indicative of the results expected for the full year 2016 or any future years or periods.

Liquidity

The Company has incurred losses since inception and negative cash flows from operating activities. As of December 31, 2015 and March 31, 2016, the Company had an accumulated deficit of \$111.5 million and \$121.1 million, respectively. The Company has financed its operations to date through issuances of redeemable convertible preferred stock (collectively, "Preferred Stock"), debt, research grants and a research collaboration. During the year ended December 31, 2015, the Company raised an additional \$39.8 million, net of issuance costs, through the issuance of convertible notes (Note 8) and Series E redeemable convertible preferred stock ("Series E Preferred") (Note 9) and \$6.8 million through the issuance of additional venture debt ("Debt") (Note 8). The Company's cash and cash equivalents as of December 31, 2015 and March 31, 2016 included \$3.0 million and

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

\$1.5 million, respectively, of unrestricted cash held by its Russian subsidiary. The future success of the Company is dependent upon its ability to obtain additional capital through issuances of equity and debt securities and from collaboration and grant agreements in order to further the development of its technology and product candidates, and ultimately upon its ability to attain profitable operations. There can be no assurance that the Company will be able to obtain the necessary financing to successfully develop and market its product candidates or attain profitability.

These factors raise substantial doubt about the Company's ability to continue as a going concern. The Company intends to pursue a private offering of equity securities or a public offering of its common stock to fund future operations. However, if the Company is unable to complete a sufficient private or public offering in a timely manner, it would need to pursue other financing alternatives. There can be no assurances that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

Unaudited pro forma financial information

The unaudited pro forma consolidated balance sheet information at March 31, 2016 has been prepared to reflect the automatic conversion of all shares of Preferred Stock outstanding at March 31, 2016 into 9,890,580 shares of common stock and cashless exercise of warrants for the purchase of 567,306 shares of common stock as if a proposed initial public offering had occurred on March 31, 2016. For purposes of pro forma basic and diluted net loss per share attributable to common stockholders, all shares of Preferred Stock and those warrants which will automatically be converted or exercised upon the filing of a registration statement on Form S-1 or closing of an initial public offering, and the preferred stock warrants which will convert into common stock warrants upon the closing of an initial public offering, have been treated as if they have been converted or exercised at the beginning of the period or on the issuance date, if later. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders do not include the effects of the accretion of Preferred Stock to redemption value and accrued dividends, or the change in fair value of redeemable convertible preferred stock warrants.

2. Summary of significant accounting policies

Principles of consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Selecta (RUS), LLC ("Selecta RUS"), a Russian limited liability corporation, and Selecta Biosciences Security Corporation, a Massachusetts Security Corporation. All significant intercompany accounts and transactions have been eliminated.

Foreign currency

The functional currency of Selecta RUS is the ruble. Assets and liabilities of Select RUS are translated at period-end exchange rates, while revenues and expenses are translated at average exchange rates for the period. Translation gains and losses are reflected in accumulated other comprehensive loss within stockholders' deficit. Foreign currency transaction gains or losses are reflected in the consolidated statements of operations and comprehensive loss.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**Use of estimates**

The preparation of consolidated financial statements in conformity with U.S. GAAP requires the Company's management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The Company's management considers many factors in selecting appropriate financial accounting policies and controls, and bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. In preparing these consolidated financial statements, management used significant estimates in the following areas, among others: revenue recognition, the fair value of common stock and other equity instruments, accounting for stock-based compensation, income taxes, collectability of accounts receivable, useful lives of long-lived assets, accrued expenses, and accounting for project development. The Company assesses the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

The Company's management makes significant estimates and assumptions in determining the fair value of its common stock. The Company utilizes various valuation methodologies in accordance with the framework of the 2004 American Institute of Certified Public Accountants' Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Segment information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, the Company's Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment, the research and development of nanoparticle immunomodulatory drugs for the treatment and prevention of human diseases.

Cash equivalents and short term investments

Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. Investments consist of securities with remaining maturities greater than 90 days when purchased. The Company classifies these investments as available-for-sale and records them at fair value in the accompanying consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying investment.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During 2015, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

Concentrations of credit risk and off-balance sheet risk

Financial instruments that potentially subject the Company to concentration of credit risk consist primarily of cash, cash equivalents, and accounts receivable. Cash and cash equivalents are deposited with federally insured financial institutions in the U.S. and may, at times, exceed federally insured limits. Management believes that the financial institutions that hold the Company's deposits are financially credit worthy and, accordingly, minimal risk exists with respect to those balances. Generally, these deposits may be redeemed upon demand and therefore bear minimal interest rate risk. As an integral part of operating our Russia subsidiary, we also maintain cash in Russian bank accounts in denominations of both rubles and U.S. dollars. As of March 31, 2016, we maintained approximately \$4.2 million in Russian bank accounts, of which \$3.0 million was held in U.S. dollars.

The Company has minimal credit risk as the majority of accounts receivable relates to amounts due under a government sponsored grant, collaboration with large pharmaceutical companies or grants from well-known and supported non-profit organizations. The Company did not have any off balance sheet arrangements as of December 31, 2014 and 2015 and March 31, 2016.

Fair value of financial instruments

The Company's financial instruments consist mainly of cash equivalents, short-term investments, restricted cash, accounts receivable, accounts payable, loans payable, common stock warrants, and redeemable convertible preferred stock warrants. The carrying amounts of cash equivalents, short term investments, restricted cash, accounts receivable, and accounts payable approximate their estimated fair value due to their short term maturities. The carrying amount of loans payable approximates their estimated fair value due to the consistency between the prevailing market rates in effect and the effective interest rate of 12.4% for the debt arrangement.

Accounting standards define fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. A three-level hierarchy is used to prioritize the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements), and the lowest priority to unobservable inputs (Level 3 measurements). The three levels of the fair value hierarchy are described below:

Level 1—Level 1 inputs are quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.

Level 2—Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. If the asset or liability has a specified (contractual) term, a Level 2 input must be observable for substantially the full term of the asset or liability.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
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Level 3—Level 3 inputs are unobservable inputs for the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

To the extent that a valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. As of December 31, 2014 and 2015, and at March 31, 2016, the Company's Preferred Stock Warrants were the only financial instruments classified as Level 3.

Fair value is a market-based measure considered from the perspective of a market participant rather than an entity-specific measure. Therefore, even when market assumptions are not readily available, the Company's own assumptions are set to reflect those that market participants would use in pricing the asset or liability at the measurement date. The Company uses prices and inputs that are current as of the measurement date, including during periods of market dislocation. In periods of market dislocation, the observability of prices and inputs may change for many instruments. This condition could cause an instrument to be reclassified within levels in the fair value hierarchy. There were no transfers within the fair value hierarchy during the years ended December 31, 2014 and 2015, and the three months ended March 31, 2016.

Property and equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the respective assets, generally seven years for furniture, five years for equipment and three years for computer and office equipment. Leasehold improvements are amortized over their useful life or the life of the lease, whichever is shorter. Major additions and betterments are capitalized. Maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to operations as incurred. Costs incurred for construction in progress are recorded as assets and are not amortized until the construction is substantially complete and the assets are ready for their intended use.

Impairment of long-lived assets

The Company periodically evaluates its long-lived assets for potential impairment. Impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends, and product development cycles. Impairment in the carrying value of each asset is assessed when the undiscounted expected future cash flows derived from the asset are less than their carrying value. The Company did not recognize any impairment charges through March 31, 2016.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
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Debt issuance costs

Debt issuance costs and fees paid to lenders are recorded as a direct deduction from the face amount of the related debt. Debt issuance costs are accounted for as additional debt discount and are amortized over the term of the related debt using the interest method and recorded as interest expense. Costs and fees paid to third parties are expensed as incurred.

Revenue recognition

The Company's revenue is primarily generated from research grants in both the United States and Russia, and a license and research collaboration agreement with Sanofi. The Company recognizes revenue in accordance with ASC Topic 605, *Revenue Recognition*. Accordingly, revenue is recognized when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;
- The seller's price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Collaboration revenue

When evaluating multiple element arrangements such as the agreement with Sanofi discussed in Note 12, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. The Company has used its best estimate of selling price to estimate the selling price for licenses to the Company's proprietary technology, since the Company does not have VSOE or TPE of selling price for these deliverables. In those circumstances, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements, estimated

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company's best estimate of selling price, the Company evaluates whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

The Company may receive upfront payments when licensing its intellectual property in conjunction with a research and development agreement. When management believes the license to its intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company generally recognizes revenue attributed to the license over the Company's contractual or estimated performance period. When management believes the license to its intellectual property has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed.

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized over the remaining period of performance.

Grant agreements

Grant revenue is generally recognized as the related research and development work is performed. Grant arrangements frequently include payment milestones which the Company has judged to be non-substantive milestones as they are typically entitled to receive payment regardless of the outcome of the research work. Revenue under such arrangements is recognized using a proportional performance method, but not in excess of cash actually received.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets.

Research and development costs

Costs incurred in the research and development of the Company's products are expensed as incurred. Research and development expenses include costs incurred in performing research and development activities, including salaries and benefits, facilities cost, overhead costs, contract services, supplies and other outside costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
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Clinical trial costs

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activation, and other information provided to the Company by its vendors.

Income taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more-likely-than-not be realized.

The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes. To date, the Company has not incurred interest and penalties related to uncertain tax positions. Should such costs be incurred, they would be classified as a component of income tax expense.

Preferred stock

The Company classifies Preferred Stock as temporary equity and initially records it at the original issuance price, net of issuance costs and discounts. The carrying value is accreted up to the redemption value over the earliest redemption period. The carrying value is also adjusted for dividends expected to be paid upon redemption or liquidation according to the preferred stock terms on each balance sheet date.

Warrants

The Company issues common stock warrants and redeemable convertible preferred stock warrants to investors and lenders. Common stock warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from other debt and equity instruments, are contingently exercisable, do not embody an obligation for the Company to repurchase its own shares, and permit the holders to receive a fixed number of common shares upon exercise. In addition, such warrants require physical settlement and do not provide any guarantee of value or return. Common stock warrants are initially recorded at their issuance date fair value and are not subsequently re-measured. These warrants are valued using the Black-Scholes option pricing model ("Black-Scholes").

Redeemable convertible preferred stock warrants are classified as a liability and are initially recorded at their fair value and re-measured on each subsequent balance sheet date while the warrants are

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

outstanding. Changes in fair value are recorded in interest expense, net in the accompanying consolidated statements of operations and comprehensive loss. The redeemable convertible warrants are valued using Black-Scholes.

Stock-based compensation

The Company accounts for all stock-based compensation granted to employees and non-employees using a fair value method. Stock-based compensation awarded to employees is measured at the grant date fair value of stock option grants and is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis, net of estimated forfeitures. Stock-based compensation awarded to non-employees are subject to revaluation over their vesting terms. The Company reduces recorded stock-based compensation for estimated forfeitures. To the extent that actual forfeitures differ from the Company's estimates, the differences are recorded as a cumulative adjustment in the period the estimates were adjusted. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Comprehensive loss

Comprehensive loss is defined as the change in the equity of a business entity during a period from transactions and other events and circumstances from non-owner sources. It includes all changes in equity during a period except those resulting from investments by owners and distributions to owners. Comprehensive loss consists of both: (i) all components of net loss and (ii) all components of comprehensive loss other than net loss, referred to as other comprehensive loss. For all periods presented, other comprehensive loss is comprised solely of foreign currency translation adjustments.

Net loss per share

Because the outstanding preferred stock is considered a participating security, the Company utilizes the "two-class" method of computing earnings per share. Under the "two-class" method, in periods in which the Company would report income from continuing operations, such income would be reduced by any dividends directly attributable to the preferred stock and the remainder would then be allocated between the preferred stock and the common stock based on their proportionate as converted interest. Net losses are not allocated to preferred stockholders as they do not have an obligation to share in the Company's net losses.

The Company has reported losses since inception and has computed basic net loss per share attributable to common stockholders by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including stock options, convertible preferred stock, and warrants outstanding during the period except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

Deferred rent

Rent expense and lease incentives from operating leases are recognized on a straight-line basis over the lease term. The difference between rent expense recognized and rental payments is recorded as deferred rent in the accompanying consolidated balance sheets.

Contingent liabilities

The Company accounts for its contingent liabilities in accordance with ASC No. 450, *Contingencies*. A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter. As of December 31, 2014 and 2015, and at March 31, 2016, the Company was not a party to any litigation that could have a material adverse effect on the Company's business, financial position, results of operations or cash flows.

Deferred issuance costs

Direct and incremental legal and accounting costs associated with the Company's proposed initial public offering totaled approximately \$2.5 million through March 31, 2016. Such costs are recorded as Other assets on the Consolidated Balance Sheet and will be used as an offset against the proceeds received in the offering. If the proposed initial public offering were no longer probable of occurring, the deferred costs would be expensed at that time.

Guarantees and indemnifications

As permitted under Delaware law, the Company indemnifies its officers, directors, consultants and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through March 31, 2016, the Company had not experienced any losses related to these indemnification obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

Recent accounting pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09"), which amends the guidance for revenue recognition to replace numerous industry-specific requirements. ASU 2014-09 implements a five-step process for customer contract revenue recognition that focuses on transfer of control, as opposed to transfer of risk and rewards. ASU 2014-09 also requires enhanced disclosures regarding the nature, amount, timing, and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The amendments in ASU 2014-09 are effective for reporting periods beginning after December 15, 2017. Early adoption is permitted, but not before December 15, 2016. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. The Company is

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
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currently in the process of evaluating the effect the adoption of ASU 2014-09 may have on its financial statements.

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements-Going Concern* ("ASU 2014-15"). ASU 2014-15 requires management to assess an entity's ability to continue as a going concern and to provide related disclosures in certain circumstances. The requirement of ASU 2014-15 will be effective for the annual financial statement period beginning after December 15, 2016, with early adoption permitted. The Company is currently in the process of evaluating the impact of adopting ASU 2014-15.

In February 2016, FASB issued ASU No.2016-02, *Leases* ("ASU 2016-02"). ASU 2016-02 requires a lessee to separate the lease components from the non-lease components in a contract and recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. It also aligns lease accounting for lessors with the revenue recognition guidance in ASU 2014-09. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years, and is to be applied at the beginning of the earliest period presented using a modified retrospective approach.

3. Net loss per share

Because the Company has reported a net loss attributable to common stockholders for all periods presented, basic and diluted net loss per share attributable to common stockholders are the same for those periods. All Preferred Stock, common stock warrants, Preferred Stock warrants, and stock options have been excluded from the computation of diluted weighted average shares outstanding because such securities would have an antidilutive impact.

Selecta Biosciences, Inc. and Subsidiaries

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
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The following table sets forth the computation of basic and diluted net loss per share and has been retrospectively adjusted to reflect the effect of a reverse common stock split effected in June 2016 (in thousands, except share and per-share data):

	Year ended December 31,		Three months ended	
	2014	2015	2015	2016
			(unaudited)	
Numerator:				
Net (loss)	\$ (12,880)	\$ (25,174)	\$ (5,733)	\$ (7,476)
Less: accretion on preferred stock	(4,951)	(7,335)	(1,561)	(2,356)
Net effect of extinguishment of preferred stock	1,459	—	—	—
Net loss attributable to common stockholders	<u>\$ (16,372)</u>	<u>\$ (32,509)</u>	<u>\$ (7,294)</u>	<u>\$ (9,832)</u>
Denominator:				
Weighted-average common shares outstanding—basic and diluted	2,090,677	2,150,422	2,126,878	2,175,037
Net loss per share attributable to common stockholders—basic and diluted	<u>\$ (7.84)</u>	<u>\$ (15.13)</u>	<u>\$ (3.43)</u>	<u>\$ (4.52)</u>

Potential common shares issuable upon conversion of Preferred Stock, warrants to purchase common or Preferred Stock, and stock options that are excluded from the computation of diluted weighted average shares outstanding are as follows:

	Year ended December 31,		Three months ended	
	2014	2015	2015	2016
			(unaudited)	
Redeemable convertible preferred stock	6,471,358	9,890,580	6,471,358	9,890,580
Stock options to purchase common stock	1,143,237	1,569,379	1,247,562	1,736,682
Stock warrants to purchase common stock	—	650,618	—	650,618
Redeemable convertible preferred stock warrants	17,094	26,832	17,094	26,832
Total	<u>7,631,689</u>	<u>12,137,409</u>	<u>7,736,014</u>	<u>12,304,712</u>

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2015, and the three months ended March 31, 2016, has been computed using the weighted average common shares outstanding after giving pro forma effect to the automatic conversion of all shares of Preferred Stock into shares of common stock, the automatic conversion of all Preferred Stock warrants into common stock warrants, and the automatic net exercise of warrants to purchase common stock upon the filing of a registration statement on Form S-1 as if such conversions or exercises had occurred at the beginning of 2015 or the date of original issuance, if later.

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The following table sets forth the computation of the pro forma net loss per share (in thousands, except share and per share data):

	Year ended <u>December 31,</u> 2015	Three months ended <u>March 31,</u> 2016
	(unaudited)	(unaudited)
Numerator:		
Net loss attributable to common stockholders	\$ (32,509)	\$ (9,832)
Less: accrued dividends and accretion on preferred stock	7,335	2,356
Change in fair value of preferred stock warrants	(83)	20
Net loss attributable to common stockholders	<u>\$ (25,257)</u>	<u>\$ (7,456)</u>
Denominator:		
Weighted-average common shares outstanding—basic and diluted	2,150,472	2,175,037
Adjustment for assumed conversion of preferred stock	7,637,239	9,890,580
Adjustment for assumed effect of cashless conversion of common stock warrants issued with Series E preferred stock	192,809	567,306
	<u>9,980,469</u>	<u>12,632,923</u>
Net loss per share attributable to common stockholders—basic and diluted	<u>\$ (2.53)</u>	<u>\$ (0.59)</u>

4. Fair Value Measurements

The tables below present information about the Company's financial assets and liabilities that are measured and carried at fair value as of December 31, 2014 and 2015 (in thousands) and indicate the level within the fair value hierarchy where each measurement is classified.

	December 31, 2014			
	(level 1)	(level 2)	(level 3)	Total
Warrants to purchase redeemable convertible preferred stock, included in other long term liabilities	\$ —	\$ —	\$ 236	\$ 236

	December 31, 2015			
	(level 1)	(level 2)	(level 3)	Total
US Treasury obligations, included in cash equivalents	\$ 14,486	\$ —	\$ —	\$ 14,486
US Treasury obligations, included in investments	\$ 3,516	\$ —	\$ —	\$ 3,516
Warrants to purchase redeemable convertible preferred stock, included in other long term liabilities	\$ —	\$ —	\$ 290	\$ 290

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	Three months ended March 31, 2016			
	(level 1)	(level 2)	(level 3)	Total
			(unaudited)	
US Treasury obligations, included in cash equivalents	\$ 8	\$ —	\$ —	\$ 8
US Treasury obligations, included in investments	\$ 6,928	\$ —	\$ —	\$ 6,928
Warrants to purchase redeemable convertible preferred stock, included in other long term liabilities	\$ —	\$ —	\$ 310	\$ 310

The maturity date for US Treasury obligations, included in cash equivalents at December 31, 2015 was 34 days and for those included within investments at December 31, 2015 and for the three months ended March 31, 2016 was 106 days and between 15 and 45 days, respectively. Fair value of US Treasury obligations approximates amortized value.

In July 2015, the Company issued warrants for the purchase of 80,813 shares of common stock at an exercise price of \$17.55 in connection with the issuance of convertible notes. These warrants expire three years from date of issuance. In August 2015, the Company issued warrants for the purchase of 569,791 shares of common stock at an exercise price of \$0.04 in connection with the issuance of the Series E Preferred. Common stock warrants are classified as permanent equity which are initially recorded at issuance date fair value and are not subsequently re-measured. The warrants to purchase common stock issued at the same time as the Series E Preferred will automatically exercise on a cashless basis upon the filing of a registration statement on Form S-1. These warrants expire four years from date of issuance.

In August 2013 and July 2014, in conjunction with the execution of a loan and security agreement (Note 8), the Company issued warrants to the lenders for the purchase of up to 66,668 shares of the Company's Series D redeemable convertible preferred stock ("Series D Preferred") at an exercise price of \$4.50 per share. These warrants are classified as liabilities in the accompanying consolidated balance sheets. These warrants expire four years from the date of issuance.

In December 2015, in conjunction with the execution of a loan and security agreement (Note 8), the Company issued warrants to the lenders for the purchase of up to 37,978 shares of the Company's Series E Preferred at an exercise price of \$4.50 per share. These warrants are classified as liabilities in the accompanying consolidated balance sheets. These warrants expire four years from the date of issuance.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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The following table sets forth a summary of the activities of the Company's Series D and Series E Preferred stock warrant liability which represents a recurring measurement that is classified within Level 3 of the fair value hierarchy wherein fair value is estimated using significant unobservable inputs:

	Year ended December 31, 2014	Year ended December 31, 2015	Three months ended March 31, 2016 (unaudited)
Balance at beginning of period	\$ 77	\$ 236	\$ 290
Fair value of additional warrants issued	121	137	—
Change in fair value	38	(83)	20
Balance at end of period	<u>\$ 236</u>	<u>\$ 290</u>	<u>\$ 310</u>

The fair value of the warrants to purchase shares of the Company's Series D Preferred at an exercise price of \$4.50 per share was estimated using Black-Scholes with the following assumptions as of December 31, 2014 and 2015 and at March 31, 2016:

	December 31, 2014	December 31, 2015	March 31, 2016 (unaudited)
Risk free interest rate	2.10%	2.15%	1.61%
Expected dividend yield	—	—	—
Expected term (in years)	9.20	8.18	7.93
Expected volatility	92.53%	85.83%	85.26%
Fair value of underlying instrument	<u>\$ 4.18</u>	<u>\$ 3.05</u>	<u>\$ 3.29</u>

The fair value of the warrants to purchase shares of the Company's Series E Preferred at an exercise price of \$4.50 per share was estimated using Black-Scholes with the following assumptions as of December 31, 2015 and at March 31, 2016:

	December 31, 2015	March 31, 2016 (unaudited)
Risk free interest rate	2.26%	1.75%
Expected dividend yield	—	—
Expected term (in years)	10.00	9.75
Expected volatility	82.22%	82.66%
Fair value of underlying instrument	<u>\$ 4.37</u>	<u>\$ 4.67</u>

The risk-free interest rate used is the rate for a U.S. Treasury zero coupon issue with a term consistent with the remaining contractual term of the associated award on the date of measurement. The Company has not paid, and does not expect to pay, any cash dividends in the foreseeable future. The Company based the expected term assumption on the actual remaining contractual term of the respective warrants as of the date of measurement. Expected volatilities are based on historical

Selecta Biosciences, Inc. and Subsidiaries**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

volatilities from guideline companies, since there is no active market for the Company's common stock. The fair value on the date of measurement of the Series D Preferred and the Series E Preferred, the underlying instruments, was estimated by management with the assistance of a third party valuation specialist.

5. Property and equipment

Property and equipment consists of the following (in thousands):

	<u>December 31,</u>		<u>March 31,</u>
	<u>2014</u>	<u>2015</u>	<u>2016</u>
			(unaudited)
Laboratory equipment	\$ 3,314	\$ 4,028	\$ 4,337
Computer equipment and software	365	409	421
Leasehold improvements	911	91	120
Furniture and fixtures	115	222	222
Office equipment	56	62	62
P,P&E—Construction in process	—	144	7
Total property and equipment	<u>4,761</u>	<u>4,956</u>	<u>5,169</u>
Less accumulated depreciation	<u>(2,778)</u>	<u>(2,927)</u>	<u>(3,129)</u>
Property and equipment, net	<u>\$ 1,983</u>	<u>\$ 2,029</u>	<u>\$ 2,040</u>

Depreciation expense for the years ended December 31, 2014 and 2015 was \$0.9 million and \$1.0 million, respectively, and \$0.2 million for the three months ended March 31, 2015 and 2016.

6. Accrued expenses

Accrued expenses consist of the following (in thousands):

	<u>December 31,</u>		<u>March 31,</u>
	<u>2014</u>	<u>2015</u>	<u>2016</u>
			(unaudited)
Payroll	\$ 189	\$ —	\$ 98
Legal	—	213	119
Bonus	515	669	150
Current portion of deferred rent and lease incentive	219	405	416
Accrued patent fees	155	219	285
Accrued R&D costs	394	1,649	1,090
Other	381	223	1,027
Accrued liabilities	<u>\$ 1,853</u>	<u>\$ 3,378</u>	<u>\$ 3,185</u>

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**7. Commitments and contingencies***Operating leases*

The Company has a non-cancellable operating lease for its laboratory and office space that expires in March 2017. The lease agreement includes a rent escalation clause, and accordingly, rent expense is being recognized on a straight-line basis over the lease term. In addition, as part of the lease agreement, the landlord provided the Company a tenant improvement allowance of up to \$0.7 million, which the Company fully utilized during 2012. The tenant improvement allowance is accounted for as a lease incentive obligation and is being amortized as a reduction to rent expense over the lease term. The leasehold improvements are capitalized as a component of property and equipment.

In connection with the lease, the Company secured a letter of credit for \$0.3 million which renews automatically each year and is classified in restricted cash and other deposits in the accompanying consolidated balance sheets.

In April 2015, the Company amended the lease agreement to exchange 13,711 square feet of space for another 15,174 square feet of space within the same building. Rental payments on the prior space ceased as of March 31, 2015 and rental payments on the new space began on October 1, 2015. The combined lease term remains unchanged and will expire in March 2017. Rent expense is recorded over the lease term on a straight-line basis.

Deferred rent and lease incentive liability totaled \$0.5 million and \$0.5 million as of December 31, 2014 and 2015, respectively, and \$0.4 million at March 31, 2016. Included in that amount, the current portion of deferred rent and lease incentive liability is classified as accrued expenses and was \$0.2 million and \$0.4 million at December 31, 2014 and 2015, respectively, and \$0.4 million at March 31, 2016.

The Company subleased a portion of its facility to a tenant with a term that expires in March 2017. In March 2015, the tenant terminated the sublease and vacated the space. The sublease amount from the tenant was recorded as a reduction of lease expense and totaled \$0.7 million and \$0.2 million for the years ended December 31, 2014 and 2015, respectively, and \$0.2 million for the three months ended March 31, 2016.

The Company has a month-to-month facility agreement for its Moscow, Russia facility. Rent expense is recognized as incurred.

Rent expense, net of sublease payments, for the years ended December 31, 2014 and 2015 was \$0.6 million and \$1.1 million, respectively, and for the three months ended March 31, 2015 and 2016 was \$0.2 million and \$0.4 million, respectively. As of December 31, 2015, future minimum lease payments for non-cancellable leases were \$1.2 million in 2016, and \$0.3 million in 2017.

Other

As permitted under Delaware law, the Company indemnifies its directors for certain events or occurrences while the director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the director's lifetime. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' insurance

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

coverage that limits its exposure and enables it to recover a portion of any future amounts paid. The Company also has indemnification arrangements under certain of its facility leases that require it to indemnify the landlord against certain costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from certain breaches, violations, or non-performance of any covenant or condition of the Company's lease. The term of the indemnification is for the term of the related lease agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. To date, the Company had not experienced any material losses related to any of its indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, accordingly, has concluded that the fair value of these obligations is negligible, and no related reserves have been established.

The Company is a party in various other contractual disputes and potential claims arising in the ordinary course of business. The Company does not believe that the resolution of these matters will have a material adverse effect on its financial position or results of operations.

8. Debt*Term loans*

On August 9, 2013, the Company entered into a loan and security agreement with two lenders to borrow up to \$7.5 million. The Company initially borrowed \$3.0 million in August 2013 and subsequently borrowed an additional \$4.5 million in July 2014. The amounts borrowed are collectively referred to as "Term Loans." In December 2015, the Company refinanced its existing debt facility that was originally entered into on August 9, 2013, as amended with Oxford Finance LLC ("Oxford") and Square 1 Bank ("Square 1"), to increase the amount of the borrowing to \$12.0 million and to extend the repayment term. The lenders for the refinanced debt facility are Oxford and Pacific Western Bank ("Pacific Western.") Pacific Western had acquired Square 1 since the time of the original loan. Such a change in lender does not constitute third party financing and, on its own, would not require extinguishment accounting. As a result of the refinancing, the stated interest rate was also adjusted to reflect the current market borrowing rate. As of December 31, 2015 and March 31, 2016, the outstanding principal balance under the Term Loans was \$12.0 million.

According to ASC 470-50-40, the refinancing and modification of the prior debt in a non-troubled debt situation must be treated as either an extinguishment or a modification based on whether the present value of the cash flows under the terms of the new debt instrument is different by greater than, or less than, 10% from the present value of the remaining cash flows under the terms of the original instrument. For cash flow changes greater than 10%, the debt modification is accounted for as a debt extinguishment, whereby the original debt is derecognized and the new debt is initially recorded at fair value, with the difference recognized as an extinguishment gain or loss. For cash flow changes of less than 10%, the new loan is considered a modification and no gain or loss is recognized. In considering all cash flow changes, the Company concluded that the refinancing of the debt as of December 31, 2015 is a modification of the debt and not a debt extinguishment, and as a result the debt is initially recorded at its amortizable value net of discounts and deferred costs.

Selecta Biosciences, Inc. and Subsidiaries**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

The Term Loans are collateralized by the assets of the Company and bear interest at 8.1% per annum. The monthly payments for the Term Loans are initially interest only through January 2017. Principal repayments for the Term Loans are due over 30 monthly installments beginning on February 1, 2017. The Term Loans may be prepaid at the Company's option at any time prior to maturity subject to a prepayment fee of 3% if prepaid prior to the first anniversary of the borrowing date, 2% if prepaid after the first anniversary but before the second anniversaries, and 1% if prepaid after the second anniversary.

The Term Loans do not include any financial covenants. The Term Loans require a final payment fee of 6.0% on the aggregate principal amounts borrowed upon repayment at maturity, on a prepayment date, or upon default. The final payment fee totaling \$0.7 million is recorded as a loan discount. In addition, the Term Loans contain a subjective acceleration clause whereby in an event of default, an immediate acceleration of repayment occurs if there is a material impairment of the lenders' lien or the value of the collateral, a material adverse change in the business condition or operations, or a material uncertainty exists that any portion of the loan may not be repaid. To date, there have been no such events and the lender has not exercised its right under this clause. As a result, the Company concluded that a material adverse change has not occurred and is unlikely to occur, therefore, no liability has been recorded in connection with the clause.

In connection with the Term Loans, the Company granted the lenders warrants in August 2013 to purchase up to 26,668 shares of the Company's Series D Preferred and additional warrants in July 2014 to purchase up to 40,000 shares of the Company's Series D Preferred. Additionally, with the refinancing of the Term Loans at December 31, 2015, the Company granted the lenders 37,978 shares of the Company's Series E Preferred. The initial grant date fair value of the warrants of \$0.1 million, \$0.1 million and \$0.1 million respectively, was recorded as a loan discount.

Term Loan discounts are amortized as additional interest expense over the term of the loans. Interest expense for the years ended December 31, 2014 and 2015 totaled \$0.6 million and \$0.6 million, respectively, and \$0.2 million and \$0.3 million for the three months ended March 31, 2015 and 2016, respectively.

Future minimum payments on the Term Loans as of December 31, 2015 are as follows (in thousands):

Year ended December 31:	
2016	\$ 972
2017	5,319
2018	5,318
2019	3,379
Total debt payments	14,988
Less: Amount representing interest	(2,268)
Less: Debt discount and deferred charges	(919)
Less: Current portion of issuance costs	54
Loans payable, net of current portion	<u>\$ 11,855</u>

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016*Convertible notes*

In April 2015, the Company issued convertible notes as a bridge loan to be automatically converted into the Company's capital stock upon the consummation of a private placement of the Company's Preferred Stock. The convertible notes bore interest at 8% per annum, compounding monthly. In the event the Company was unable to consummate the private placement by July 15, 2015, the Company would be required to issue warrants to purchase shares of the Company's common stock equal to 20% of the convertible note principal divided by \$17.55. On July 24, 2015, the Company issued warrants to the convertible note holders to purchase up to 80,813 shares of the Company's common stock at an exercise price of \$17.55 per share for a term of three years. The carrying value and accrued interest of the outstanding convertible notes were automatically converted into 1,619,550 shares of Series E Preferred. As part of the Series E Preferred issuance, the convertible note holders also received warrants to purchase up to 103,817 shares of the Company's common stock (Note 9). The difference between the carrying value and accrued interest of the convertible notes that were converted and the combined fair value of the Series E Preferred shares and common stock warrants issued were negligible. Interest expense incurred on the convertible notes totaled \$0.3 million for the year ending December 31, 2015 and zero during the three months ended March 31, 2016.

9. Preferred stock

The Company issued Preferred Stock with a \$0.0001 par value to investors for cash or as settlement for outstanding debt under convertible notes. As of December 31, 2014 and 2015, the Company had 28,804,969 and 37,835,623 authorized shares of Preferred Stock, respectively, and at March 31, 2016 had 37,835,623 authorized shares of Preferred Stock.

As of December 31, 2015 and at March 31, 2016, the Company had issued and outstanding Preferred Stock of (i) 2,589,868 shares of Series A redeemable convertible preferred stock ("Series A Preferred"), (ii) 7,437,325 shares of Series B redeemable convertible preferred stock ("Series B Preferred"), (iii) 5,000,002 shares of Series C redeemable convertible preferred stock ("Series C Preferred"), (iv) 8,099,994 shares of Series D Preferred, (v) 2,111,109 shares of Series SRN Redeemable Convertible Preferred Stock ("Series SRN Preferred") and (vi) 8,888,888 shares of Series E Preferred.

In April 2014 and August 2014, the Company issued an additional 3,211,105 shares of Series D Preferred at \$4.50 per share for total net proceeds of \$14,349,239. In July 2014, the Company issued an additional 1,333,332 shares of Series SRN Preferred at \$4.50 per share for total net proceeds of \$5.8 million. In connection with the issuance of the additional shares of Series SRN Preferred, the Series SRN Preferred terms were amended. Significant terms that were amended included a change of the Series SRN Preferred optional and mandatory conversion price (other than a special conversion event, as defined in the certificate of incorporation) to \$16.77 per share, the elimination of a time-based tranche investment requirement, and the removal of a call option for the Company to repurchase the Series SRN Preferred shares. Based upon the qualitative characteristics of the amendments, the Company determined that the changes significantly modified the terms of Series SRN Preferred resulting in an extinguishment of the then outstanding SRN Preferred shares. As a result, the carrying value of Series SRN Preferred of \$5.0 million at the date of the amendment was derecognized.

Selecta Biosciences, Inc. and Subsidiaries

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

and the amended Series SRN Preferred shares were recorded at their fair value of \$4.50 per share. The difference of \$1.5 million was recorded as additional paid in capital.

In August 2015 and September 2015, the Company issued an aggregate of 7,269,338 shares of Series E Preferred at \$4.50 per share for total gross proceeds of \$32.7 million with issuance costs totaling \$0.2 million. In addition, the Company issued 1,619,550 shares of Series E Preferred in connection with the conversion of convertible notes (Note 8). In connection with the Series E Preferred issuances, each Series E Preferred stockholder also received warrants to purchase a number of shares of the Company's common stock that equal to 25% of the number of Series E Preferred shares issued. The fair value of the issued common stock warrants is accounted for as an issuance discount on the Series E Preferred. The common stock warrants are classified as permanent equity and were recorded as additional paid-in capital.

Series A Preferred, Series B Preferred, Series C Preferred, and Series D Preferred are hereinafter collectively referred to as "Tier II Preferred." Tier II Preferred and Series E Preferred are hereinafter collectively referred to as "Senior Preferred."

The rights, preferences, and privileges of the Preferred Stock are summarized below:

Voting

Series SRN Preferred are nonvoting. Except for matters that require a vote by a separate class or by separate series, Senior Preferred stockholders have full voting rights and powers similar to the rights and powers of the holders of common stock on an as-converted basis (disregarding the special conversion ratio applicable to Series E Preferred). Certain significant actions, including the amendment of the certificate of incorporation and any changes or transactions that may affect the preferences and priority of Senior Preferred such as dividends, dilution, sale and disposal of assets, mergers and acquisitions, voluntary dissolution or liquidation, merger, consolidation, recapitalization, and number of directors, must be approved by a majority vote of Senior Preferred stockholders voting as a single class on an as-converted basis.

Dividends

Holders of all series of Preferred Stock are entitled to receive dividends when and if declared by the Company's board of directors. In the event of liquidation, dissolution, or winding up of business, Senior Preferred stockholders are entitled to receive unpaid accrued dividends, whether or not declared by the board of directors. Senior Preferred dividends are to be calculated daily and accrued on a cumulative basis (adjusted for stock split, stock dividends, or other recapitalizations) at the rate of: \$0.0579 per share for Series A Preferred, \$0.1218 per share for Series B Preferred, \$0.18 per share for Series C Preferred, \$0.27 per share for Series D Preferred, and \$0.27 per share for Series E Preferred. Dividends accumulated on Preferred Stock totaled \$3.8 million, \$4.9 million, \$1.0 million and \$1.6 million during the years ended December 31, 2014 and 2015, and the three months ended March 31, 2015 and 2016, respectively. Series SRN Preferred stockholders are not entitled to receive accrued dividends.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

After accrued dividends due to Senior Preferred stockholders are satisfied in full, holders of all series of Preferred Stock are entitled to participate in other dividends payable to holders of common stock on an as-converted basis, when and if declared by the board of directors. Holders of Preferred Stock are not entitled to participate in stock dividends.

Optional conversion

Series A Preferred, Series B Preferred, and Series C Preferred are convertible into common stock at the stockholders' option at any time at the original issuance price of \$0.9653 per share for Series A Preferred, \$2.0303 per share for Series B Preferred, and \$3.00 per share for Series C Preferred, respectively, divided by the then effective conversion prices which are currently the original issuance price multiplied by 3.9 (3.9:1 conversion ratio), plus any declared but unpaid dividends (excluding accrued dividends).

Series D Preferred are convertible into common stock at the stockholders' option at any time at the original issuance price of \$4.50 per share divided by the then effective conversion price which is currently \$4.30 per share multiplied by 3.9 (1:0.2683 conversion ratio), plus any declared but unpaid dividends (excluding accrued dividends).

Series SRN Preferred are convertible into common stock at the stockholders' option only upon a deemed liquidation event or an initial public offering ("IPO") (whether or not a firm commitment underwritten IPO for an aggregate offering price of at least \$30.0 million, referred to as a qualified IPO), at the original issuance price of \$4.50 per share divided by \$16.77 per share (1:0.2683 conversion ratio), plus any declared but unpaid dividends. Upon the occurrence of a special conversion event (as defined in the certificate of incorporation), Series SRN Preferred are convertible at a special conversion price of \$14.04 per share (1:0.3205 conversion ratio), plus any declared but unpaid dividends.

Upon liquidation, dissolution, or winding up of business, including deemed liquidation events, Series E Preferred stockholders can elect to (1) convert their shares of Series E Preferred into common stock at the original Series E Preferred issuance price of \$4.50 per share divided by the then effective conversion price (currently the original issuance price of \$4.50 multiplied by 3.9) multiplied by 1.15 (1:0.2949 conversion ratio), or (2) receive a liquidation preference at 1.15 times the per-share original issuance price, or \$5.175, plus any declared but unpaid dividends (excluding accrued dividends). When not associated with a liquidation, dissolution, winding up of business, or deemed liquidation event, Series E Preferred are convertible into common stock at the stockholders' option at any time at the original issuance price of \$4.50 per share divided by the then effective conversion price which is currently the original issuance price of \$4.50 per share multiplied by 3.9 (1:0.2564 conversion ratio), plus any declared but unpaid dividends (excluding accrued dividends).

Mandatory conversion

All series of Preferred Stock are automatically converted at the then effective conversion price upon the completion of a qualified IPO. Currently, the effective conversion price is \$3.7647 per share for Series A Preferred, \$7.9182 per share for Series B Preferred, \$11.70 per share for Series C Preferred, \$16.77 per share for Series D Preferred, and \$16.77 per share of Series SRN Preferred. The Series E

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

Preferred effective conversion price upon a qualified IPO is determined based on the number of common stock shares issuable calculated as the highest of: (a) \$5.175 (Series E Preferred liquidation price) divided by the IPO price per share paid by the underwriters; (b) each shares of Series E Preferred converting into 0.2949 shares of common stock, or (c) \$4.50 divided by the then effective Series E Preferred conversion price (currently \$17.55 per share).

Tier II Preferred are also automatically convertible as a single class upon, the vote of at least two-thirds of the voting power of all Tier II Preferred at the then effective conversion price (3.9:1 conversion ratio, except Series D Preferred which is 1:0.2683). Series E Preferred are automatically convertible as a single class upon a majority vote of Series E Preferred stockholders at the then effective conversion price (currently \$17.55 per share) times 1.15 (1:0.2949 conversion ratio). Series SRN Preferred are automatically convertible as a single class upon (a) the sale of a majority of the Company's outstanding capital stock, (b) an IPO (whether or not a qualified IPO), or (c) an agreement among the majority of Series SRN Preferred stockholders, at the then effective conversion price (currently \$16.77 per share).

Liquidation preference

Upon liquidation, dissolution, or winding up of business, including deemed liquidation events, Series E Preferred stockholders can elect to (1) convert into common stock at the original Series E Preferred issuance price of \$4.50 per share divided by the then effective conversion price (currently the original issuance price of \$4.50 multiplied by 3.9) multiplied by 1.15 (1:0.2949 conversion ratio), or (2) receive liquidation preference at 1.15 times the per-share original issuance price, or \$5.175, plus any unpaid accrued dividends (whether or not declared), and any additional declared but unpaid dividends. Series E Preferred shares have preferences in priority to Tier II Preferred, Series SRN Preferred, and common stock. If assets available for distribution are insufficient to satisfy the Series E Preferred liquidation payment amounts in full, assets available for distribution will be allocated among Series E Preferred shares ratably and in proportion to the full preferential amount of shareholding.

After Series E Preferred stockholders are satisfied, any remaining assets available will be distributed to the Tier II Preferred stockholders at an amount equal to their original issuance price plus any unpaid accrued dividends (whether or not declared), and any additional declared but unpaid dividends. If assets available for distribution are insufficient to satisfy the Tier II Preferred liquidation payment amounts in full, assets available for distribution will be allocated among shares of Tier II Preferred shares ratably and in proportion to the full preferential amount of shareholding.

After the Senior Preferred stockholders are satisfied, any remaining assets available will be distributed to the Series SRN Preferred stockholders at an amount equal to their original issuance price plus any declared but unpaid dividends. Series SRN Preferred are not entitled to accrued dividends. If assets available for distribution are insufficient to satisfy the Series SRN Preferred liquidation payment amounts in full, assets available for distribution will be allocated among Series SRN Preferred shares ratably and in proportion to the full preferential amount of shareholding.

In the event any series of Preferred Stock would have received a greater amount of distribution than the amounts summarized above if those series of Preferred Stock had been converted into common stock, then all shares of such series of Preferred Stock would receive the higher distribution amount as

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

if they had been converted into common stock. This option does not apply to any holders of Preferred Stock who converted their shareholdings prior to or independent of the liquidation or deemed liquidation event.

After all series Preferred Stock are satisfied in full, any excess assets available for distribution will be allocated ratably among common stock based on the ratable common stock shares held by each stockholder.

Redemption rights

Senior Preferred are redeemable at the option of the stockholders at any time on or after November 7, 2019 upon a written notice by at least $\frac{2}{3}$ of the Senior Preferred stockholders then outstanding voting as a single class, at a price that equals their respective original issuance price per share, plus all accrued but unpaid dividends and all other declared and unpaid dividends, to be paid in four equal annual installments. Any unpaid redemption amounts will be accelerated prior to the effective date of Series SRN Preferred redemption, if elected.

As long as the Company has outstanding loans or similar commitments, Series SRN Preferred shares are not redeemable. In the absence of outstanding loans or similar commitments, Series SRN Preferred are redeemable at the option of each stockholder at any time on or after November 7, 2019, at a price per share that equals the original issuance price per share plus a 16.5% internal rate of return. In the event the Company's cash funds are insufficient to redeem all Series SRN Preferred shares including the 16.5% internal rate of return, the Company will issue a promissory note for the unredeemed shares with a term up to two years and accrues interest at 16.5%. Series SRN Preferred shares are not entitled to receive additional dividends once the redemption option is elected.

10. Common stock

The voting, dividend and liquidation rights of the common stockholders are subject to and qualified by the rights, powers and preferences of the Preferred Stock. The common stock has the following characteristics:

Voting

The common stockholders are entitled to one vote for each share of common stock held with respect to all matters voted on by the stockholders of the Company. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the Senior Preferred.

Dividends

The common stockholders are entitled to receive dividends, if and when declared by the Board of Directors. The Company may not declare or pay any cash dividends to the common stockholders unless dividends are first declared and paid to the holders of Preferred Stock in accordance with their respective terms. Through March 31, 2016, no dividends have been declared or paid on common stock.

Selecta Biosciences, Inc. and Subsidiaries**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016****Liquidation**

After holders of Preferred Stock are satisfied of their liquidation preferences upon any voluntary or involuntary liquidation, dissolution or winding up of the affairs of the Company, the common stockholders are then entitled to receive that portion of the remaining funds to be distributed to all holders of the Company's stock on an as-converted basis.

Reserved shares

The Company has authorized shares of common stock for future issuance as follows:

	Periods ending		
	December 31, 2014	December 31, 2015	March 31, 2016 (unaudited)
Conversion of Series A Preferred	664,068	664,068	664,068
Conversion of Series B Preferred	1,907,006	1,907,006	1,907,006
Conversion of Series C Preferred	1,282,051	1,282,051	1,282,051
Conversion of Series D Preferred	2,094,015	2,191,412	2,191,412
Conversion of Series SRN Preferred	1,438,746	1,798,433	1,798,433
Conversion of Series E Preferred with warrants	—	2,662,885	2,662,885
Exercise of common warrants	—	650,618	650,618
Shares available for future stock incentive awards	1,544	100,034	7,091
Exercise of outstanding common stock options	1,143,237	1,569,379	1,736,681
Total	<u>8,530,667</u>	<u>12,825,886</u>	<u>12,900,245</u>

11. Stock incentive plans

The Company maintains the 2008 Equity Incentive Plan (the "Plan") for employees, consultants, advisors, and directors. The Plan provides for the granting of incentive and non-qualified stock option and restricted stock awards as determined by the Board. As of March 31, 2016, a total of 2,200,592 shares of common stock are authorized for grants under the Plan with 7,091 shares available for future grant. All stock options granted under the 2008 Plan may be exercised into restricted stock subject to forfeiture provisions upon termination.

The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the grant date for participants who own less than 10% of the total combined voting power of the Company, and not less than 110% for participants who own more than 10% of the Company's voting power. Options and restricted stock granted under the Plan vest over periods as determined by the Board, which are generally four years and with terms that generally expire ten years from the grant date. The fair value of each option award is estimated on the grant date using Black-Scholes. Expected volatilities are based on historical volatilities from guideline companies, since there is no active market for the Company's common stock. The Company uses the "simplified" method to estimate the expected life of options granted and are expected to be

Selecta Biosciences, Inc. and Subsidiaries**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

outstanding. The risk-free interest rate used is the rate for a U.S. Treasury zero coupon issue with a remaining life consistent with the options expected life on the grant date. The Company has not paid, and does not expect to pay, any cash dividends in the foreseeable future. Forfeitures are estimated at the time of grant and are adjusted, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The Company has estimated a forfeitures rate of 10% based on historical attrition trends. The Company records stock-based compensation expense only on the awards that are expected to vest.

The weighted average assumptions used for employee stock option grants issued in 2014 and 2015 and for the three months ended March 31, 2016 are as follows:

	Year ended December 31,		March 31,
	2014	2015	2016
			(unaudited)
Risk-free interest rate	1.93%	1.79%	1.54%
Expected dividend yield	—	—	—
Expected life	5.94	6.02	6.03
Expected volatility	100.81%	79.80%	75.26%
Weighted-average fair value of common stock	\$ 8.97	\$ 7.35	\$ 7.02

The resulting weighted average grant date fair value of stock options granted to employees during the years ended December 31, 2014 and 2015 was \$6.86 and \$5.03, respectively, and \$7.14 and \$4.64 for the three months ended March 31, 2015 and 2016, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 2014 and 2015 was \$0.3 million and \$0.3 million, respectively, and less than \$0.1 million for the three months ended March 31, 2015 and 2016.

As of December 31, 2014 and December 31, 2015, and at March 31, 2016, total unrecognized compensation expense related to unvested employee stock options was \$0.9 million, \$2.3 million and \$2.4 million, respectively, which is expected to be recognized over a weighted average period of 2.3 years, 3.1 years and 3.0 years, respectively.

The weighted average assumptions used for unvested non-employee stock options are as follows:

	Year ended December 31,		Three months ended March 31,
	2014	2015	2016
			(unaudited)
Risk-free interest rate	1.22%	1.57%	1.89%
Expected dividend yield	—	—	—
Expected life (in years)	5.87	6.46	9.94
Expected volatility	98.25%	98.18%	82.48%

The unvested options held by non-employees are revalued using the Company's estimate of fair value on each vesting and reporting date through the remaining vesting period. Non-employee stock-based compensation expense of \$0.5 million and \$0.4 million was recorded for the years ended

Selecta Biosciences, Inc. and Subsidiaries
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

December 31, 2014 and 2015, respectively, and of \$0.1 million and less than \$0.1 million for the three months ended March 31, 2015 and March 31, 2016, respectively.

As of December 31, 2014 and 2015 and March 31, 2016, total unrecognized compensation expense related to unvested non-employee stock options was \$0.4 million, \$0.1 million and \$0.5 million, respectively, which is expected to be recognized over a weighted average period of 0.8 years, 2.2 years and 3.5 years, respectively.

The following table summarizes the activity under the Plan for the year ended December 31, 2015 and the quarter ended March 31, 2016:

	Number of options	Weighted-average exercise price	Weighted-average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Employee				
Outstanding at December 31, 2014	800,165	\$ 3.24	6.99	\$ 4,895
Granted	485,833	\$ 7.91		
Exercised	(20,861)	\$ 1.21		
Forfeited	(17,977)	\$ 6.32		
Outstanding at December 31, 2015	<u>1,247,160</u>	\$ 5.05	7.41	\$ 3,130
Vested at December 31, 2015	<u>668,465</u>	\$ 2.61	5.71	\$ 2,946
Vested and expected to vest at December 31, 2015	<u>1,171,380</u>	\$ 4.84	7.26	\$ 3,138
Outstanding at December 31, 2015 (unaudited)	1,247,160	\$ 5.05	7.41	\$ 3,130
Granted	94,871	\$ 7.02		\$
Exercised	(2,564)	\$ 0.62		\$
Forfeited	(1,928)	\$ 7.47		\$
Outstanding at March 31, 2016	<u>1,337,539</u>	\$ 5.19	7.36	\$ 4,376
Vested at March 31, 2016	<u>726,702</u>	\$ 3.09	5.73	\$ 3,790
Vested and expected to vest at March 31, 2016	<u>1,254,639</u>	\$ 5.01	7.21	\$ 4,318
Non-Employee				
Outstanding at December 31, 2014	343,072	\$ 2.93	6.5	\$ 2,207
Granted	—	\$ —		
Exercised	(20,852)	\$ 2.91		
Forfeited	—	\$ —		
Outstanding at December 31, 2015	<u>322,200</u>	\$ 2.93	5.50	\$ 1,288
Vested at December 31, 2015	<u>310,680</u>	\$ 2.70	5.40	\$ 1,288
Vested and expected to vest at December 31, 2015	<u>322,219</u>	\$ 2.93	5.50	\$ 1,288
Outstanding at December 31, 2015 (unaudited)	322,220	\$ 2.91	5.50	\$ 1,288
Granted	76,923	\$ 7.02		\$
Exercised	—	\$ —		\$
Forfeited	—	\$ —		\$
Outstanding at March 31, 2016	<u>399,143</u>	\$ 3.72	6.16	\$ 1,787
Vested at March 31, 2016	<u>316,770</u>	\$ 2.79	5.23	\$ 1,705
Vested and expected to vest at March 31, 2016	<u>399,143</u>	\$ 3.72	6.16	\$ 1,787

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

Restricted stock

During the year ended December 31, 2013, the Company issued 30,317 shares of restricted common stock to employees upon the early exercise of stock options. During the year ended December 31, 2014, the Company issued 2,564 shares of restricted common stock to employees. Under the terms of each agreement, the Company has a repurchase provision whereby the Company has the right to repurchase any unvested shares when/if the shareholders terminate their business relationship with the Company, at a price equal to the original exercise price. Accordingly, the Company recorded the cumulative payments received of \$0.1 million for the purchase of the restricted shares as a liability. The Company records payment received from the granting of restricted stock as a liability which is amortized over the vesting period. As of December 31, 2014 and 2015 and at March 31, 2016, the remaining liability was less than \$0.1 million.

Total fair value of restricted shares that vested during the years ended December 31, 2014 and 2015, was \$0.1 million and less than \$0.1 million, respectively, and for the three months ended March 31, 2016 was less than \$0.1 million.

The following table summarizes the restricted stock award activity of the Plan during the year ended December 31, 2014 and 2015 and for the three months ended March 31, 2016:

	<u>December 31, 2014</u>		<u>December 31, 2015</u>		<u>Three months ended March 31, 2016</u>	
	<u>Shares</u>	<u>Weighted- average exercise price</u>	<u>Shares</u>	<u>Weighted- average exercise price</u>	<u>Shares</u>	<u>Weighted- average exercise price</u>
Unvested at beginning of period	70,804	\$ 1.56	15,264	\$ 2.77	7,574	\$ 2.77
Issued	2,564	0.62	—	—	—	—
Vested	(58,104)	1.44	(7,690)	2.72	(1,895)	2.77
Unvested at end of period	<u>15,264</u>	<u>\$ 2.77</u>	<u>7,574</u>	<u>\$ 2.77</u>	<u>5,679</u>	<u>2.77</u>

As of December 31, 2014 and 2015 and for the three months ended March 31, 2016, total unrecognized compensation expense related to restricted stock awards was less than \$0.1 million, which the Company expects to recognize over a weighted average period of approximately 2.0 years, 1.0 year and 0.8 years, respectively.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

During the years ended December 31, 2014 and 2015 and for the three months ended March 31, 2015 and 2016, the Company recorded stock-based compensation expense as follows (in thousands):

	Year ended December 31,		Three months ended March 31,	
	2014	2015	2015	2016
			(unaudited)	
Research and development	\$ 384	\$ 495	\$ 132	\$ 167
General and administrative	840	630	170	115
Total	\$ 1,224	\$ 1,125	\$ 302	\$ 282

12. Revenue arrangements

Sanofi collaboration agreement

On November 27, 2012, the Company and Sanofi entered into a license and research collaboration agreement focused on the identification and development of vaccines against food allergies. Under the arrangement, the Company will perform research to identify an initial vaccine candidate for development and commercialization by Sanofi under an exclusive license.

In November 2014, Sanofi exercised the option to include celiac disease as an additional indication and the Sanofi Agreement was amended to add terms specific to the celiac disease indication and to terminate Sanofi's right to exercise its option for any additional indications in May 2015.

Each party will carry out its obligations under the collaboration in accordance with a research plan approved by a Joint Research Committee ("JRC"). The Company will perform the majority of the research work to identify the potential candidate, and once identified, Sanofi will primarily be responsible for the clinical development of the candidate.

At any time during the term of the development plan, but before the fifth anniversary of the start of the research term for the applicable indication, Sanofi and the Company may agree to replace the previously nominated development candidate with a new development candidate. The Company would be entitled to additional consideration for any research services performed at such time.

The research term for the first indication continues until the earlier of (a) the nomination of a development candidate for the initial indication or (b) the third anniversary of the agreement. The research term for the second indication (celiac disease) will expire upon the earlier of (a) the nomination of a development candidate for the second indication and (b) May 7, 2019. In the event that the Company is unable to complete its research obligations by the expiration of the applicable research term, its obligation will be limited to exercising commercially reasonable efforts to complete such research up to one year after the end of the research term. Each party is responsible for its own internal costs, as well as any third-party or out-of-pocket costs incurred in the performance of the activities laid out in the research plan. If the parties agree to expand the Company's scope of work, such costs will be reimbursed by Sanofi based on an agreed upon budget. Once a development candidate is nominated, all development activities will be under the direction of Sanofi pursuant to a

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

development plan to be negotiated and agreed to at that time and Sanofi will pay the Company for expenses incurred within certain approved limits.

Under the terms of the research collaboration portion of the Sanofi Agreement, the Company is required to use commercially reasonable efforts to perform the activities set out for the Company in the research and development plans created and overseen by a joint research committee. The Company is responsible for manufacturing all vaccines required for research, development and commercialization of licensed products. Pursuant to the Sanofi Agreement, Sanofi has paid the Company an initial payment of \$2.0 million for the initial indication and an additional \$2.0 million for the second indication of celiac disease. Sanofi is obligated to make additional payments to the Company during preclinical research totaling up to \$3.0 million for each indication, which has been received for the food allergy indication. For each indication, the Company is also eligible for (i) a \$5.0 million development candidate milestone payable to the Company at the start of preclinical development, (ii) further development milestones up to an aggregate of \$127.0 million, which includes up to an aggregate of \$57.0 million following the initiation of Phase I, Phase II and Phase III clinical trials for the indication and filing of the first biologic license application, more than two-thirds of which is attributable to the initiation of the Phase 3 clinical trial and the filing of the first biologic license application, and an aggregate of \$70.0 million upon achieving various regulatory approvals in the United States, European Union, Japan and Brazil, Russia, India or China, of which the majority is attributable to regulatory approvals in the United States, (iii) sales milestones of up to an aggregate of \$170.0 million, and (iv) tiered royalties on annual net sales of licensed products at percentages ranging from mid-single to low double digits.

As per the agreement, the research term expired for the first indication on the third anniversary (November 27, 2015) of the agreement. The Company completed its research obligations within the initial three year period and is not obligated to perform any further research on the specific indication under the agreement. A vaccine candidate for development and commercialization was not selected by Sanofi by the end of the research plan, and therefore no further milestone payments have been received. However, the Company is in discussions with Sanofi to extend the research term for the first indication by one year (until November 27, 2016).

The Company identified the deliverables under the arrangement as the license, the research necessary to identify the development candidate, and participation on the JRC. The Company determined that the exclusive license granted to Sanofi did not have standalone value from the research to be performed to identify the vaccine development candidate. As a result, each upfront and milestone consideration was allocated to the combined unit of account comprising the license and research services, and is being recognized over the estimated development period using a proportional performance method. The consideration allocated to participation on the JRC was not material. The Company recognized \$2.1 million of revenue during each of the years ended December 31, 2014 and 2015, and \$0.5 million and \$0.1 million during the three months ended March 31, 2015 and 2016, respectively.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**Other research and collaboration agreements**

The Company has entered into other research and collaboration agreements in 2014 and 2015 for which the Company did not recognize any revenue for the period ended December 31, 2014 and recognized revenue in the amount of \$0.3 million for the period ended December 31, 2015, and less than \$0.1 million for the three months ended March 31, 2015 and 2016.

Grant agreements

The Company receives funding in the form of grants from the National Institutes of Health ("NIH"), the Juvenile Diabetes Research Foundation ("JDRF"), the Bill and Melinda Gates Foundation, the Russian Ministry of Industry and Trade ("Minpromtorg"), and the Russia based Development Fund of New Technologies Development and Commercialization Center ("Skolkovo").

NIH

The Company has two grants through the Department of Health and Human Services, National Institutes of Health ("NIH"). The first grant, for an aggregate amount of \$8.1 million, was awarded in May 2014 to support research in the development of a next generation vaccine for smoking cessation and relapse prevention. The Company recognized \$0.6 million and \$2.4 million of revenue for the periods ending December 31, 2014 and 2015, respectively, and \$0.4 million and \$1.8 million for the three months ended March 31, 2015 and 2016, respectively, under the arrangement.

The second grant is for an aggregate amount of \$0.2 million, which was awarded in September 2015 for the development of nanoparticles for immune tolerance to factor VIII. The company recognized revenue in the amount of \$0.1 million for the year ended December 31, 2015 and less than \$0.1 million for the three months ended March 31, 2016.

JDRF

The Company had two contracts in effect with JDRF during 2014, and only one of those contracts was in effect during 2015. The first contract was a continuation and completion of the 2011 grant for \$0.8 million. The Company recognized the remaining \$0.2 million of revenue during the year ended December 31, 2014 under this contract. The second JDRF grant is a joint grant with Sanofi entered into in September 2014 for \$0.4 million to conduct Type 1 Diabetes research. The Company recognized less than \$0.1 million and \$0.2 million of revenue related to this contract during the years ended December 31, 2014 and 2015, respectively, and less than \$0.1 million and \$0.1 million for the three months ended March 31, 2015 and 2016, respectively.

Bill and Melinda Gates Foundation

The Company received a grant in 2013 from the Bill and Melinda Gates Foundation for \$1.2 million to fund the Company's immunology research on malaria antigens. During 2014, the grant amount was increased to a total of \$1.6 million and the term was extended to a three-year research term. Revenue recognized for the years ending December 31, 2014 and 2015 was \$0.2 million and \$0.6 million, respectively, and was less than \$0.1 million and \$0.1 million for the three months ended March 31,

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

2015 and 2016, respectively. Revenue is recognized on a proportional performance basis as it relates to employee time expended on the research, along reimbursement for external costs directly related to, and approved, by the grant terms.

Minpromtorg

The Company had a contract awarded from Minpromtorg for approximately \$4.6 million to fund the Company's nicotine cessation vaccine clinical trial to be conducted in Russia. The grant covered a term from July 9, 2013 through December 31, 2015, and provided for reimbursement of expenses incurred by the Company from the clinical trial. Under the agreement term, the Company was subject to a penalty in the event that clinical trial was delayed or terminated prior to completion. As a result of the penalty provision, the Company concluded the amounts received under the agreement were not fixed or determinable. Therefore, no revenue has been recognized to date. Through December 31, 2014, the Company received payments totaling approximately \$1.4 million, which has been recorded as a contingently repayable grant funding liability in the accompanying consolidated balance sheets. The agreement also required the Company to maintain a deposit in a restricted bank account equal to approximately one year of expected contract payments, which approximates \$1.0 million, to cover the potential penalty. The amount is classified as restricted cash in the consolidated balance sheets for the years ended December 31, 2014 and 2015. In January 2016, the deposit was released from the restricted deposit requirement. In 2014, the Company terminated its plan to conduct the clinical trial in Russia subjecting the Company to the penalty obligation.

In February 2015, the Company received an executed final settlement agreement from Minpromtorg that included the repayment of funds previously received by the Company totaling \$0.2 million, and a penalty fee that equaled to 10% of the contract value, or \$0.2 million. The Company paid the settlement payment in March 2015 and all mutual claims under the contract were terminated. According to the terms of the agreement, Minpromtorg has the right to audit the expenditure incurred under the agreement for a period up to three years from each research milestone date. All grant funding received in excess of the penalty settlement will remain as a liability on the balance sheet until such time the audit period has expired and at which time, the amount will be recognized as revenue. The first audit period expired on December 31, 2015, and as a result \$0.4 million of revenue was recognized for the year ending December 31, 2015. The remaining amount of unrecognized revenue is classified contingent repayable grant funding in the consolidated balance sheets.

Skolkovo

On November 28, 2014, the Company executed a grant awarded by Skolkovo for the development of a therapeutic vaccine using nanoparticles to treat chronic infection caused by HPV and diseases associated with this infection. The grant covers a period from August 1, 2014 through July 21, 2017. The grant provides for up to \$2.7 million that covers 48.5% of the estimated total cost of the research plan with the remaining 51.5% of estimated costs to be contributed by the Company. The Company received from Skolkovo \$1.0 million in 2014, no additional funds were received for the year ending December 31, 2015 and \$0.7 million was received for the three months ended March 31, 2016.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

At any time during the term of the grant agreement, but not more than once per quarter, Skolkovo has the right to request information related to the project and to conduct an audit of the expenses incurred by the Company. In the event the project or the expenses do not meet predefined requirements, the Company may be required to reimburse the funds received up to three years after the completion of the project. As a result, the Company has determined that the grant funding is not fixed or determinable and all amounts received to date are recorded as deferred revenue in the consolidated balance sheet until the completion of Skolkovo's audit or the expiration of the audit term.

13. Related-party transactions

As part of the Series B Preferred and Series D Preferred financings (as described in Note 9), the Company's landlord (the "Landlord") purchased 49,254 shares of Series B Preferred at \$2.0303 per share for total proceeds of \$0.1 million and 488,888 shares of Series D Preferred at \$4.50 per share for total proceeds of \$2.2 million. Additionally, in April 2015, the Landlord participated in the Company's bridge loan in the amount of \$0.2 million, which converted into Series E Preferred (see note 9). The Landlord paid the same price as the price paid by other investors in each of these Preferred Stock purchases.

The Company incurred expenses for consulting services provided by its founders totaling \$0.3 million during each of the years ended December 31, 2014 and 2015, and \$0.1 million for each of the three months ended March 31, 2015 and 2016.

14. Technology license agreements

On November 25, 2008, the Company entered into an Exclusive Patent License agreement with the Massachusetts Institute of Technology ("MIT"). The Company received an exclusive royalty-bearing license to utilize patents held by MIT in exchange for upfront consideration and annual license maintenance fees. Such fees are expensed as incurred and have not been material to any period presented. In the event the Company sublicenses the MIT patents to a third party, it will be required to remit to MIT a percentage (ranging from 10% to 30%) of sublicense income. In addition, the Company is obligated to pay MIT a certain amount upon the achievement of defined clinical milestones, up to a total of \$1.5 million. On December 18, 2008, the Company entered into a patent-cross-license agreement with BIND Therapeutics, Inc. whereby each party receives a license for the use of the other patents in their respective fields of use. In exchange for this license, the Company paid a one-time expense in 2008.

In May 2014, the Company entered into a license agreement with Shenyang Sunshine Pharmaceutical Co., Ltd., or 3SBio, which is referred to as the 3SBio License. Pursuant to the 3SBio License, the Company was granted an exclusive license to certain pepsitacase-related patents and related "know-how" owned or in-licensed by 3SBio for the worldwide (except for Greater China and Japan) development and commercialization of products based thereupon for human therapeutic, diagnostic and prophylactic use. The Company was also granted a worldwide (except for Greater China) exclusive license to develop, commercialize and manufacture or have manufactured products combining the Company's proprietary SVP technology with pepsitacase or related compounds supplied by 3SBio (or otherwise supplied if the Company's rights to manufacture are in effect) for human

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

therapeutic, diagnostic and prophylactic use. The Company was also granted a co-exclusive license to manufacture and have manufactured pegsiticase and related compounds for preclinical and clinical use or, if the 3SBio License is terminated for 3SBio's material breach, for any use under the 3SBio License. Otherwise, the Company is obligated to obtain all of its supply of such compounds for Phase 3 clinical trials and commercial use from 3SBio under the terms of supply agreements to be negotiated.

Pursuant to the 3SBio License, the Company is required to use commercially reasonable efforts to develop and commercialize a product containing pegsiticase or a related compound. If the Company does not commercialize any such product in a particular country in Asia, Africa or South America within 48 months after approval of any such product in the U.S. or a major European country, then 3SBio will have the right to do so, but only until the Company commercializes a product combining the Company's SVP technology with any such compound in such country. The Company has paid to 3SBio an aggregate of \$1.0 million in upfront and milestone-based payments under the 3SBio License. The Company is required to make future payments to 3SBio contingent upon the occurrence of events related to the achievement of clinical and regulatory approval milestones of up to an aggregate of \$21.0 million for products containing the Company's SVP technology, and up to an aggregate of \$41.5 million for products without the Company's SVP technology. The Company is also required to pay 3SBio tiered royalties on annual worldwide net sales (on a country-by-country and product-by-product basis) related to the pegsiticase component of products at percentages ranging from the low-to-mid single digits for products containing the Company's SVP technology, and a range of no more than ten percentage points from the mid-single digits to low double-digits for products without the Company's SVP technology. The Company will pay these royalties to 3SBio, subject to specified reductions, on a country-by-country and product-by-product basis until the later of (i) the date that all of the patent rights for that product have expired in that country, or (ii) a specified number of years from the first commercial sale of such product in such country.

The 3SBio License expires on the date of expiration of all of the Company's royalty payment obligations unless earlier terminated by either party for an uncured material default or for the other party's bankruptcy. Any such termination by 3SBio for material default may be on a country-by-country or product-by-product basis in certain circumstances. The Company may also terminate the 3SBio License on a country-by-country or product-by-product basis for any reason effective upon 60 days' prior written notice to 3SBio or, with respect to a given product, immediately upon written notice to 3SBio if the Company identifies a safety or efficacy concern related to such product.

15. Income taxes

The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse.

Selecta Biosciences, Inc. and Subsidiaries**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016**

For the years ended December 31, 2014 and 2015, the Company did not record a current or deferred income tax expense or benefit. A reconciliation of the Company's effective tax rate to the statutory federal rate is as follows:

	2014	2015
Statutory U.S. federal rate	34.0%	34.0%
State income taxes—net of federal benefit	5.9	5.7
Permanent items	(0.7)	(0.7)
Research tax credits/others	1.6	1.0
Valuation allowance, net	(33.0)	(40.0)
Other	(7.8)	—
Net deferred tax assets	—%	—%

The tax effects of temporary differences that give rise to the Company's net deferred tax assets as of December 31 are as follows (in thousands):

	2014	2015
	(in thousands)	
Deferred Tax Assets		
Net operating loss carryforwards	\$ 22,444	\$ 31,958
Research and development credits	1,835	2,305
Stock-based compensation expense	355	570
Deferred rent and other expenses	284	493
Deferred revenue	2,283	1,582
Patent costs/amortization	2,796	3,500
Tenant improvement allowance	131	—
Warrant liability	93	114
Gross deferred tax assets	30,221	40,522
Deferred Tax Liabilities		
Depreciation	\$ (388)	\$ (197)
Debt discount	(59)	(97)
Unrealized foreign exchange gain	(1,352)	(1,728)
Gross deferred tax liabilities	(1,799)	(2,022)
Net deferred tax assets	28,422	38,500
Valuation allowance	(28,422)	(38,500)
Net deferred tax assets	\$ —	\$ —

The Company has provided a full valuation allowance against its net deferred tax assets, as the Company believes that it is more likely than not that the deferred tax assets will not be realized. Realization of future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

concluded that it is more likely than not that the Company will not realize the benefit of its deferred tax assets. The valuation allowance increased by \$4.3 million and \$10.1 million for the years ended December 31, 2014 and 2015, respectively, primarily as a result of an increase in net operating loss. In 2014, the Company's Russian subsidiary was granted a 10 year tax holiday in Russia. As a result, previously reported deferred tax assets were adjusted for the change in tax rate. There has been no change to the tax holiday status for the subsidiary as of December 31, 2015.

At December 31, 2015, the Company had federal and state net operating loss carryforwards of \$82.4 million and \$76.3 million, which will expire at various times through 2035. Included in the net operating loss above is approximately \$0.2 million related to excess stock option deductions. The Company also has federal and state research and development tax credit carryforwards of \$1.6 million and \$1.1 million available to reduce future tax liabilities, which will expire at various times through 2035.

Utilization of the net operating loss and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously, or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively.

The Company applies ASC 740, Income Taxes to uncertain tax positions. As of the adoption date on January 1, 2009 and through December 31, 2015, the Company had no unrecognized tax benefits or related interest and penalties accrued.

The Company has not, as of yet, conducted a study of its research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. As a result, there would be no impact to the consolidated balance sheets, statements of operations and comprehensive loss, or cash flows if an adjustment was required.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statement of operations and comprehensive loss. As of December 31, 2015, the Company had no accrued interest related to uncertain tax positions.

The statute of limitations for assessment by the Internal Revenue Service and Massachusetts tax authorities is open for tax years since inception. The Company files income tax returns in the United States and Massachusetts. There are currently no federal, state or foreign audits in progress.

16. 401(k) Savings Plan

The Company maintains a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. The 401 (k) Plan provides for matching contributions on a portion of participant

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

contributions pursuant to the 401(k) Plan's matching formula. All matching contributions vest ratably over 4 years and participant contributions vest immediately.

Contributions by the Company totaling \$0.1 million and \$0.1 million for the years ended December 31, 2014 and 2015, respectively, and \$0.1 million for each of the three months ended March 31, 2015 and 2016, have been recorded in the consolidated statements of operations and comprehensive loss.

17. Subsequent Events**a) License Agreement (unaudited)**

In May 2016, the Company entered into a license agreement with the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc., or, collectively, MEE, referred to as the MEE License. Under the MEE License, the Company was granted an exclusive commercial worldwide license, with the right to grant sublicenses through multiple tiers, to make, have made, use, offer to sell, sell and import certain products and to practice certain processes, the sale, use or practice of which are covered by patents and proprietary know-how owned or controlled by MEE, for use of Anc80 gene therapy vectors for gene augmentation therapies expressing certain target sequences.

MEE also granted the Company exclusive options to exclusively license certain of their intellectual property rights relating to several additional target sequences and variations thereof each linked to a specified disease. During a defined option period, the Company may exercise this right for up to a designated number of target sequences. If the Company exercises its options, under certain circumstances, the Company may substitute alternative target sequences for previously selected target sequences.

The Company agreed to use commercially reasonable efforts to develop and commercialize licensed products pursuant to a development plan, and to market and sell at least one product for each target sequence for which the Company exercised its option as soon as reasonably practicable. Subject to certain exceptions, following commercial launch, the Company must use commercially reasonable efforts to market, sell, and maintain public availability of licensed products in a certain number of specified major markets.

Pursuant to the MEE Agreement, the Company agreed to pay MEE a license fee in the low six figures, annual license maintenance fees ranging from the mid-twenty thousands to mid-seventy thousands and an option maintenance fee in the low five figures for each exercisable option. The Company also agreed to reimburse MEE for a specified percentage of the past patent expenses for the patents licensed to the Company. The Company also agreed to pay development milestones on a licensed product-by-licensed product basis, totaling up to an aggregate of between \$4,175,000 to \$37,025,000 and sales milestones on a licensed product-by-licensed product basis, totaling up to an aggregate of between \$50,000,000 to \$70,000,000; tiered royalties on a licensed product-by-licensed product and country-by-country basis equal to a percentage of net sales ranging from mid-single digits to mid-teens, subject to the prevalence of the targeted disease and certain reductions; and a percentage, in a range expected to be in the mid-teens depending on timing, of any sublicense income the Company receives from sublicensing its rights granted thereunder, subject to certain reductions and exclusions. Upon

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)
Years Ended December 31, 2014 and 2015 and Unaudited Three Months Ended March 31, 2015 and 2016

exercise of each option, the Company agreed to pay MEE an option exercise fee ranging from low-six figures to mid-six figures, depending on the prevalence of the targeted disease.

The MEE License will continue until the expiration of the last to expire of the patent rights licensed thereunder. The Company may terminate the MEE License in whole or in part upon prior written notice. MEE may terminate the MEE License on a target sequence-by-target sequence basis if the Company fails to make any scheduled payments in respect of such target sequence or if the Company materially breaches a diligence obligation in respect of such target sequence, in each case if the Company fails to cure within a specified time period. MEE may terminate the MEE License in its entirety if the Company materially breaches certain of its obligations related to diligence, representations and warranties, and maintenance of insurance; if the Company challenges the validity or enforceability of any patents licensed thereunder; if any of the Company's executive officers are convicted of a felony relating to manufacture, use, sale or importation of licensed products; or upon the Company's insolvency or bankruptcy.

b) Reverse Stock Split

The Company's Board of Directors and stockholders approved a 1-for-3.9 reverse stock split of the Company's common stock. The reverse stock split became effective on June 7, 2016. All common stock share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split. The shares of common stock retained a par value of \$0.0001 per share. Accordingly, the stockholder's deficit reflects the reverse stock split by reclassifying from common stock to additional paid in capital an amount equal to the par value of the decreased shares resulting from the effect of the reverse stock split.

c) Equity Plan (unaudited)

The Company's Board of Directors adopted and the Company's stockholders approved the Selecta Bioscience, Inc. 2016 incentive plan ("2016 Plan"), which will become effective on the date that is immediately prior to the date of effectiveness of the registration statement on Form S-1 for the Company's initial public offering. The 2016 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2016 Plan.



Until _____, 2016 (the 25th day after the date of this prospectus), all dealers that buy, sell, or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the NASDAQ listing fee.

	Amount
Securities and Exchange Commission registration fee	\$ 7,875
FINRA filing fee	12,230
NASDAQ initial listing fee	125,000
Accountants' fees and expenses	1,050,000
Legal fees and expenses	2,461,866
Printing and engraving expenses	120,000
Miscellaneous	123,030
Total expenses	\$ 3,900,000

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our restated certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability

but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our restated certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favour by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, or the Securities Act, against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding securities issued by us within the past three years. Also included is the consideration received by us for such shares and information relating to the section of

the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock.

From April 7, 2014 to August 14, 2014, the registrant issued an aggregate of 3,211,105 shares of Series D Preferred Stock for aggregate consideration of \$14.4 million to accredited investors pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

On July 15, 2014, the registrant also issued an aggregate of 1,333,332 shares of Series SRN Preferred Stock for aggregate consideration of \$6.0 million to accredited investors pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

On August 27, 2015, September 3, 2015 and September 17, 2015, the registrant issued an aggregate of 7,269,338 shares of Series E Preferred Stock for aggregate consideration of \$32.7 million to accredited investors and 1,619,550 shares of Series E Preferred upon the cancellation of debt totaling \$7.3 million pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

(b) Equity Grants.

Since December 31, 2012, the registrant granted stock options to purchase an aggregate of 1,056,748 shares of its common stock with exercise prices ranging between \$2.77 and \$9.36 per share, including stock options that were exercised prior to vesting in exchange for 30,318 shares of restricted stock, and 2,564 shares of restricted common stock to employees, non-employees, and directors in connection with services provided to the registrant by such parties.

In May 2016, the registrant granted stock options to purchase an aggregate of 390,805 shares of common stock, which will become effective in connection with this offering, to some of our executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering in connection with services provided to the registrant.

The issuances of such stock options, the shares of common stock issuable upon the exercise of such options and such restricted shares of common stock were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

(c) Warrants.

On August 9, 2013 and July 25, 2014, the registrant issued warrants to purchase an aggregate of 66,668 shares of Series D preferred stock to Oxford Finance LLC, or Oxford, and Square 1 Bank pursuant to Section 4(a)(2) of the Securities Act as a transaction not involving a public offering

On July 24, 2015, the registrant issued warrants to purchase up to 80,820 shares of common stock to accredited investors pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

On August 27, 2015, September 3, 2015 and September 17, 2015, the registrant issued warrants to purchase up to an aggregate of 569,791 shares of common stock to accredited investors pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

On December 31, 2015, the registrant issued warrants to purchase up to an aggregate of 37,978 shares of Series E Preferred Stock to Oxford and Pacific Western Bank pursuant to Section 4(a)(2) of the Securities Act as a transaction not involving a public offering.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit number	Description of exhibit
1.1**	Form of Underwriting Agreement
3.1**	Certificate of Incorporation of the Registrant, as amended (currently in effect)
3.2**	Bylaws of the Registrant (currently in effect)
3.3**	Form of Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4**	Form of Restated Bylaws of the Registrant (to be effective upon the closing of this offering)
4.1**	Fifth Amended and Restated Investors' Rights Agreement, dated as of August 26, 2015, by and between the Registrant and each of the stockholders party thereto, as amended by Amendment No. 1 to Fifth Amended and Restated Investors' Rights Agreement, dated as of June 7, 2016
4.2**	Specimen Stock Certificate evidencing the shares of common stock
4.3**	Form of Warrant to Purchase Common Stock, dated July 24, 2015, issued by the Registrant to Investors in the Registrant's April 2015 Convertible Notes Financing, together with a schedule of warrant holders
4.4**	Form of Warrant to Purchase Common Stock, dated August 27, 2015, September 3, 2015 or September 17, 2015, issued by the Registrant to Investors in the Registrant's Series E Preferred Stock Financing, together with a schedule of warrant holders
4.5**	Form of Warrant to Purchase Shares of Series D Preferred Stock, dated August 9, 2013 or July 25, 2014, issued by the Registrant to Oxford Finance LLC and Square One Bank, together with a schedule of warrant holders
4.6**	Form of Warrant to Purchase Shares of Series E Preferred Stock, dated December 31, 2015, issued by the Registrant to Oxford Finance LLC and Square One Bank, together with a schedule of warrant holders
5.1**	Opinion of Latham & Watkins LLP
10.1	2008 Stock Incentive Plan, as amended, and form of option agreements thereunder
10.2**	2016 Incentive Award Plan and form of award agreements thereunder
10.3**	2016 Employee Stock Purchase Plan
10.4**	Non-Employee Director Compensation Program
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10.7(a)†**	Exclusive Patent License Agreement, dated as of November 25, 2008, by and between the Registrant and the Massachusetts Institute of Technology
10.7(b)†**	First Amendment to Exclusive Patent License Agreement, dated as of January 12, 2010, by and between the Registrant and the Massachusetts Institute of Technology

Exhibit number	Description of exhibit
10.7(c)†**	Letter Agreement, dated as of November 27, 2012, by and among the Registrant, Massachusetts Institute of Technology and Sanofi
10.7(d)†**	Letter Amendment, dated as of November 27, 2012, by and between the Registrant and the Massachusetts Institute of Technology
10.7(e)†**	Second Amendment to Exclusive Patent License Agreement, dated as of August 29, 2013, by and between the Registrant and the Massachusetts Institute of Technology
10.8(a)†**	License and Research Collaboration Agreement, dated as of November 27, 2012, by and between the Registrant and Sanofi
10.8(b)†**	Supplemental Agreement No. 1 to License and Research Collaboration Agreement, dated as of May 7, 2015, by and between the Registrant and Sanofi
10.9†**	License Agreement, dated as of May 12, 2014, by and between the Registrant and Shenyang Sunshine Pharmaceutical Co., Ltd.
10.10†**	Manufacturing Services Agreement, dated as of August 1, 2014, by and between the Registrant and Shenyang Sunshine Pharmaceutical Co., Ltd.
10.11†**	Patent Cross-License Agreement, dated as of December 18, 2008, by and between the Registrant and BIND Therapeutics, Inc. (formerly BIND Biosciences, Inc.)
10.12†**	Exclusive License Agreement, dated as of May 17, 2016, by and among the Registrant, the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc.
10.13†**	Lease, dated as of September 30, 2008, as amended by the First Amendment, dated as of July 12, 2011, the Second Amendment, dated as of October 11, 2011 and the Third Amendment, dated as of April 6, 2015, by and between the Registrant and ARE-480 Arsenal Street, LLC
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10.15**	Consulting Agreement, dated as of March 10, 2008, as amended by the First Amendment to Consulting Agreement, dated as of January 1, 2012, by and between the Registrant and Omid Farokhzad
10.16**	Summary of Oral Agreement, by and between the Registrant and Omid Farokhzad
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10.18**	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and Takashi Kei Kishimoto
10.19**	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and Peter Keller
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10.21**	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and Lloyd P. M. Johnston, Ph.D.
10.22**	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and David Abraham

Exhibit number	Description of exhibit
10.23**	Employment Agreement, dated as of June 6, 2016, by and between the Registrant and David Siewers
10.24**	Independent Director Consulting Agreement, dated as of May 5, 2009, as amended by the First Amendment to Independent Director Consulting Agreement, dated as of July 22, 2009, by and between the Registrant and George R. Siber, M.D., as terminated by a letter, dated as of June 1, 2016
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10.29**	Offer Letter, dated as of June 30, 2015, by and between the Registrant and Earl E. Sands, M.D.
10.30**	Offer Letter, dated as of June 2, 2008, by and between the Registrant and Lloyd P. M. Johnston, Ph.D.
10.31**	Offer Letter, dated as of April 4, 2011, by and between the Registrant and David Abraham
10.32**	Offer Letter, dated as of September 4, 2009, by and between the Registrant and David Siewers
21.1**	Subsidiaries of the Registrant
23.1	Consent of Ernst & Young LLP
23.2**	Consent of Latham & Watkins LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)
99.1**	Consent of Director Nominee

** Previously filed.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 406 under the Securities Exchange Act of 1933.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the consolidated financial statements or notes thereto.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise,

the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Signatures

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Watertown, Commonwealth of Massachusetts, on this 20th day of June, 2016.

SELECTA BIOSCIENCES, INC.

By: /s/ WERNER CAUTREELS, PH.D.

Werner Cautreels, Ph.D.
President and Chief Executive Officer

Signatures and power of attorney

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ WERNER CAUTREELS, PH.D.</u> Werner Cautreels, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	June 20, 2016
<u>/s/ DAVID SIEWERS</u> David Siewers	Chief Financial Officer (principal financial officer and principal accounting officer)	June 20, 2016
<u>*</u>		
<u>Omid Farokhzad, M.D.</u>	Director	June 20, 2016
<u>*</u>		
<u>Carl Gordon, Ph.D.</u>	Director	June 20, 2016
<u>*</u>		
<u>Peter Barton Hutt</u>	Director	June 20, 2016
<u>*</u>		
<u>Edwin M. Kania, Jr.</u>	Director	June 20, 2016
<u>*</u>		
<u>Robert S. Langer, Sc.D.</u>	Director	June 20, 2016
<u>*</u>		
<u>Amir Nashat, Sc.D.</u>	Director	June 20, 2016
<u>*</u>		
<u>Aymeric Sallin, M.S.</u>	Director	June 20, 2016
<u>*</u>		
<u>Leysan Shaydullina, M.D.</u>	Director	June 20, 2016
<u>*</u>		
<u>George Siber, M.D.</u>	Director	June 20, 2016
<u>*By: /s/ WERNER CAUTREELS, PH.D.</u> Werner Cautreels, Ph.D. <i>Attorney-in-fact</i>		

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10.32**	Offer Letter, dated as of September 4, 2009, by and between the Registrant and David Siewers
21.1**	Subsidiaries of the Registrant
23.1	Consent of Ernst & Young LLP
23.2**	Consent of Latham & Watkins LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)
99.1**	Consent of Director Nominee

** Previously filed.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 406 under the Securities Exchange Act of 1933.

SELECTA BIOSCIENCES, INC.

2008 Stock Incentive Plan

1. Purpose.

The purpose of this plan (the "Plan") is to secure for Selecta Biosciences, Inc., a Delaware corporation (the "Company") and its shareholders the benefits arising from capital stock ownership by employees, officers and directors of, and consultants or advisors to, the Company and its parent and subsidiary corporations who are expected to contribute to the Company's future growth and success. Under the Plan recipients may be awarded both (i) Options (as defined in Section 2.1) to purchase the Company's common stock, par value \$0.0001 ("Common Stock") and (ii) shares of the Company's Common Stock ("Restricted Stock Awards"). Except where the context otherwise requires, the term "Company" shall include any parent and all present and future subsidiaries of the Company as defined in Sections 424(e) and 424(f) of the Internal Revenue Code of 1986, as amended or replaced from time to time (the "Code"). Those provisions of the Plan which make express reference to Section 422 of the Code shall apply only to Incentive Stock Options (as that term is defined below).

2. Types of Awards and Administration.

2.1 **Options.** Options granted pursuant to the Plan ("Options") shall be authorized by action of the Board of Directors of Selecta Biosciences, Inc. (the "Board" or "Board of Directors") and may be either incentive stock options ("Incentive Stock Options") meeting the requirements of Section 422 of the Code or non-statutory Options which are not intended to meet the requirements of Section 422. The vesting of Options may be conditioned upon the completion of a specified period of employment with the Company and/or such other conditions or events as the Board may determine. The Board may also provide that Options are immediately exercisable subject to certain repurchase rights in the Company dependent upon the continued employment of the optionee and/or such other conditions or events as the Board may determine.

2.1.1 **Incentive Stock Options.** All Options when granted are intended to be non-statutory Options, unless the applicable Option Agreement (as defined in Section 5.1) explicitly states that the Option is intended to be an Incentive Stock Option. Incentive Stock Options may only be granted to employees of the Company. For so long as the Code shall so provide, Options granted to any employee under the Plan (and any other incentive stock option plans of the Company) which are intended to constitute Incentive Stock Options shall not constitute Incentive Stock Options to the extent that such Options, in the aggregate, become exercisable for the first time in any one calendar year for shares of Common Stock with an aggregate fair market value (determined as of the respective date or dates of grant) of more than \$100,000. If an

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Option is intended to be an Incentive Stock Option, and if for any reason such Option (or any portion thereof) shall not qualify as an Incentive Stock Option, then, to the extent of such nonqualification, such Option (or portion thereof) shall be regarded as a non-statutory Option appropriately granted under the Plan provided that such Option (or portion thereof) otherwise meets the Plan's requirements relating to non-statutory Options.

2.2 **Restricted Stock Awards.** The Board in its discretion may grant Restricted Stock Awards, entitling the recipient to acquire, for a purchase price determined by the Board, shares of Common Stock subject to such restrictions and conditions as the Board may determine at the time of grant ("Restricted Stock"), including continued employment and/or achievement of pre-established performance goals and objectives.

2.3 **Administration.** The Plan shall be administered by the Board, whose construction and interpretation of the terms and provisions of the Plan shall be final and conclusive. The Board may in its sole discretion issue Restricted Stock and grant Options and issue shares upon exercise of such Options as provided in the Plan. The Board shall have authority, subject to the express provisions of the Plan, to construe Restricted Stock Agreements, Option Agreements and the Plan, to prescribe, amend and rescind rules and regulations relating to the Plan, to determine the terms and provisions of Restricted Stock Agreements and Option Agreements, and to make all other determinations in the judgment of the Board necessary or desirable for the administration of the Plan. The Board may correct any defect or supply any omission or reconcile any inconsistency in the Plan or in any Restricted Stock Agreement or Option Agreement in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. No director or person acting pursuant to authority delegated by the Board shall be liable for any action or determination under the Plan made in good faith. The Board may, to the full extent permitted by or consistent with applicable laws or regulations, delegate any or all of its powers under the Plan to a committee (the "Committee") appointed by the Board, and if the Committee is so appointed all references to the Board in the Plan shall mean and relate to such Committee, other than references to the Board in this sentence and in Section 18 (as to amendment or termination of the Plan) and Section 21.

3. Eligibility.

Options may be granted, and Restricted Stock may be issued, to persons who are, at the time of such grant or issuance, employees, officers or directors of, or consultants or advisors to, the Company; *provided*, that the class of persons to whom Incentive Stock Options may be granted shall be limited to employees of the Company.

3.1 **10% Shareholder.** If any employee to whom an Incentive Stock Option is to be granted is, at the time of the grant of such Option, the owner of stock possessing more than 10% of the total combined voting power of all classes of stock of the

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Company (after taking into account the attribution of stock ownership rules of Section 424(d) of the Code) (a "Greater Than 10% Shareholder"), any Incentive Stock Option granted to such individual must: (i) have an exercise price per share of not less than 110% of the fair market value of one share of Common Stock at the time of grant; and (ii) expire by its terms not more than five years from the date of grant.

4. Stock Subject to Plan.

Subject to adjustment as provided in Section 14.2 below, the maximum number of shares of Common Stock which may be issued under the Plan is 2,213,412 shares. If an Option shall expire or terminate for any reason without having been exercised in full, the unpurchased shares subject to such Option shall again be available for subsequent Option grants or Restricted Stock Awards under the Plan. If shares of Restricted Stock shall be forfeited to, or otherwise repurchased by, the Company pursuant to a Restricted Stock Agreement, such repurchased shares shall again be available for subsequent Option grants or Restricted Stock Awards under the Plan. If shares issued upon exercise of an Option are tendered to the Company in payment of the exercise price of an Option, such tendered shares shall again be available for subsequent Option grants or Restricted Stock Awards under the Plan.

5. Forms of Restricted Stock Agreements and Option Agreements.

5.1 **Option Agreement.** Each recipient of an Option shall execute an option agreement ("Option Agreement") in such form not inconsistent with the Plan as may be approved by the Board of Directors. Such Option Agreements may differ among recipients.

- 5.2 **Restricted Stock Agreement.** Each recipient of a grant of Restricted Stock shall execute an agreement (“Restricted Stock Agreement”) in such form not inconsistent with the Plan as may be approved by the Board of Directors. Such Restricted Stock Agreements may differ among recipients.
- 5.3 **“Lock-Up” Agreement.** Unless the Board specifies otherwise, each Restricted Stock Agreement and Option Agreement shall provide that upon the request of the Company or the managing underwriter(s) of any offering of securities of the Company that is the subject of a registration statement filed under the United States Securities Act of 1933, as amended from time to time (the “Act”), the holder of any Option or the purchaser of any Restricted Stock shall, in connection therewith, agree in writing (in such form as the Company or such managing underwriter(s) shall request) to the general effect that for a period of time (not to exceed 180 days, plus such additional number of days (not to exceed 35) as may reasonably be requested to enable the underwriter(s) of such offering to comply with Rule 2711(f) of the Financial Industry Regulatory Authority or any amendment or successor thereto) from the effective date of the registration statement under the Act for such offering, the holder or purchaser will not sell, make any short sale of, loan, grant any option for the purchase of, or otherwise

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dispose of any shares of the common stock of the Company owned or controlled by him or her.

6. Purchase Price.

- 6.1 **General.** The purchase price per share of Restricted Stock and per share of stock deliverable upon the exercise of an Option shall be determined by the Board, provided, however, that in the case of any Option, the exercise price shall not be less than 100% of the fair market value of such stock, as determined by the Board, at the time of grant of such Option, or less than 110% of such fair market value in the case of any Incentive Stock Option granted to a Greater Than 10% Shareholder.
- 6.2 **Payment of Purchase Price.** Option Agreements may provide for the payment of the exercise price by delivery of cash or a check to the order of the Company in an amount equal to the exercise price of such Options, or, to the extent provided in the applicable Option Agreement, by one of the following methods:
- (i) with the consent of the Board by delivery to the Company of shares of Common Stock; such surrendered shares shall have a fair market value equal in amount to the exercise price of the Options being exercised,
 - (ii) with the consent of the Board a personal recourse note issued by the optionee to the Company in a principal amount equal to such aggregate exercise price and with such other terms, including interest rate and maturity, as the Company may determine in its discretion; *provided, however*, that the interest rate borne by such note shall not be less than the lowest applicable federal rate, as defined in Section 1274(d) of the Code,
 - (iii) with the consent of the Board if the class of Common Stock is registered under the Securities Exchange Act of 1934 at such time, subject to rules as may be established by the Board, by delivery to the Company of a properly executed exercise notice along with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company for the purchase price,
 - (iv) with the consent of the Board by reducing the number of Option shares otherwise issuable to the optionee upon exercise of the Option by a number of shares of Common Stock having a fair market value equal to such aggregate exercise price,
 - (v) with the consent of the Board by any combination of such methods of payment.

The fair market value of any shares of the Company’s Common Stock or other non-cash consideration which may be delivered upon exercise of an Option shall be determined by the Board of Directors. Restricted Stock Agreements may provide for the payment of any purchase price in any manner approved by the Board of Directors at the time of authorizing the issuance thereof.

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7. Option Period.

Notwithstanding any other provision of the Plan or any Option Agreement, each Option and all rights thereunder shall expire on the date specified in the applicable Option Agreement, provided that such date shall not be later than ten years after the date on which the Option is granted (or five years in the case of an Incentive Stock Option granted to a Greater Than 10% Shareholder), and in either case, shall be subject to earlier termination as provided in the Plan or Option Agreement.

8. Exercise of Options.

- 8.1 **General.** Each Option shall be exercisable either in full or in installments at such time or times and during such period as shall be set forth in the agreement evidencing such Option, subject to the provisions of the Plan. To the extent not exercised, installments shall accumulate and be exercisable, in whole or in part, at any time after becoming exercisable, but not later than the date the Option expires.
- 8.2 **Notice of Exercise.** An Option may be exercised by the optionee by delivering to the Company on any business day a written notice specifying the number of shares of Common Stock the optionee then desires to purchase and specifying the address to which the certificates for such shares are to be mailed (the “Notice”), accompanied by payment for such shares. In addition, the Company may require any individual to whom an Option is granted, as a condition of exercising such Option, to give written assurances in a substance and form satisfactory to the Company to the effect that such individual is acquiring the Common Stock subject to the Option for his or her own account for investment and not with a view to the resale or distribution thereof, and to such other effects as the Company deems necessary or advisable in order to comply with any securities law(s).
- 8.3 **Delivery.** As promptly as practicable after receipt of such written notification and payment, the Company shall deliver or cause to be delivered to the optionee certificates for the number of shares with respect to which such Option has been so exercised, issued in the optionee’s name; provided, however, that such delivery shall be deemed effected for all purposes when the Company or a stock transfer agent shall have deposited such certificates in the United States mail, addressed to the optionee, at the address specified in the Notice.

9. Transferability of Options.

No Incentive Stock Option shall be assignable or transferable by the person to whom it is granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and during the life of an optionee, an Incentive Stock Option shall be exercisable only by the optionee. The Board may, in its discretion, determine the extent to which a non-statutory Option shall be transferable.

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10. Termination of Employment; Disability; Death.

Except as may be otherwise expressly provided in the terms and conditions of the Option Agreement, Options shall terminate on the earliest to occur of:

- (i) the date of expiration thereof;

- (ii) 90 days after termination of the optionee's employment with, or provision of services to, the Company by the Company for Cause (as hereinafter defined);
- (iii) 90 days after the date of voluntary termination of the optionee's employment with, or provision of services to, the Company by the optionee (other than for death or permanent disability as defined below); or
- (iv) 90 days after the date of termination of the optionee's employment with, or provision of services to, the Company by the Company without Cause (other than for death or permanent disability as defined below).

Until the date on which the Option so expires, the optionee may exercise that portion of his or her Option which is exercisable at the time of termination of the employment or service relationship.

An employment or service relationship between the Company and the optionee shall be deemed to exist during any period during which the optionee is employed by or providing services to the Company. Whether an authorized leave of absence or an absence due to military or government service shall constitute termination of the employment relationship between the Company and the optionee shall be determined by the Board at the time thereof.

For purposes of this Section 10, the term "Cause" shall mean (a) any material breach by the optionee of any agreement to which the optionee and the Company are both parties, (b) any act (other than retirement) or omission to act by the optionee which may have a material and adverse effect on the Company's business or on the optionee's ability to perform services for the Company, including, without limitation, the commission of any crime (other than minor traffic violations), or (c) any material misconduct or material neglect of duties by the optionee in connection with the business or affairs of the Company.

In the event of the permanent and total disability or death of an optionee while in an employment or other relationship with the Company and before the date of expiration of such option, such option shall terminate on the earlier of such date of expiration or one (1) year following the date of such disability or death. After disability or death, the optionee (or in the case of death, his or her executor, administrator or any person or persons to whom this option may be transferred by will or by laws of descent and distribution) shall have the right, at any time prior to such termination, to exercise the option to the extent the optionee was entitled to exercise such option as of the date of his or her disability or death. An optionee is permanently and totally disabled if he or she is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to last for a

continuous period of not less than 12 months; permanent and total disability shall be determined in accordance with Section 22(e)(3) of the Code and the regulations issued thereunder.

- 11. **Rights as a Shareholder.** The holder of an Option shall have no rights as a shareholder with respect to any shares covered by the Option (including, without limitation, any rights to receive dividends or non-cash distributions with respect to such shares) until the date of issue of a stock certificate to him or her for such shares. No adjustment shall be made for dividends or other rights for which the record date is prior to the date such stock certificate is issued.
- 12. **Additional Provisions.** The Board of Directors may, in its sole discretion, include additional provisions in Restricted Stock Agreements and Option Agreements, including, without limitation, restrictions on transfer, rights of the Company to repurchase shares of Restricted Stock or shares of Common Stock acquired upon exercise of Options, commitments to pay cash bonuses, to make, arrange for or guaranty loans or to transfer other property to optionees upon exercise of Options, or such other provisions as shall be determined by the Board of Directors; *provided that* such additional provisions shall not be inconsistent with any other term or condition of the Plan and such additional provisions shall not be such as to cause any Incentive Stock Option to fail to qualify as an Incentive Stock Option within the meaning of Section 422 of the Code.
- 13. **Acceleration, Extension, Etc.** The Board of Directors may, in its sole discretion, (i) accelerate the date or dates on which all or any particular Option or Options may be exercised or (ii) extend the period or periods of time during which all, or any particular, Option or Options may be exercised.
- 14. **Adjustment Upon Changes in Capitalization**
 - 14.1 **No Effect of Options upon Certain Corporate Transactions.** The existence of outstanding Options shall not affect in any way the right or power of the Company to make or authorize any or all adjustments, recapitalizations, reorganizations or other changes in the Company's capital structure or its business, or any merger or consolidation, or any issue of Common Stock, or any issue of bonds, debentures, preferred or prior preference stock ahead of or affecting the Common Stock or the rights thereof, or the dissolution or liquidation of the Company, or any sale or transfer of all or any part of its assets or business, or any other corporate act or proceeding, whether of a similar character or otherwise.
 - 14.2 **Adjustment Provisions.** If, through or as a result of any merger, consolidation, sale of all or substantially all of the assets of the Company, reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar transaction, (i) the outstanding shares of Common Stock are increased, decreased or exchanged for a different number or kind of shares or other securities of the Company, or (ii) additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Common Stock or other securities, an appropriate

and proportionate adjustment shall be made in (x) the maximum number and kind of shares reserved for issuance under the Plan, (y) the number and kind of shares or other securities subject to any then outstanding Options, and (z) the price for each share or other security subject to any then outstanding Options, so that upon exercise of such Options, in lieu of the shares of Common Stock for which such Options were then exercisable, the relevant optionee shall be entitled to receive, for the same aggregate consideration, the same total number and kind of shares or other securities, cash or property that the owner of an equal number of outstanding shares of Common Stock immediately prior to the event requiring adjustment would own as a result of the event.

- 14.3 **No Adjustment in Certain Cases.** Except as hereinbefore expressly provided, the issue by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, for cash or property or for labor or services, either upon direct sale or upon the exercise of rights or warrants to subscribe therefore, or upon conversion of shares or obligations of the Company convertible into such shares or other securities, shall not affect, and no adjustment by reason thereof shall be made with respect to, the number or price of shares of Common Stock then subject to outstanding options.
- 14.4 **Board Authority to Make Adjustments.** Any adjustments under this Section 14 will be made by the Board of Directors, whose determination as to what adjustments, if any, will be made and the extent thereof will be final, binding and conclusive. No fractional shares will be issued under the Plan on account of any such adjustments.
- 15. **Effect of Certain Transactions.**
 - 15.1 **General.** Except as provided in any Option Agreement or Restricted Stock Agreement to the contrary, if the Company is merged with or into or consolidated with another corporation under circumstances where the stockholders of the Company immediately prior to such merger or consolidation do not own after such merger or consolidation shares representing at least fifty percent (50%) of the voting power of the Company or the surviving or resulting corporation, as the case may be, or if shares representing fifty percent (50%) or more of the voting power of the Company are transferred to an Unrelated Third Party, as hereinafter defined, or if the Company is liquidated, or sells or otherwise disposes of all or substantially all its assets (each such transaction is referred to herein as a "Change in Control Transaction"), the Board, or the board of directors of any corporation assuming the obligations of the Company, may, in its discretion, take any one or more of the following actions, as to some or all outstanding Options or Restricted Stock Awards (and need not take the same action as to each such Option or Restricted Stock Award): (i) provide that such Options shall be assumed, or equivalent Options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof),

Options will terminate immediately prior to the consummation of the Change in Control Transaction unless exercised by the optionee to the extent otherwise then exercisable within a specified period following the date of such notice, (iii) upon written notice to the grantees, provide that all unvested shares of Restricted Stock shall be repurchased at cost, (iv) make or provide for a cash payment to the optionees equal to the difference between (A) the fair market value of the per share consideration (whether cash, securities or other property or any combination of the above) the holder of a share of Common Stock will receive upon consummation of the Change in Control Transaction (the "Per Share Transaction Price") times the number of shares of Common Stock subject to outstanding vested Options (to the extent then exercisable at prices not equal to or in excess of the Per Share Transaction Price) and (B) the aggregate exercise price of such outstanding vested Options, in exchange for the termination of such Options, or (v) provide that all or any outstanding Options shall become exercisable and all or any outstanding Restricted Stock Awards shall vest in part or in full immediately prior to such event. To the extent that any Options are exercisable at a price equal to or in excess of the Per Share Transaction Price, the Board may provide that such Options shall terminate immediately upon the consummation of the Change in Control Transaction without any payment being made to the holders of such Options. "Unrelated Third Party" shall mean any person who is not, on the date of adoption of this Plan by the Board, a holder of stock of any class or preference or any stock option of the Company.

15.2 **Substitute Options.** The Company may grant Options in substitution for options held by employees of another corporation who become employees of the Company, as the result of a merger or consolidation of the employing corporation with the Company or as a result of the acquisition by the Company, of property or stock of the employing corporation. The Company may direct that substitute Options be granted on such terms and conditions as the Board considers appropriate in the circumstances.

15.3 **Restricted Stock.** In the event of a business combination or other transaction of the type detailed in Section 15.1, any securities, cash or other property received in exchange for shares of Restricted Stock shall continue to be governed by the provisions of any Restricted Stock Agreement pursuant to which they were issued, including any provision regarding vesting, and such securities, cash, or other property may be held in escrow on such terms as the Board of Directors may direct, to insure compliance with the terms of any such Restricted Stock Agreement.

16. **No Special Employment Rights.** Nothing contained in the Plan or in any Option or Restricted Stock Agreement shall confer upon any optionee or holder of Restricted Stock any right with respect to the continuation of his or her employment by the Company or interfere in any way with the right of the Company at any time to terminate such employment or to increase or decrease the compensation of such person.

17. **Other Employee Benefits.** The amount of any compensation deemed to be received by an employee as a result of the issuance of shares of Restricted Stock or the grant or exercise of an Option or the sale of shares received upon such award or exercise will not constitute compensation with respect to which any other employee benefits of such employee are determined, including, without limitation, benefits under any bonus, pension, profit-sharing, life insurance or salary continuation plan, except as otherwise specifically determined by the Board of Directors.

18. **Amendment of the Plan.**

18.1 The Board may at any time, and from time to time, modify or amend in any respect or terminate the Plan. If shareholder approval is not obtained within twelve months after any amendment increasing the number of shares authorized under the Plan or changing the class of persons eligible to receive Options under the Plan, no Options granted pursuant to such amendments shall be deemed to be Incentive Stock Options and no Incentive Stock Options shall be issued pursuant to such amendments thereafter.

18.2 The termination or any modification or amendment of the Plan shall not, without the consent of an optionee or the holder of Restricted Stock, adversely affect his or her rights under an Option or Restricted Stock Award previously granted to him or her. With the consent of the recipient of Restricted Stock or optionee affected, the Board may amend outstanding Restricted Stock Agreements or Option Agreements in a manner not inconsistent with the Plan.

19. **Withholding.** The Company shall have the right to deduct from payments of any kind otherwise due to the optionee or recipient of Restricted Stock, any federal, state or local taxes of any kind required by law to be withheld with respect to issuance of any shares of Restricted Stock or shares issued upon exercise of Options. Prior to delivery of any Common Stock pursuant to the terms of this Plan, the Board has the right to require that the optionee or recipient of Restricted Stock remit to the Company an amount sufficient to satisfy any minimum tax withholding obligation. Subject to the prior approval of the Company, which may be withheld by the Company in its sole discretion, the obligor may elect to satisfy any minimum withholding obligations, in whole or in part, (i) by causing the Company to withhold shares of Common Stock otherwise issuable, or (ii) by delivering to the Company a sufficient number of shares of Common Stock. The shares so withheld shall have a fair market value equal to such minimum withholding obligation. The fair market value of the shares used to satisfy such minimum withholding obligation shall be determined by the Company as of the date that the amount of tax to be withheld is to be determined. A person who has made an election pursuant to this Section 19 may only satisfy his or her withholding obligation with shares of Common Stock which are not subject to any repurchase, forfeiture, unfulfilled vesting or other similar restrictions.

20. **Effective Date and Duration of the Plan.**

20.1 **Effective Date.** The Plan shall become effective when adopted by the Board of Directors. If shareholder approval is not obtained within twelve months after the

date of the Board's adoption of the Plan, no Options previously granted under the Plan shall be deemed to be Incentive Stock Options and no Incentive Stock Options shall be granted thereafter. Amendments to the Plan not requiring shareholder approval shall become effective when adopted by the Board. Amendments requiring shareholder approval shall become effective when adopted by the Board, but if shareholder approval is not obtained within twelve months of the Board's adoption of such amendment, any Incentive Stock Options granted pursuant to such amendment shall be deemed to be non-statutory Options provided that such Options are authorized by the Plan. Subject to this limitation, Options may be granted under the Plan at any time after the effective date and before the date fixed for termination of the Plan.

20.2 **Termination.** Unless sooner terminated by action of the Board of Directors, the Plan shall terminate upon the close of business on the day next preceding the tenth anniversary of the date of its adoption by the Board of Directors.

21. **Requirements of Law.** The Company shall not be required to sell or issue any shares under any Option or Restricted Stock Agreement if the issuance of such shares shall constitute a violation by the optionee, the Restricted Stock Award recipient, or by the Company of any provisions of any law or regulation of any governmental authority. In addition, in connection with the Act, the Company shall not be required to issue any shares upon exercise of any Option unless the Company has received evidence satisfactory to it to the effect that the holder of such Option will not transfer such shares except pursuant to a registration statement in effect under the Act or unless an opinion of counsel satisfactory to the Company has been received by the Company to the effect that such registration is not required in connection with any such transfer. Any determination in this connection by the Board shall be final, binding and conclusive. In the event the shares issuable on exercise of an Option are not registered under the Act or under the securities laws of each relevant state or other jurisdiction, the Company may imprint on the certificate(s) appropriate legends that counsel for the Company considers necessary

or advisable to comply with the Act or any such state or other securities law. The Company may register, but in no event shall be obligated to register, any securities covered by the Plan pursuant to the Act; and in the event any shares are so registered the Company may remove any legend on certificates representing such shares. The Company shall not be obligated to take any affirmative action in order to cause the exercise of an Option or the issuance of shares pursuant thereto to comply with any law or regulation of any governmental authority.

22. **Non-Exclusivity of this Plan; Non-Uniform Determinations.** Neither the adoption of this Plan by the Board of Directors nor the approval of this Plan by the stockholders of the Company shall be construed as creating any limitations on the power of the Board of Directors to adopt such other incentive arrangements as it may deem desirable, including, without limitation, the granting of stock options otherwise than under this Plan, and such arrangements may be either applicable generally or only in specific cases.

The determinations of the Board of Directors under this Plan need not be uniform and may be made by it selectively among persons who receive or are eligible to receive Options or Restricted Stock Awards under this Plan (whether or not such persons are similarly situated). Without limiting the generality of the foregoing, the Board of Directors shall be entitled, among other things, to make non-uniform and selective determinations, and to enter into non-uniform and selective Option Agreements and Restricted Stock Agreements, as to (a) the persons to receive Options or Restricted Stock Awards under this Plan, (b) the terms and provisions of Options or Restricted Stock Awards, (c) the exercise by the Board of Directors of its discretion in respect of the exercise of Options pursuant to the terms of this Plan, and (d) the treatment of leaves of absence pursuant to Section 10 hereof.

23. **Governing Law.** This Plan and each Option or Restricted Stock Agreement shall be governed by the laws of The Commonwealth of Massachusetts, without regard to its principles of conflicts of law.

INCENTIVE STOCK OPTION

Granted by

Selecta Biosciences, Inc. (the "Company")

Under the 2008 Stock Incentive Plan

This Option is and shall be subject in every respect to the provisions of the Company's 2008 Stock Incentive Plan, as amended from time to time, which is incorporated herein by reference and made a part hereof. The holder of this Option (the "Holder") hereby accepts this Option subject to all the terms and provisions of the Plan and agrees that (a) in the event of any conflict between the terms hereof and those of the Plan, the latter shall prevail, and (b) all decisions under and interpretations of the Plan by the Board or the Committee shall be final, binding and conclusive upon the Holder and his or her heirs and legal representatives.

1. **Name of Holder:** [Name of Optionee]
2. **Date of Grant:** [Date]
3. **Vesting Start Date:** [Date of Hire]
4. **Maximum number of shares for which this Option is exercisable:** [number]
5. **Exercise (purchase) price per share:** [\$.]
6. **Payment method:**
 - (i) a personal, certified or bank check or postal money order payable to the order of the Company for an amount equal to the exercise price of the shares being purchased; or
 - (ii) with the consent of the Company, any of the other methods set forth in the Plan.
7. **Expiration Date of Option:** [Grant Date + 10 years]
8. **Vesting Schedule:** This Option shall become exercisable for 25% of the maximum number of shares granted on the first anniversary of the Vesting Start Date, and shall become exercisable for an additional 2.0833% on the last day of each month thereafter until the Option is fully vested, [provided, however, that the Option shall be deemed to be fully vested immediately prior to the consummation of a Qualified Sale (as defined below)]. All vesting shall cease upon the date of termination of employment or provision of services.

["Qualified Sale" shall mean the sale of all or substantially all of assets or issued and outstanding capital stock of the Company, or merger or consolidation involving the Company in which stockholders of the Company immediately before such merger or

consolidation do not own immediately after such merger or consolidation capital stock or other equity interests of the surviving corporation or entity representing more than fifty percent in voting power of capital stock or other equity interests of such surviving corporation or entity outstanding immediately after such merger or consolidation.]

In addition to the foregoing, upon the Holder's election at any time after the date of Grant of this Option, the Holder shall be entitled to exercise this Option immediately and in full for the Maximum Number of shares as set forth herein, whether or not fully vested, provided that, upon such exercise, the Holder shall execute a stock restriction agreement containing a "reverse vesting" schedule effectively equivalent to the Vesting Schedule set forth herein, pursuant to which the Holder agrees to sell back any unvested shares at cost should he or she leave the employment of the Company prior to full vesting.

9. **Termination of Employment.** This Option shall terminate on the earliest to occur of:
- (i) the date of expiration thereof;
 - (ii) 90 days after termination of the Holder's employment with or services to the Company by the Company for Cause (as defined in the Plan);
 - (iii) 90 days after the date of voluntary termination of employment or services by the Holder (other than for death or permanent disability as defined in the Plan); or
 - (iv) 90 days after the date of termination of the Holder's employment with or services to the Company by the Company without Cause (other than for death or permanent disability as defined in the Plan).

10. **Company's Right of First Refusal.** Prior to the effective date of a registration statement covering shares of the Company's Common Stock, any shares of stock issued pursuant to exercise of this Option shall be subject to the Company's right of first refusal as set forth at Appendix A.
11. **Lock-Up Agreement.** The Holder agrees for a period of up to 180 days from the effective date of any registration of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), upon request of the Company or underwriters managing any underwritten offering of the Company's securities, not to sell, make any short sale of, loan, grant any option for the purchase of, or otherwise dispose of any shares issued pursuant to the exercise of this Option, without the prior written consent of the Company and such underwriters.
12. **Tax Withholding.** The Company's obligation to deliver shares shall be subject to the Holder's satisfaction of any federal, state and local income and employment tax withholding requirements.
13. **Notice.** Any notice to be given to the Company hereunder shall be deemed sufficient if addressed to the Company and delivered to the office of the Company, Selecta Biosciences, Inc., 480 Arsenal Street, Building One, Watertown, MA 02472, to the attention of the President, or such other address as the Company may hereafter designate.

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Any notice to be given to the Holder hereunder shall be deemed sufficient if addressed to and delivered in person to the Holder at his or her address furnished to the Company or when deposited in the mail, postage prepaid, addressed to the Holder at such address.

IN WITNESS WHEREOF, the parties have executed this Option, or caused this Option to be executed, as of the Date of Grant.

Selecta Biosciences, Inc.

By:

[Robert L. Bratzler, President]

The undersigned Holder hereby acknowledges receipt of a copy of the Plan and this Option (including Appendix A hereto), and agrees to the terms of this Option and the Plan.

[Optionee]

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APPENDIX A

Right of First Refusal

1. **General.** Prior to the effective date of a registration statement under the Securities Act, covering any shares of the Company's Common Stock and until such time as the Company shall have effected a public offering of its Common Stock registered under the Securities Act, in the event that, at any time when the Holder (which term for purposes of this section shall mean the Holder and his or her executors, administrators and any other person to whom this Option may be transferred by will or the laws of descent and distribution) is permitted to do so, the Holder desires to sell, assign or otherwise transfer any of the shares issued upon the exercise of this Option, the Holder shall first offer such shares to the Company by giving written notice of the Holder's desire so to sell, assign or transfer such shares.
2. **Notice of Intended Transfer.** The notice shall state the number of shares offered, the name of the person or persons to whom it is proposed to sell, assign or transfer such shares and the price at which such shares are intended to be sold, assigned or transferred. Such notice shall constitute an offer to the Company for the Company to purchase the number of shares set forth in the notice at a price per share equal to the price stated therein.
3. **Company to Accept or Decline Within 30 Days.** The Company may accept the offer as to all, but not less than all, such shares by notifying the Holder in writing within 30 days after receipt of such notice of its acceptance of the offer. If the offer is accepted, the Company shall have 60 days within which to purchase the offered shares at a price per share as aforesaid. If within the applicable time periods the Holder does not receive notice of the Company's intention to purchase the offered shares, or if payment in full of the purchase price is not made by the Company, the offer shall be deemed to have been rejected and the Holder may transfer title to such shares within 90 days from the date of the Holder's written notice to the Company of the Holder's intention to sell, but such transfer shall be made only to the proposed transferee and at the proposed price as stated in such notice and after compliance with any other provisions of this Option applicable to the transfer of such shares.
4. **Transferred Shares to Remain Subject to Right of First Refusal.** Shares that are so transferred to such transferee shall remain subject to the rights of the Company set forth in this Appendix A. As a condition to such transfer, such transferee shall execute and deliver all such documents as the Company may require to evidence the binding agreement of such transferee so to remain subject to the rights of the Company.
5. **Remedies of Company.** No sale, assignment, pledge or transfer of any of the shares covered by this Option shall be effective or given effect on the books of the Company unless all of the applicable provisions of this Appendix A have been duly complied with, and the Company may inscribe on the face of any certificate representing any of such shares a legend referring to the provisions of this Appendix A. If any transfer of shares is made or attempted in violation of the foregoing restrictions, or if shares are not offered to the Company as required hereby, the Company shall have the right to purchase such shares from the owner thereof or his transferee at any time before or after the transfer, as herein provided. In addition to any other legal or equitable remedies which it may have, the Company may enforce its rights by actions for

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specific performance (to the extent permitted by law) and may refuse to recognize any transferee as one of its stockholders for any purpose, including, without limitation, for purposes of dividend and voting rights, until all applicable provisions hereof have been complied with.

6. **Shares Subject to Right of First Refusal.** For purposes of the Right of First Refusal pursuant to this Appendix A, the term "shares" shall mean any and all new, substituted or additional securities or other property issued to the Holder, by reason of his or her ownership of Common Stock pursuant to the exercise of this Option, in connection with any stock dividend, liquidating dividend, stock split or other change in the character or amount of any of the outstanding securities of the Company, or any consolidation, merger or sale of all or substantially all of the assets of the Company.

7. **Legends on Stock Certificates.** Any certificate representing shares of stock subject to the provisions of this Appendix A may have endorsed thereon one or more legends, substantially as follows:

- (i) "Any disposition of any interest in the securities represented by this certificate is subject to restrictions, and the securities represented by this certificate are subject to certain options, contained in a certain agreement between the record holder hereof and the Company, a copy of which will be mailed to any holder of this certificate without charge upon receipt by the Company of a written request therefor."

- (ii) "The shares of stock represented by this certificate have not been registered under the Securities Act of 1933 or under the securities laws of any state and may not be pledged, hypothecated, sold or otherwise transferred except upon such registration or upon receipt by the Company of an opinion of counsel satisfactory to the Company, in form and substance satisfactory to the Company, that such registration is not required."

8. Right of First Refusal to Lapse Upon Registration. The restrictions imposed by this Appendix A shall terminate in all respects upon the effective date of a registration statement under the Securities Act covering any of the Company's Common Stock.

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NON-STATUTORY STOCK OPTION

Granted by

Selecta Biosciences, Inc. (the "Company")

Under the 2008 Stock Incentive Plan

This Option is and shall be subject in every respect to the provisions of the Company's 2008 Stock Incentive Plan, as amended from time to time, which is incorporated herein by reference and made a part hereof. The holder of this Option (the "Holder") hereby accepts this Option subject to all the terms and provisions of the Plan and agrees that (a) in the event of any conflict between the terms hereof and those of the Plan, the latter shall prevail, and (b) all decisions under and interpretations of the Plan by the Board or the Committee shall be final, binding and conclusive upon the Holder and his or her heirs and legal representatives.

1. **Name of Holder:** [Name of Optionee]
2. **Date of Grant:** [Date]
3. **Vesting Start Date:** [Date of Hire / Date of Grant]
4. **Maximum number of shares for which this Option is exercisable:** [number]
5. **Exercise (purchase) price per share:** [\$.]
6. **Payment method:**
 - (i) a personal, certified or bank check or postal money order payable to the order of the Company for an amount equal to the exercise price of the shares being purchased; or
 - (ii) with the consent of the Company, any of the other methods set forth in the Plan.
7. **Expiration Date of Option:** [Grant Date + 10 years]
8. **Vesting Schedule:** This Option shall become exercisable for 2.0833% of the maximum number of shares granted on [last day of month of Vesting Start Date], and shall become exercisable for an additional 2.0833% on the last day of each month thereafter until the Option is fully vested, [provided, however, that the Option shall be deemed to be fully vested immediately prior to the consummation of a Qualified Sale (as defined below)]. All vesting shall cease upon the date of termination of employment or provision of services.

["Qualified Sale" shall mean the sale of all or substantially all of assets or issued and outstanding capital stock of the Company, or merger or consolidation involving the Company in which stockholders of the Company immediately before such merger or

consolidation do not own immediately after such merger or consolidation capital stock or other equity interests of the surviving corporation or entity representing more than fifty percent in voting power of capital stock or other equity interests of such surviving corporation or entity outstanding immediately after such merger or consolidation.]

In addition to the foregoing, upon the Holder's election at any time after the date of Grant of this Option, the Holder shall be entitled to exercise this Option immediately and in full for the Maximum Number of shares as set forth herein, whether or not fully vested, provided that, upon such exercise, the Holder shall execute a stock restriction agreement containing a "reverse vesting" schedule effectively equivalent to the Vesting Schedule set forth herein, pursuant to which the Holder agrees to sell back any unvested shares at cost should he or she leave the employ of the Company prior to full vesting.

9. **Termination of Employment.** This Option shall terminate on the earliest to occur of:
 - (i) the date of expiration thereof;
 - (ii) 90 days after termination of the Holder's employment with or services to the Company for any reason other than for death or permanent disability as defined in the Plan); or
 - (iv) one year following the date of Holder's death or permanent disability as defined in the Plan.
10. **Company's Right of First Refusal.** Prior to the effective date of a registration statement covering shares of the Company's Common Stock, any shares of stock issued pursuant to exercise of this Option shall be subject to the Company's right of first refusal as set forth at Appendix A.
11. **Lock-Up Agreement.** The Holder agrees for a period of up to 180 days from the effective date of any registration of securities of the Company under the Securities Act of 1933, as amended (the "Securities Act"), upon request of the Company or underwriters managing any underwritten offering of the Company's securities, not to sell, make any short sale of, loan, grant any option for the purchase of, or otherwise dispose of any shares issued pursuant to the exercise of this Option, without the prior written consent of the Company and such underwriters.
12. **Tax Withholding.** The Company's obligation to deliver shares shall be subject to the Holder's satisfaction of any federal, state and local income and employment tax withholding requirements.

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13. **Notice.** Any notice to be given to the Company hereunder shall be deemed sufficient if addressed to the Company and delivered to the office of the Company, Selecta Biosciences, Inc., 480 Arsenal Street, Building One, Watertown, MA 02472, to the attention of the President, or such other address as the Company may hereafter designate.

Any notice to be given to the Holder hereunder shall be deemed sufficient if addressed to and delivered in person to the Holder at his or her address furnished to the Company or when deposited in the mail, postage prepaid, addressed to the Holder at such address.

IN WITNESS WHEREOF, the parties have executed this Option, or caused this Option to be executed, as of the Date of Grant.

Selecta Biosciences, Inc.

By: _____
[Robert L. Bratzler, President]

The undersigned Holder hereby acknowledges receipt of a copy of the Plan and this Option (including Appendix A hereto), and agrees to the terms of this Option and the Plan.

[Optionee]

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APPENDIX A

Right of First Refusal

1. **General.** Prior to the effective date of a registration statement under the Securities Act, covering any shares of the Company's Common Stock and until such time as the Company shall have effected a public offering of its Common Stock registered under the Securities Act, in the event that, at any time when the Holder (which term for purposes of this section shall mean the Holder and his or her executors, administrators and any other person to whom this Option may be transferred by will or the laws of descent and distribution) is permitted to do so, the Holder desires to sell, assign or otherwise transfer any of the shares issued upon the exercise of this Option, the Holder shall first offer such shares to the Company by giving written notice of the Holder's desire so to sell, assign or transfer such shares.
2. **Notice of Intended Transfer.** The notice shall state the number of shares offered, the name of the person or persons to whom it is proposed to sell, assign or transfer such shares and the price at which such shares are intended to be sold, assigned or transferred. Such notice shall constitute an offer to the Company for the Company to purchase the number of shares set forth in the notice at a price per share equal to the price stated therein.
3. **Company to Accept or Decline Within 30 Days.** The Company may accept the offer as to all, but not less than all, such shares by notifying the Holder in writing within 30 days after receipt of such notice of its acceptance of the offer. If the offer is accepted, the Company shall have 60 days within which to purchase the offered shares at a price per share as aforesaid. If within the applicable time periods the Holder does not receive notice of the Company's intention to purchase the offered shares, or if payment in full of the purchase price is not made by the Company, the offer shall be deemed to have been rejected and the Holder may transfer title to such shares within 90 days from the date of the Holder's written notice to the Company of the Holder's intention to sell, but such transfer shall be made only to the proposed transferee and at the proposed price as stated in such notice and after compliance with any other provisions of this Option applicable to the transfer of such shares.
4. **Transferred Shares to Remain Subject to Right of First Refusal.** Shares that are so transferred to such transferee shall remain subject to the rights of the Company set forth in this Appendix A. As a condition to such transfer, such transferee shall execute and deliver all such documents as the Company may require to evidence the binding agreement of such transferee so to remain subject to the rights of the Company.
5. **Remedies of Company.** No sale, assignment, pledge or transfer of any of the shares covered by this Option shall be effective or given effect on the books of the Company unless all of the applicable provisions of this Appendix A have been duly complied with, and the Company may inscribe on the face of any certificate representing any of such shares a legend referring to the provisions of this Appendix A. If any transfer of shares is made or attempted in violation of the foregoing restrictions, or if shares are not offered to the Company as required hereby, the Company shall have the right to purchase such shares from the owner thereof or his transferee at any time before or after the transfer, as herein provided. In addition to any other legal or equitable remedies which it may have, the Company may enforce its rights by actions for

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specific performance (to the extent permitted by law) and may refuse to recognize any transferee as one of its stockholders for any purpose, including, without limitation, for purposes of dividend and voting rights, until all applicable provisions hereof have been complied with.

6. **Shares Subject to Right of First Refusal.** For purposes of the Right of First Refusal pursuant to this Appendix A, the term "shares" shall mean any and all new, substituted or additional securities or other property issued to the Holder, by reason of his or her ownership of Common Stock pursuant to the exercise of this Option, in connection with any stock dividend, liquidating dividend, stock split or other change in the character or amount of any of the outstanding securities of the Company, or any consolidation, merger or sale of all or substantially all of the assets of the Company.
7. **Legends on Stock Certificates.** Any certificate representing shares of stock subject to the provisions of this Appendix A may have endorsed thereon one or more legends, substantially as follows:
 - (i) "Any disposition of any interest in the securities represented by this certificate is subject to restrictions, and the securities represented by this certificate are subject to certain options, contained in a certain agreement between the record holder hereof and the Company, a copy of which will be mailed to any holder of this certificate without charge upon receipt by the Company of a written request therefor."
 - (ii) "The shares of stock represented by this certificate have not been registered under the Securities Act of 1933 or under the securities laws of any state and may not be pledged, hypothecated, sold or otherwise transferred except upon such registration or upon receipt by the Company of an opinion of counsel satisfactory to the Company, in form and substance satisfactory to the Company, that such registration is not required."
8. **Right of First Refusal to Lapse Upon Registration.** The restrictions imposed by this Appendix A shall terminate in all respects upon the effective date of a registration statement under the Securities Act covering any of the Company's Common Stock.

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Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated March 30, 2016 (except for Note 17(b) as to which the date is June 8, 2016) in the Amendment No. 2 to the Registration Statement (Form S-1 No. 333-211555) and related Prospectus of Selecta Biosciences, Inc. for the registration of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts
June 20, 2016
