Seres Therapeutics, Inc.
Form 10-K
March 14, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2015

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission File Number: 001-37465

Seres Therapeutics, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	27-4326290
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)
215 First Street	02142

Cambridge, Massachusetts
(Address of Principal Executive Offices) (Zip Code)

(617) 945-9626

(Registrant's Telephone Number, Including Area Code)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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	o	Accelerated filer	o
Non-accelerated filer	x (Do not check if a smaller reporting company)	Smaller reporting company	o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No x

The aggregate market value of common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on the Nasdaq Global Select Market on June 30, 2015, was $422,395,134.

As of March 7, 2016, there were 39,187,017 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2016 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission are incorporated by reference into Part III of this Annual Report on

Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. 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” o of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K 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 report and are subject to a number of risks, uncertainties and assumptions described under the sections in this report titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report. These forward-looking statements are subject to numerous risks, including, without limitation, the following:

- our status as a development-stage company and our expectation to incur losses in the future;
- our future capital needs and our need to raise additional funds;
- our ability to build a pipeline of product candidates and develop and commercialize drugs;
- our unproven approach to therapeutic intervention;
- our ability to enroll patients in clinical trials, timely and successfully complete those trials and receive necessary regulatory approvals;
- our ability to establish our own manufacturing facilities and to receive or manufacture sufficient quantities of our product candidates;
- our ability to protect and enforce our intellectual property rights;
- federal, state, and foreign regulatory requirements, including FDA regulation of our product candidates;
- our ability to obtain and retain key executives and attract and retain qualified personnel; and
- our ability to successfully manage our growth

PART I

Item 1. Business

Overview

We are a microbiome therapeutics platform company developing a novel class of biological drugs, which we refer to as Ecobiotic microbiome therapeutics. The human microbiome is an ecology of microorganisms, including bacteria, fungi and viruses, that, when unhealthy, or dysbiotic, can leave the body more susceptible to infections, metabolic disorders, allergies, autoimmune disease, inflammation and other serious conditions. Our drugs are designed to restore health by repairing the function of a dysbiotic microbiome. We are initially focused on implementing our microbiome therapeutics platform to develop Ecobiotic microbiome therapeutics that treat dysbiosis in the colonic microbiome, one of the most diverse microbiomes in the human body. SER-109, our lead product candidate, is designed to prevent further recurrences of Clostridium difficile infection, or CDI, a debilitating infection of the colon and, if approved by the U.S. Food and Drug Administration, or FDA, could be a first-in-field drug. In our Phase 1b/2 clinical study of SER-109 in recurrent CDI patients, 97% of patients achieved a clinical cure, which we defined as the absence of CDI requiring antibiotic treatment during the eight-week period after SER-109 dosing; 87 % of patients met the predefined endpoint of preventing recurrent CDI within eight weeks following administration of SER-109.

SER-109 has been granted Breakthrough Therapy designation by the FDA for the treatment of recurrent CDI. Breakthrough Therapy designation is intended to expedite the development and review of drugs or biologics that treat serious or life-threatening diseases or conditions and where preliminary clinical evidence indicates the drug candidate may be a substantial improvement over existing therapies. In addition, SER-109 has received Orphan Drug designation from the FDA for the treatment of recurrent CDI. We initiated a Phase 2 clinical study of SER-109 for recurrent CDI and dosed the first patient in May 2015. We expect initial study results in the middle of 2016.

The human microbiome is one of the richest and most diverse ecosystems on earth, with a population of more than 100 trillion microorganisms that live in our intestines, mouth, skin and elsewhere in the body. In a healthy, symbiotic state the colonic microbiome plays an important role in human health, helping the body digest food, resist pathogens, regulate the metabolic systems, develop and regulate the immune system and synthesize essential nutrients and vitamins. However, the colonic microbiome may change in composition for a variety of reasons, including in response to long-term or high-dose antibiotics and following gastrointestinal infection. These changes in composition result in the loss of key microbes, resulting in a state of dysbiosis. Dysbiosis of the colonic microbiome is associated with a wide range of serious disease and infections, such as gastrointestinal infection and inflammatory and metabolic diseases.

While the study of the human microbiome is not new, the scientific community’s understanding of the microbiome, and the colonic microbiome in particular, has been significantly advanced through metagenomics, which has enabled the broader understanding of the human microbiome at the organismal, functional and community level. Scientific research has correlated dysbiosis in the colonic microbiome with numerous diseases and conditions in humans and in animal models, including: infections, metabolic disorders, allergies, autoimmune disease, inflammation and other non-specific conditions, such as inflammatory bowel disease, or IBD. Information regarding the impact of the colonic microbiome on various disease states continues to grow rapidly.

We are developing a new approach to treating disease by restoring a dysbiotic colonic microbiome to a healthy state using our Ecobiotic microbiome therapeutics. Our approach is premised on the hypothesis that the proximal cause of many diseases is a dysbiosis in the natural state of the colonic microbiome that perpetuates the conditions that allow

disease to take hold and flourish. We believe that the restoration of a dysbiotic colonic microbiome using rationally designed therapeutics represents a paradigm shift in the approach to treating the underlying disease. Our Ecobiotic microbiome therapeutics, which are derived from our microbiome therapeutics platform, are rationally designed ecological compositions, consisting of discrete combinations of beneficial microorganisms with targeted functional properties that provide the ability to re-establish keystone features of a functional microbiome in settings of disease. There are currently no FDA-approved therapeutics that are designed to restore the microbiome to a healthy state.

Our approach to discovery and design is based on an iterative bedside-to-bench-to-bedside drug discovery strategy that begins with data on the human microbiome that we gather from clinical studies. From these data, we identify the ecological differences between a healthy and a diseased microbiome, which we then use to rationally design potential Ecobiotic microbiome therapeutics. After further in-lab testing, selected Ecobiotic microbiome therapeutic candidates are moved back into the clinic for testing with humans. We apply a comparative genomic systems biology framework that leverages proprietary computation, microbiology and screening capabilities to design lead candidates targeted at these ecological deficiencies. We are able to apply this framework and experience to existing clinical data sets, as well as to the proprietary clinical data set we have generated through our SER-109 clinical trials. We believe we can utilize our knowledge and data to design Ecobiotic microbiome therapeutics to treat various medical

conditions, such as non-Clostridium difficile infection and inflammatory and metabolic diseases. We also have advanced capabilities in the fermentation of colonic bacteria and the formulation of vegetative and spore forms of bacteria into therapeutics. We believe that the combination of experience, proprietary data and proprietary know-how that comprise our microbiome therapeutics platform provides us with a competitive advantage in the design and development of microbiome therapeutics. Further, our approach and platform, which enable the rational design, testing, optimization, formulation and manufacturing of Ecobiotic microbiome therapeutics, provide a framework that we believe can significantly reduce the time typically required to advance therapeutics to the clinic.

Using our microbiome therapeutics platform, we are developing our lead clinical product candidate, SER-109, which is designed to durably repair dysbiosis in the colonic microbiome in the setting of recurrent CDI. CDI is most often caused by the use of broad spectrum antibiotics which induce dysbiosis of the microbiome causing susceptibility to infection by Clostridium difficile, or C. difficile, a spore forming bacterium. CDI leads to severe and persistent diarrhea in infected individuals, but can also lead to more severe outcomes, such as inflammation of the colon, toxic megacolon and death. The U.S. Centers for Disease Control, or CDC, has identified CDI as one of the top three most urgent antibiotic-resistant bacterial threats in the United States. It is the most common cause of hospital acquired infection in the United States and has overtaken methicillin-resistant Staphylococcus aureus, or MRSA. CDI is responsible for the deaths of approximately 29,000 Americans each year. We estimate the incidence of primary CDI in the United States is between 640,000 and 820,000 patients per year. While the epidemiological data are varied outside the United States, we believe that, due to the widespread use of antibiotics, CDI is a growing global disease. The standard of care for CDI is to treat with antibiotics. In many cases, antibiotic treatments may resolve the acute infection caused by C. difficile. However, these antibiotic treatments kill bacteria broadly, inducing a dysbiosis of the microbiome and potentially making patients more susceptible to a recurrence of CDI. For those patients who experience a recurrence of their CDI, we believe it is this dysbiosis of the microbiome, not the presence of C. difficile, which is the proximal cause of disease. Research suggests that the risk of recurrence is approximately 25% after the primary CDI, 40% after a first recurrence and greater than 60% for those experiencing two or more recurrences. In addition, a recent randomized trial comparing two antibiotics for the treatment of primary CDI indicated that 8% of patients receiving fidaxomicin and 9% of patients receiving vancomycin did not respond to these antibiotics. We estimate that the addressable population of patients in the United States with recurrent CDI, defined as patients who have experienced at least three occurrences of CDI in the past nine months, is between 85,000 and 110,000 patients per year.

SER-109 is a bacterial spore ecology consisting of an average of approximately 50 bacterial species derived from healthy donors' fecal matter. SER-109 is designed to prevent further recurrences of CDI in patients suffering from recurrent CDI by restoring the dysbiotic microbiome to a state of health. In our recently completed open label Phase 1b/2 clinical study, results demonstrated that 87 percent of patients (26 of 30) met the predefined endpoint of preventing recurrent CDI within eight weeks following administration of SER-109. 97 percent of patients (29 of 30), achieved a clinical cure, which we defined as the absence of CDI requiring antibiotic treatment during the eight-week period after SER-109 dosing. The study demonstrated that SER-109 is well-tolerated and has a favorable safety profile with no serious adverse events considered by the investigators to be attributable to SER-109 treatment. We also performed an analysis of the microbiome using next-generation sequencing technology and microbiological analysis. These studies demonstrated a re-establishment of keystone organisms and a rapid increase in bacterial diversity, which enable the restoration of the microbiome to a healthy state. SER-109 has been granted both Breakthrough Therapy and Orphan Drug designations by the FDA. We initiated a Phase 2 clinical study of SER-109 for recurrent CDI and dosed the first patient in May 2015. We expect initial study results in the middle of 2016. We have conducted manufacturing process pre-validation studies of SER-109 to support a Phase 3 clinical trial and a potential biologics license application and commercial launch.

We believe the results of our open label Phase 1b/2 clinical study of SER-109 provide validation of the hypothesis underlying our microbiome therapeutics platform, supporting its further use to develop additional Ecobiotic microbiome therapeutics. Using the data we obtained from the SER-109 clinical trial, we are developing SER-262 as an Ecobiotic microbiome therapeutic designed to be used following antibiotic treatment of primary CDI to prevent the initial recurrence of CDI. SER-262 consists of bacteria that are a subset of the bacterial ecology comprising SER-109. Unlike SER-109, SER-262 strains are clonally isolated and produced in fermenters and do not require sourcing raw materials from human donations. There are several advantages to using a synthetic approach to developing microbiome therapeutics. Synthetically derived product candidates can be scaled up to meet global demand in a reliable reproducible manner, with well-defined characteristics. Based on our metagenomics expertise, proprietary in silico algorithms, world-leading, proprietary bacterial library, and field-leading manufacturing capabilities, we believe we can design synthetically produced microbiome therapeutic candidates for specific target indications. Importantly, our unique capabilities provide Seres with a significant competitive advantage in developing synthetically produced microbiome therapies. Pre-clinical studies of SER-262 have demonstrated efficacy in preventing the initial recurrence of CDI in mouse and hamster models. We intend to initiate clinical studies of SER-262 in patients with primary CDI to prevent recurrence in the middle of 2016.

In addition to our ongoing SER-109 clinical trial, we initiated our Phase 1b study for our inflammatory bowel disease, or IBD, drug candidate, SER-287, in December 2015 and are enrolling subjects with active mild to moderate ulcerative colitis to evaluate the

safety and efficacy of SER-287 added to standard of care treatment. The randomized, placebo-controlled multiple dose Phase 1b study of SER-287 is expected to enroll up to 55 subjects with active mild-to-moderate UC who are failing current therapies. The primary endpoint of the study will evaluate the change in the microbiome resulting from SER-287 treatment. The study will also evaluate clinical response, mucosal healing, as well as metabolomic, immunological and safety findings. The clinical development of SER-287 to treat UC is supported by preclinical studies in multiple animal models of colitis that provide evidence that SER-287 administration results in reduced pathology. Published clinical reports furthermore suggest that modulation of the microbiome through repetitive fecal microbiota transplants may lead to meaningful clinical response in certain UC patients.

In addition to our CDI and IBD product candidates, we are utilizing our microbiome therapeutics platform to develop SER-155 for the prevention of transplant-related mortality (due to infection and graft versus host disease, or, GvHD) in allogeneic hematopoietic stem cell transplant, or allo-HSCT, recipients. Published clinical evidence shows that allo-HSCT patients with reduced microbiome diversity due to antibiotic exposure are far more likely to die due to infection or GvHD (Taur et al., Blood, 2015). Notably, the SER-109 Phase 1b/2 study results demonstrated the elimination of drug-resistant organisms and other pathobiont species from a patient's gastrointestinal tract. We are also researching Ecobiotic microbiome therapeutics for the treatment of metabolic diseases, such as early-stage, non-insulin dependent diabetes, non-alcoholic steatohepatitis (NASH), obesity and metabolic syndrome. Research in these indications is focused on developing Ecobiotic drugs that address specific functional defects in the microbiome, including the specific metabolic products made by the microbes. We believe this approach may enable pursuit of a range of disorders including various forms of liver disease and rare genetic diseases of metabolism. The role of the microbiome in immuno-oncology therapies has also become apparent with recent important publications in humans and animal models (Dublin K. et al., Nature, 2016; Vetizou M. et al., Science 2015; Sivan A. et al., Science 2015) and we are applying our platform here as well.

The following chart summarizes our current product pipeline:

We have assembled a world class group of scientists, clinicians, directors and investors, who have established our leadership in the field of microbiome therapeutics. We were co-founded by Drs. Noubar Afeyan, David Berry and Geoffrey von Maltzahn of Flagship VentureLabs, the innovation foundry of Flagship Ventures, which has founded over 25 life sciences companies. Through Flagship VentureLabs' contribution of foundational scientific concepts and intellectual property, assembly of our management team and critical early-stage support, we launched as the first company focused on the ecological nature of the microbiome. Led by Dr. Roger Pomerantz, our Chairman, President and Chief Executive Officer, our experienced management team possesses core capabilities in microbiome therapeutics, infectious disease, drug development, commercialization, chemistry, manufacturing and controls, or CMC, public company management and finance. Dr. Pomerantz, an infectious disease physician-scientist, has extensive experience in infectious disease drug development and commercialization, licensing and acquisitions gained over a 10-year career in senior executive positions at Merck & Co, Johnson & Johnson and Tibotec Pharmaceuticals. Dr. Pomerantz led the development and commercialization of eight FDA-approved infectious disease drugs in his career. Collectively, our management team has successfully developed 18 approved pharmaceutical drugs in infectious disease and other indications. Our management team has extensive

experience in microbial ecology, microbiology and live biologicals, with over 25 years studying the microbiome and over 60 published papers on the science of the microbiome. Additionally, our team has extensive experience in building out commercial capabilities in specialty diseases and has a track record for success in launching vaccine products, which have analogous manufacturing processes to that of Ecobiotic microbiome therapeutics.

In January 2016 we entered into a Collaboration and License Agreement, or the License Agreement, with Nestec Ltd., or NHS, for the development and commercialization of certain of our product candidates in development for the treatment and management of CDI and IBD, including ulcerative colitis and Crohn's disease. The License Agreement will support the development of our portfolio of products for CDI and IBD in markets outside of the United States and Canada, or the Licensed Territory, and is expected to provide substantial financial support for our ongoing worldwide research and development. We have retained full commercial rights to our entire portfolio of product candidates with respect to the United States and Canada, where we plan to build our own commercial organization.

Under the License Agreement, we granted to NHS an exclusive, royalty-bearing license to develop and commercialize, in the Licensed Territory, certain products based on our microbiome technology that are being developed for the treatment of CDI and IBD, including SER-109, SER-262, SER-287 and SER-301, or, collectively, the NHS Collaboration Products. Upon mutual agreement, one or more other products based on our microbiome technology for CDI or IBD may be added to the License Agreement in lieu of or in addition to the then-existing NHS Collaboration Products. NHS' exclusive license in the Licensed Territory to develop and commercialize NHS Collaboration Products extends to any indications for which the parties agree to develop such products. We also granted to NHS a non-exclusive license to export, develop and make NHS Collaboration Products in the licensed fields worldwide solely for commercialization in the licensed fields and in the Licensed Territory. Additionally, the rights to develop and commercialize a given Collaboration Product in certain non-EU countries within the Licensed Territory may revert to us if NHS either elects not to pursue commercialization of such Collaboration Product in such country, or fails to meet certain agreed upon milestones for commercialization of such Collaboration Product in such country. If the licensed rights in any country revert to us in this way, then we would pay to NHS a royalty in the mid-single digits on net sales of such Collaboration Product in such country.

The License Agreement sets forth our and NHS' respective obligations for development, commercialization, regulatory and manufacturing and supply activities for the NHS Collaboration Products with respect to the licensed fields and the Licensed Territory. Under the License Agreement, our and NHS' development activities will be governed by global and regional development plans, including the conduct of additional clinical studies. We agreed to manufacture and supply NHS Collaboration Products to support development and commercialization of NHS Collaboration Products in the licensed fields and in the Licensed Territory. We also agreed to use diligent efforts to develop NHS Collaboration Products under a global development plan and to obtain approval for such NHS Collaboration Products in the European Union, or EU.

In exchange for the license, NHS is obligated to pay the Company an upfront cash payment of $120 million, which the Company received in February 2016. NHS has also agreed to pay the Company tiered royalties, at percentages ranging from the high single digits to high teens, of net sales of NHS Collaboration Products in the Licensed Territory. Additionally, NHS has agreed to pay the Company up to $660 million for the achievement of certain development and regulatory milestones and up to an aggregate of $1.125 billion for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products. We expect to receive a total of $30 million in milestone payments in 2016 associated with the planned initiation of a Phase 1b study for SER-262 in CDI and the anticipated initiation of the Phase 3 clinical trial for SER-109 in CDI.

For the development of NHS Collaboration Products for IBD under a global development plan, we are obligated to pay the costs of clinical trials of such products up to and including Phase 2 clinical trials, and 67% of the costs for Phase 3 and other clinical trials of such products, with NHS bearing the remaining 33% of such costs. For other clinical development of NHS Collaboration Products for IBD, we will pay the costs of such activities to support approval in the United States and Canada, and NHS will bear the cost of such activities to support approval of NHS Collaboration Products in the Licensed Territory.

With respect to development of NHS Collaboration Products for CDI under a global development plan, we agreed to pay all costs of an ongoing Phase 2 clinical trial for SER-109 and of Phase 3 clinical trials for SER-109. We agreed to bear all costs of conducting any Phase 1 or Phase 2 clinical trials under a global development plan for NHS Collaboration Products other than SER-109 for CDI. We agreed to pay 67% and NHS agreed to pay 33% of other costs of Phase 3 clinical trials conducted for NHS Collaboration Products other than SER-109 for CDI under a global development plan. For other clinical development of NHS Collaboration Products for CDI, we agreed to pay costs of such development activities to support approval in the United States and Canada, and NHS agreed to bear the cost of such activities to support approval of NHS Collaboration Products in the Licensed Territory.

The License Agreement continues in effect until terminated by either us or NHS on the following bases: (i) NHS may terminate the License Agreement in the event of serious safety issues related to any of the NHS Collaboration Products; (ii) we may terminate the License Agreement if NHS challenges the validity or enforceability of any of our licensed patents; and (iii) either we or NHS may terminate the License Agreement in the event of the other party's uncured material breach or insolvency. Upon termination of the License Agreement, all licenses granted to NHS by us will terminate, and all rights in and to the NHS Collaboration Products in the Licensed Territory will revert to us. If we commit a material breach of the License Agreement, NHS may elect not to terminate the License Agreement but instead apply specified adjustments to its payment obligations and other terms and conditions of the License Agreement.

The License Agreement contains customary representations and warranties, intellectual property protection provisions, certain indemnification rights in favor of each party and customary confidentiality provisions and limitations of liability.

Our Strategy

Our goal is to become the leading biopharmaceutical company developing and commercializing microbiome therapeutics to address significant unmet medical needs. The critical components of our strategy include:

- Rapidly advancing the development of our lead product candidate, SER-109, for the prevention of further recurrences of CDI in patients with recurrent CDI. SER-109 has been granted both Orphan Drug and Breakthrough Therapy designation by the FDA for the treatment of CDI. Breakthrough Therapy designation provides for intensive guidance from the FDA in an effort to expedite the drug development process. Based on the results from our recently completed Phase 1b/2 clinical study of SER-109, we dosed the first patient in a Phase 2 clinical study in May 2015 in patients with three or more occurrences of CDI within the previous nine months. We expect to enroll 87 patients in a double-blinded and placebo-controlled clinical trial, with patients randomized in a ratio of 2:1 into a SER-109 arm or placebo arm. The primary endpoint of the trial is the absence of CDI recurrence requiring antibiotic treatment during the eight-week follow-up period after dosing. We also plan to follow patients for an additional 16 weeks to document the safety profile of SER-109 compared to placebo. Secondary endpoints include the time to CDI recurrence and the proportion of patients experiencing CDI recurrence at four weeks, 12 weeks and 24 weeks. We also plan to compare changes in the composition of the colonic microbiome from baseline to Week 24 post-treatment using genomic analysis. In addition, subjects that recur in either arm of the study will have the option to enroll in a parallel open label safety study in which patients will receive SER-109. We expect results from the Phase 2 clinical study in the middle of 2016. Following the analysis of the data from our Phase 2 clinical study, we plan to meet with the FDA to present Phase 2 safety and efficacy results and a proposed protocol for the Phase 3 clinical trial. We plan to initiate the Phase 3 clinical trial in the second half of 2016.
- Advancing the clinical development of SER-262 to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI. We are developing SER-262 as a therapeutic to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI. SER-262 contains a subset of the bacterial ecology comprising SER-109, however, SER-262 is not derived from human stool and, in contrast, is made in bacterial fermenters in a rational in vitro design. Pre-clinical studies of SER-262 have demonstrated efficacy similar to SER-109 in mouse and hamster models of CDI. We intend to initiate clinical studies of SER-262 in the middle of 2016.
- Continued clinical development of SER-287 for the treatment of IBD, including ulcerative colitis. In December of 2015, we initiated a Phase 1b clinical trial evaluating SER 287 in patients with mild to moderate ulcerative colitis. The randomized, placebo-controlled multiple dose Phase 1b study of SER-287 is expected to enroll up to 55 subjects with active mild-to-moderate ulcerative colitis who are

failing current therapies. The primary endpoint of the study will evaluate the change in the microbiome resulting from SER-287 treatment. The study will also evaluate clinical response, mucosal healing, as well as metabolomic, immunological and safety findings. The clinical development of SER-287 to treat UC is supported by preclinical studies in multiple animal models of colitis that provide evidence that SER-287 administration results in reduced pathology. Published clinical reports furthermore suggest that modulation of the microbiome through repetitive fecal microbiota transplants may lead to meaningful clinical response in certain UC patients.

- Developing SER-155 for the treatment of antibiotic resistant bacteria. We are designing and developing SER-155, an Ecobiotic microbiome therapeutic candidate for the prevention of transplant-related mortality (due to infection and GvHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients.
- Leveraging our leading microbiome therapeutics platform to develop additional innovative and novel Ecobiotic microbiome therapeutics across a range of serious medical conditions with high unmet need including infectious disease, metabolic disease, inflammatory disease, rare genetic disease, and applications in immuno-oncology. We

believe that the combination of experience, proprietary data and proprietary know-how related to the microbiome and of the production of microbial strains provides us a competitive advantage in the design and development of microbiome therapeutics. Our platform enables us to build upon our existing and growing clinical experience to rationally approach the treatment of acute and complex chronic diseases. We intend to leverage this advantage to develop additional innovative Ecobiotic microbiome therapeutics.

- Commercializing our Ecobiotic microbiome therapeutics, including SER-109, directly in the United States and Canada and with collaborators outside of North America. In January 2016, we announced a strategic collaboration with Nestlé Health Science for microbiome-based Clostridium difficile and inflammatory bowel disease therapies in markets outside the United States and Canada. We have retained the worldwide rights for therapies developed outside of these indications. We believe the market for recurrent CDI is sufficiently concentrated to permit us to effectively commercialize SER-109 in the United States with a highly focused and specialized sales force of less than 100 individuals. We intend to leverage the experience gained by commercializing SER-109 in the United States to further build our direct sales force to address the larger patient population to be addressed by SER-262.
- Developing manufacturing capabilities sufficient to support commercialization of any approved Ecobiotic microbiome therapeutic candidates. If approved by the FDA, we believe SER-109 could be a first-in-field drug, which will require manufacturing capabilities that are distinct from other biologic drugs. We intend to make strategic investments in manufacturing capabilities to help ensure that we maintain control of our know-how and also because we believe these capabilities will be necessary and highly advantageous for the development of future Ecobiotic microbiome therapeutics such as SER-287 and SER-262. Our bioprocess and manufacturing personnel are focused on creating a platform of manufacturing expertise that will set the stage for further advances in the emerging field of microbiome therapeutics.

Understanding the Microbiome and Its Impact on Disease

The human microbiome is one of the richest and most diverse ecosystems on earth with a population of approximately 40 trillion microorganisms that live in our intestines, mouth, skin and elsewhere in the body. These microbiomes have numerous beneficial functions necessary to supporting health, such as digesting food, preventing disease-causing bacteria from invading the body, regulating our immune system and synthesizing essential nutrients and vitamins. Among the various microbiomes in the human body, the colonic microbiome is one of the most diverse microbial communities. At up to 100 billion to one trillion cells per milliliter, it is among the densest microbial ecosystems ever observed. In a healthy, symbiotic state the colonic microbiome enables the body to function normally. However, the colonic microbiome can change in composition, such as in response to long-term or high-dose exposure to antibiotics or following a gastrointestinal infection. As a result, there can be a loss of key microbes that results in a state of dysbiosis. Dysbiosis of the microbiome is associated with a wide range of disease and infections.

Although bacteria are often associated with infection and disease, much of the bacteria that colonize the human body are essential for life. Until recently, few scientific studies existed that focused on the benefits of the bacteria comprising the microbiome. In 2005, the National Institutes of Health funded the Human Microbiome Project, or HMP, which had as one of its goals the characterization of the microbiome with enough specificity to enable the study of variations in the microbiome and their influence on disease.

Historically, researchers studied microbes in patients by isolating pathogens and growing them in culture. This process typically identifies only a limited diversity of microbial species. The HMP used genomic sequencing technologies to analyze 5,000 samples, representing more than 3.5 terabases of genome sequence data, to identify specific genetic signals found only in bacteria. HMP researchers estimate that more than 5,000 unique microbial species occupy the human ecosystem, and these researchers believe they have characterized the normal range of microbial variation in the U.S. population. Importantly, HMP researchers have discovered that different consortia of microbes may accomplish the same metabolic activity, and the presence of those metabolic activities is more important than the exact species of

microbe providing the function. Results from the HMP have provided a robust baseline microbiome against which disease states can be compared.

Compared to the baseline data developed by the HMP, numerous scientific studies are emerging in both animals and humans, suggesting that many human diseases can be correlated with dysbiosis of the microbiome. These include infections, such as CDI or vancomycin-resistant Enterococcus, or VRE; metabolic disorders, such as early-stage, non-insulin dependent diabetes, obesity and non-alcoholic fatty liver disease; allergies; autoimmune disease; inflammatory diseases, such as ulcerative colitis, Crohn's disease and pouchitis, and immune-oncology related applications. Examples of some studies include:

- The results of a study published in PLOS Pathogens in 2012 suggested that a mixture of six different bacteria found naturally in the gastrointestinal system of mice, when isolated from stool and reintroduced into the infected mice, was effective at

suppressing CDI (Lawley et al., PLOS Pathogens, 2012). Researchers in the study found that a single treatment of the bacteria was sufficient and that the suppression lasted for months.

- A placebo-controlled, randomized, blinded clinical study published in Gastroenterology in 2015 showed that repetitive fecal microbiota transplant, or FMT, delivered via enema weekly for 6 weeks could induce clinical remissions in patients with active ulcerative colitis (Moayyedi et al., Gastroenterology, 2015) This study used an established measure of colonic mucosal healing to assess the efficacy of FMT compared to placebo, thus demonstrating the role of the microbiome in treating active ulcerative colitis.

- A placebo-controlled, randomized, blinded clinical study published in Gastroenterology in 2012 showed that administration of FMT derived from lean donors to obese subjects with metabolic syndrome could transiently increase insulin sensitivity (Vrieze et al, Gastro, 2012). This study furthermore identified changes in the microbiome of the small intestine that might have caused the effect.

- Two studies in mouse cancer models, both published in Science in 2015, demonstrated that the anti-tumor response to checkpoint inhibitors could be enhanced by altering the microbiome (Velizou et al., Science 2015; Slvan et al., Science 2015). In addition, a prospective study in melanoma patients receiving anti-CTLA4 therapy for their cancer was published in Nature in 2016 and showed that a difference in the microbiome prior to treatment of patients who suffer from anti-CTLA4 induced colitis compared to patients who do not experience colitis (Dubin et al., Nature, 2016). Taken together, these results suggest that microbiome therapies might improve the safety and efficacy of checkpoint inhibitors in immuno-oncology treatments.

- A study published in the Journal of Clinical Investigation in 2015 demonstrated that the microbiome of mice could be engineered to treat hyperammonemia, a clinical consequence of a set of rare genetic diseases known as Urea Cycle Disorders (Shen et al., JCI, 2015). In this preclinical model, gut microbes that lack a functional urease gene were able to alter ammonia balance in the blood, suggesting a new route to novel therapeutics.

There are currently no microbiome therapeutics approved by the FDA. We believe that the ability to develop drugs that are able to modulate the microbiome and return a dysbiotic microbiome to its healthy state presents a significant opportunity to improve human health.

Our Microbiome Therapeutics Platform

We are developing a new approach to restoring health in settings of microbiome dysbiosis by using our microbiome therapeutics platform to develop Ecobiotic microbiome therapeutics. Our microbiome therapeutics platform is premised on the hypothesis that the proximal cause or significant contributor to multifactorial diseases is a dysbiosis of the colonic microbiome. We believe this represents a paradigm shift in approaching the way the underlying disease is defined and can be treated. Our microbiome therapeutics are a novel class of biological drugs designed to treat disease by restoring a dysbiotic microbiome to a state of health. They represent rationally defined ecological compositions, consisting of discrete combinations of beneficial microorganisms with targeted functional properties

that provide the ability to re-establish keystone features of a functional microbiome in settings of disease.

Our microbiome therapeutics platform integrates genomic and related data sets, proprietary algorithms and computational analysis, sequencing and screening and clinical insights. This platform allows us to rationally design, test, optimize, formulate and manufacture Ecobiotic microbiome therapeutics. Our microbiome therapeutics platform provides a framework that we believe can significantly reduce the time typically required to advance therapeutics to the clinic. The following diagram depicts the steps in our fully end-to-end microbiome therapeutics platform:

Clinical Trials and Cohort Studies

Our discovery process begins with human data derived from clinical trials and cohort studies, which we use as a basis for designing our Ecobiotic microbiome therapeutics. This allows us to compare the colonic microbiome of healthy normal individuals to those in a dysbiotic state, revealing the ecological and functional signatures of microbiome differences that we target using our Ecobiotic microbiome therapeutics. Additionally, our experience with SER-109 serves as a critical dataset for humans, instructing us on how the introduction of certain keystone microbes can facilitate and augment the restoration of a dysbiotic colonic microbiome for other indications. Using these proprietary insights and tools we can evaluate emerging data sets that link a change in the microbiome

with various diseases and define therapeutic lead candidates.. By using our genomic data sets and our proprietary tools combined with our experience with SER-109, we integrate clinical results into bench research to design our Ecobiotic microbiome therapeutics.

Ecobiotic Candidate Design

We have developed a candidate design program to assist us in identifying the keystone structural and functional elements of healthy microbiomes, the deficiencies present in disease states and the functional profile of a microbial ecological network that can return the microbiome to a healthy state. The following diagram depicts the steps in our candidate design program:

Our candidate design program applies computational comparative genomics and systems biology methods to analyze existing clinical data sets, such as those derived from the SER-109 Phase 1b/2 clinical study, to elucidate the structure and function of a healthy microbiome relative to a microbiome in a disease state. The structure is defined in terms of the organisms that comprise the ecology of the microbiome while the function is defined in terms of the genes and metabolic pathways inherent to the organisms that comprise that ecology. Structure and functional properties of a microbiome are determined using our proprietary algorithms that derive actual ecological networks that characterize the microbiome of subjects with a particular disease or that are in a state of health. Our algorithms define those organisms that impact the structure of the microbial communities and the health of the microbiome, which we refer to as keystone organisms, and their associated critical, functional biological pathways. Keystone organisms and their associated critical, functional biological pathways may exist in low, moderate, or high abundance in an ecology of microbes, but are often missing or at reduced levels in an individual with disease. By comparing the ecologies in healthy and disease states, we are able to identify the ecological deficiencies and missing keystone components that characterize the disease state and are the target of our Ecobiotic microbiome therapeutics.

Ecobiotic microbiome therapeutics are rationally designed to solve for the microbiome ecological deficiencies identified between disease and health states. Rational design involves the determination, prioritization and optimization of microbial network ecologies with the greatest therapeutic potential based on critical factors, such as the evolutionary relationships of the microbes, theoretical and empirically defined functional capabilities, safety profile of strains and various bioprocessing parameters. We maintain a proprietary design and discovery database that captures and integrates key information about microbial strains. Our design algorithms in combination with our functional screening capabilities enable us to identify lead candidate compositions that possess the necessary functional profile to restore the ecological deficiency that causes the dysbiosis.

Strain Library Screening and Lead Optimization and Ecobiotic Candidate Nomination

To facilitate the screening of network ecologies and individual strains, we have developed and maintain proprietary know-how on the isolation, cultivation and fermentation of microbial strains. Our proprietary library comprises over 13,000 strains isolated from healthy donors. Using information from our strain library, we develop and execute moderate- to high-throughput in vitro and ex vivo screens that evaluate the efficacy and functional properties of candidates and individual microbial strains that comprise the lead candidate ecologies. Once we have a lead candidate we optimize its efficacy and functional properties by screening variants in disease relevant models, including in vivo models on a reduced set of candidates that are relevant to the disease indications we are investigating. The final candidate that meets our predefined criteria is nominated for clinical development.

Bioprocess and Formulation

Our Ecobiotic microbiome therapeutics in development consist of combinations of bacteria or bacterial spores rather than single strains. As a result, we must be able to produce, purify and formulate multiple strains of bacteria economically and be able to test the composition of a combination product for quality control. Our bioprocess development and manufacturing processes are designed to address each of these elements.

- Fermentation: We employ platform fermentation processes as starting conditions for current good manufacturing processes, or cGMP, production schemes and, when required, develop strain specific process parameters.

- Purification: Similar to fermentation, we use small-scale purification operations to complete bench-scale manufacturing and quickly assess the final process yield, quality and robustness.
- Formulation: Our Ecobiotic microbiome therapeutics are combinations of cells and bacterial spores and can be administered by a number of methods and by different routes to effect the primary goal of delivering the bacteria to the intended location in a condition where they are able to replicate and correct dysbiosis. Currently, our Ecobiotic microbiome therapeutics are designed to be administered in oral form.
- Analytical: We address quality control requirements for our Ecobiotic microbiome therapeutics using proprietary microbiological and sequence-based testing schemes, including high-throughput quantitative analytics to assess the identity, potency and purity of the final product.

Pre-clinical and Clinical Testing

One of the key competitive advantages of microbiome therapeutics is that we believe they will not need to undergo the same pre-clinical testing that other modalities such as small molecules require. Because the components of our Ecobiotic microbiome therapeutics are found naturally in the body, we do not expect to need carcinogenicity studies or studies designed to evaluate how our Ecobiotic microbiome therapeutics interact with other drugs. Further, we expect that we will not need to conduct traditional Phase 1 pharmacokinetic studies. Clinical pharmacokinetic studies are performed to examine the absorption, distribution, metabolism and excretion of a drug under investigation. Because our Ecobiotic microbiome therapeutics are not absorbed and, therefore, remain in the colonic microbiome, we believe such trials will not be necessary and we expect to proceed directly to patients with the disease that we are studying. These pre-clinical and clinical studies are costly and time- consuming and the ability to proceed in development without them provides an advantage as compared to traditional drug development. For example, based on our correspondence with the FDA, further pre-clinical studies will not be needed for SER-109. In addition, we have confirmed with the FDA that we do not need Phase 2 dose ranging studies for SER-109. We were also not required to perform pre-clinical toxicology studies on SER-287, our investigational product for ulcerative colitis, and we have received written feedback from FDA that traditional pre-clinical toxicology will not be required for SER-262, our Ecobiotic drug candidate for primary CDI. We believe many of the same requirements may apply across our future product candidates.

Our Product Pipeline

We believe our Ecobiotic microbiome therapeutics represent a novel approach with potential application across a broad range of human diseases. Our most advanced drug development program, SER-109, focuses on recurrent CDI. SER-109 is in a Phase 2 study in the U.S. and has been designated as a Breakthrough Therapy and an Orphan Drug by FDA. SER-262 is an Ecobiotic drug candidate under development for treatment of dysbiosis following primary CDI, in order to prevent recurrence, and we expect to initiate a Phase 1b study in mid-2016. SER-287 is under development for the treatment of active mild-to-moderate ulcerative colitis and we commenced a Phase 1b study in the fourth quarter of 2015. We are designing and developing SER-155, an Ecobiotic microbiome therapeutic candidate for the prevention of transplant-related mortality (due to infection and GvHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients; for the treatment of metabolic disorders such as non-alcoholic fatty liver disease and early-stage and non-insulin dependent diabetes; for inflammatory conditions such as Crohn’s disease; for enhancing the safety and efficacy of immuno-oncology agents including checkpoint inhibitors used in cancer treatment; and for treating rare genetic disorders such as urea cycle disorders.

The following chart summarizes our current product pipeline:

Our CDI Product Candidates

We are developing SER-109 as an Ecobiotic microbiome therapeutic designed to prevent further recurrences of CDI in patients suffering from recurrent CDI, defined as at least three occurrences of CDI in a nine-month period, by restoring the dysbiotic microbiome to a healthy state. In our Phase 1b/2 clinical study, 26 of 30 patients, or 87% of patients, achieved the primary efficacy endpoint of experiencing no diarrhea associated with a positive C. difficile test during the eight weeks post-treatment. Additionally, 29 of 30 patients, or 97% of patients, achieved a clinical cure, which we defined as the absence of CDI requiring antibiotic treatment during the eight- week period after SER-109 dosing. The results of the trial suggest a favorable safety profile with no serious adverse events considered by the investigators to be attributable to SER-109. We also performed an analysis of the microbiome using next-generation sequencing technology and microbiological analysis. These studies demonstrated a re-establishment of keystone organisms and a rapid increase in bacterial diversity, which enable the restoration of the microbiome towards a healthy state. SER-109 has been granted Orphan Drug and Breakthrough Therapy designation by the FDA. We initiated a Phase 2 clinical study of SER-109 for recurrent CDI and dosed the first patient in May 2015. We expect initial study results in the middle of 2016. We have conducted manufacturing process pre- validation studies of SER-109 to support a Phase 3 clinical trial and a potential biologics license application and commercial launch.

We are also developing SER-262 to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI. Pre-clinical studies of SER-262 have demonstrated efficacy similar to SER-109 in mouse models of CDI. We intend to initiate clinical studies of SER-262 in the middle of 2016.

If approved, we believe these two product candidates will enable us to provide a more effective and safer treatment for preventing the recurrence of CDI than the current standard of care.

Clostridium difficile Infection, or CDI

C. difficile is a Gram-positive, toxin-producing, spore forming bacterium that causes severe and persistent diarrhea in infected individuals, but can also lead to more severe outcomes, such as pseudomembraneous colitis, toxic megacolon and death. C. difficile bacteria express toxins that disrupt the structural architecture of cells causing leakage of fluids through the gastrointestinal epithelium. The cells disrupted by these toxins eventually undergo apoptosis and die, releasing their contents into the colon, resulting in inflammation of the colon, severe and persistent diarrhea and, in the most serious cases, death.

CDI is generally not present in healthy adults, although approximately 1% to 5% of adults may carry low levels of C. difficile without clinical symptoms. CDI is most often associated with the prior use of antibiotics, although age and poor immune status are

important risk factors as well. Antibiotics are thought to decrease resistance to CDI by causing dysbiosis in the microbiome. Since C. difficile spores are able to survive for long periods of time outside the body, and because healthcare settings are often sites of significant antibiotic use, CDI transmission rates in hospitals, long-term acute care facilities and nursing homes have been increasing. CDI is also a cause of morbidity and mortality among hospitalized cancer patients and bone marrow transplant patients as their immune systems are suppressed by cytotoxic drugs, which are drugs that inhibit or prevent the function of cells, and they may be heavily treated with antibiotics to prevent or treat infections. More recently, the rise of community-acquired CDI has been recognized as a growing problem.

The CDC has identified C. difficile as one of the top three most urgent antibiotic-resistant bacterial threats in the United States. It is the most common cause of hospital acquired infection in the United States, having overtaken MRSA. CDI is responsible for the deaths of approximately 29,000 Americans each year. CDI is also very costly to the healthcare system. According to a study published in Clinical Infectious Diseases, the economic burden of CDI in 2008 in U.S. acute care facilities alone was estimated to be as much as $4.8 billion. In addition, a summary of studies published in 2009 in The Journal of Hospital Infection, calculated that the treatment cost per episode of primary CDI was as much as $5,000 and as much as $18,000 per recurrence of CDI (Ghantoji et al., 2010).

The CDC estimates the incidence of primary CDI by focusing on 10 catchment areas covering 11 million residents. Based on this analysis, it is estimated that there are approximately 453,000 new cases of primary CDI per year. Further, according to a 2014 article in the American Journal of Infection Control, from 2001 to 2010, incidence of CDI per 1,000 patients discharged increased from 4.5 to 8.2 with an average hospital stay of eight days. We believe the CDC method underestimates incidence based on several factors. First, residents who are diagnosed outside of their catchment area are not included in estimates. Second, many of the CDC diagnostic labs use a lower sensitivity test, which results in about 20% lower detection rates than the current most sensitive method. In addition, the CDC approach misses community cases, which are estimated to account for 30% to 40% of total cases. As a result, we estimate the incidence of primary CDI in the United States is between 640,000 and 820,000 patients per year. Additional research suggests that the risk of recurrence is approximately 25% after primary CDI, 40% after a first recurrence and greater than 60% for those experiencing two or more recurrences. In addition, in a recent randomized trial comparing two antibiotics for primary CDI, 8% of patients receiving fidaxomicin and 9% of patients receiving vancomycin did not respond after completing their antibiotic regimen. We estimate that the addressable population of patients in the United States with recurrent CDI, defined as patients who have experienced at least three occurrences of CDI in the past nine months, is between 85,000 and 110,000 patients per year.

The European Hospital and Healthcare Federation, or HOPE, estimates that there are approximately 172,000 cases of CDI per year in the EU. In 2013, CDI was estimated to occur in one in 435 admissions per hospital. Based on a 2010 report from HOPE and other studies on the incidence of CDI in the EU, we estimate that the annual incidence rate of CDI in the EU is 4.1 per 10,000 individuals.

Current and developing treatment alternatives and their limitations

Patients with CDI utilize antibiotics, fecal microbiota transplantation FMT, and unapproved over-the-counter probiotics. Several therapeutic antibodies and vaccines are also being developed.

Antibiotics

The current standard of care for CDI is to treat with antibiotics, such as metronidazole and vancomycin. Metronidazole has been found to be effective for primary CDI, but approximately 29% of patients experience

recurrence. It is not recommended for severe disease, nor is it used beyond first recurrence due to lack of efficacy. Vancomycin is more expensive, with a reported relapse rate of 25%. In addition, fidaxomicin, an approved antibiotic for CDI, may have higher initial efficacy compared to metronidazole, but it does not have a label claim to reduce or prevent CDI recurrence. No antibiotic therapeutics are currently approved for treatment of recurrence of CDI.

Recurrent CDI, defined as three or more occurrences of CDI in a nine-month period, is not well addressed by any of the available antibiotics. When a patient has recurred two or more times after the initial occurrence, antibiotic relapse rates are greater than 60% and the probability of additional relapse increases with successive cycles. Some physicians resort to pulse-taper regimens of vancomycin lasting six weeks or more, but there are no well-controlled clinical studies that show such regimens are effective. In extreme cases, patients are treated continuously for years with vancomycin, even while they continue to experience gastrointestinal symptoms including diarrhea and abdominal discomfort.

The primary limitation of antibiotics is that their use appears to exacerbate dysbiosis. Recent research in animal models has shown that antibiotic use not only eliminates many healthy bacteria in the gastrointestinal tract, but also leads to the release of nutrients that facilitate the growth of C. difficile. Antibiotics have also been shown to change the ratio of primary versus secondary

bile acids in the colon by killing bacteria required to metabolize bile acids. This shift to a predominance of primary bile acids further facilitates the growth of C. difficile, as it requires primary bile acids for germination of its spores. As a result, antibiotic use may induce a lasting dysbiosis that makes it possible for C. difficile to colonize a person and then cause, or further perpetuate, disease.

Fecal microbiota transplantation

FMT, also known as a stool transplantation, is a procedure during which donated stool, including fecal microbes, is typically instilled via colonoscopy into a patient with CDI. We believe that the efficacy of FMT, which has resulted in cure rates for recurrent CDI of 81% in a randomized controlled study reported in 2013 in the New England Journal of Medicine, essentially confirms the role of dysbiosis as a cause of CDI recurrence. However, FMT presents several challenges for effective treatment of the disease. FMT has the potential to transmit infectious or allergenic agents between hosts, involves the transmission of potentially hundreds of unknown strains of bacteria, fungi and viruses from donor to subject, and is difficult to perform on a mass scale. Additionally, FMT is inherently non-standardized so that different desired and/or undesired material may be transmitted in any given donation. FMT is not approved by the FDA and we believe it may be unable to gain such approval since the product, to our knowledge, cannot be standardized and characterized according to current regulatory requirements for identity, potency, purity and safety.

Probiotic therapies

Probiotics represent a group of products typically available over the counter in supplements and in some foods, which contain a small number of species of bacteria. However, to date there have been no clinical studies that have established the ability of probiotics to repair a dysbiosis of the microbiome. Further, there is neither a legally recognized definition of, nor a standard of identity for, the term probiotic in the United States or Europe. Recently, the European Food Safety Authority rejected many of the claims of health benefits associated with probiotics because the microbes had not been sufficiently characterized, the claimed effect was not considered beneficial and human studies in support of the claims had not been made available. As a result, after December 14, 2012, food and nutritional supplements companies were no longer allowed to communicate health benefits for their products on account of probiotic content in the EU.

Antibodies and vaccines

Antibodies and vaccines are also in development to treat CDI. Antibodies suppress toxins to alleviate the symptoms of CDI, but they do not address the underlying dysbiosis of the microbiome, which we believe is the cause of recurrent CDI. Antibodies also require intravenous infusion and are more costly to produce relative to other treatments, such as antibiotics. The efficacy of vaccines in treating CDI in humans currently remains unproven. In addition, it is difficult to define a target population for a CDI vaccine, given that the at-risk patient population is largely elderly individuals who typically respond less robustly to vaccination therapies.

SER-109

SER-109 is a bacterial spore ecology consisting of an average of approximately 50 bacterial species derived from healthy donors' fecal matter that is designed to prevent further recurrences of CDI in patients suffering from recurrent CDI by restoring a dysbiotic microbiome to a state of health. In our open label Phase 1b/2 clinical study of SER-109, we evaluated the effect of treatment with SER-109 in patients with three or more occurrences of CDI in a 12-month period. Of the 30 patients enrolled in the trial, 29, or 97%, achieved a clinical cure, which we defined as the absence of CDI requiring antibiotic treatment during the eight-week period after SER-109 dosing. In the trial SER-109 was

well- tolerated and had a favorable safety profile with no serious adverse events considered by the investigators to be attributable to the SER-109 treatment. We also performed an analysis of the microbiome using next-generation sequencing technology and microbiological analysis. These studies demonstrated a re-establishment of keystone organisms and a rapid increase in bacterial diversity, which enable the restoration of the microbiome to a healthy state.

SER-109 is formulated as oral capsules for single-dose administration after completion of antibiotics. A single dose of SER-109 comprises 100 million spores that are delivered in four small oral capsules. The spores in SER-109 are intended to germinate in the gastrointestinal tract and immediately compete for the same nutrients required by C. difficile. The spore forming organisms from SER-109 are also intended to shift the balance of bile acids toward secondary acids that are less efficient for promoting germination of C. difficile spores. The following picture is a commercial prototype of a single dose of SER-109:

Phase 1b/2 clinical study design

The Phase 1b/2 clinical study was a two part trial designed to evaluate the safety and efficacy of SER-109 in 30 patients with recurrent CDI, defined as three or more occurrences of CDI in the previous 12 months.

Part 1 of the study evaluated a single dose of SER-109 administered orally in 30 capsules over two days, with the dose derived from approximately 75 grams of stool. Part 2 of the study evaluated a single dose of SER-109 administered orally in a range of one to 12 capsules over one day. The dose in Part 2 was based on spore count, as opposed to fecal mass, which is expected to allow for a more precise dosing regimen. The target dose in Part 2 was $1x10^8$ spores per dose, which was approximately 17-fold lower than the mean dose in Part 1. The SER-109 doses were derived from seven different healthy human donors. Prior to receiving treatment with SER-109, patients were on antibiotic therapy consisting of either fidaxomicin, vancomycin or metronidazole. At least 24 hours prior to starting treatment with SER-109, antibiotic therapy was discontinued.

The trial was designed to enroll patients between the ages of 18 and 90 years, with relapsed, laboratory-confirmed CDI with three or more occurrences in the previous 12 months. Enrolled patients must have undergone treatment for CDI with at least three courses of antibiotic therapy in the last 12 months and have a life expectancy of greater than three months. Patients with acute leukemia, recent bone marrow transplant or recent chemotherapy, as well as patients with a history of IBD or IBS with diarrhea, total colectomy or liver cirrhosis were excluded from the trial. The following table identifies patient demographics following enrollment in the trial:

Cohort	Mean Dose (spore units)	Male/Female	Age Median (Range)	Number of CDI Recurrences in Prior 12 months Median (Range)
1	$1.7x10^9$	5 / 10	71 years (22 – 88)	3 (2 – 6)
2	$1.0x10^8$	5 / 10	58 years (39 – 83)	3 (2 – 5)

The primary safety measures were an evaluation of adverse events, laboratory values, vital signs and physical examination of findings prior to and after dosing with SER-109 over a 24-week time period. Evaluations occurred by telephone calls, in-home assessments or clinic visits by qualified personnel. Patients were assessed at Days 2 and 4 and Weeks 1, 2, 4, 8 and 24 post-treatment. The primary efficacy measure was the absence of CDI (defined in this study as more than three unformed bowel movements in a 24-hour period with laboratory confirmation of the presence

of C. difficile toxin in the stool) during the eight weeks after initiating therapy. Eight weeks was selected as the measurement period for the primary endpoint based on our clinical advisory board's experience that a significant majority of CDI recurrences occur within eight weeks. Secondary efficacy measures included minimum effective dose, time to CDI recurrence following SER-109, time without diarrhea during the follow-up period and change in diversity

of the colonic microbiome at Day 4 and Weeks 1, 2, 4 and 8 as measured by deep sequencing of patient stool samples. Stool samples were collected pre- treatment and on Day 4 and Weeks 1, 2, 4, 8 and 24 post-treatment.

Phase 1b/2 clinical study results

Efficacy. Twenty-six of 30 patients, or 87% of patients, in the Phase 1b/2 clinical study achieved the primary efficacy endpoint of experiencing no recurrence of CDI during the eight weeks post- treatment. These 26 patients consisted of 13 patients in each of Part 1 and Part 2 of the study. Among the 26 patients was one patient who experienced an initial recurrence on Day 26 and was re-treated, per protocol, with a dose from the same donor. Following re-treatment, this patient also achieved the primary efficacy endpoint. Efficacy results were not dependent upon the initial human donor or the dose over the range of $3.4x10^7$ to $2.3x10^{10}$ spores.

Of those patients who did not meet the primary efficacy endpoint, one patient had a recurrence of CDI on Day 5 and did not receive a second treatment with SER-109. The three other patients who failed the protocol-defined primary efficacy endpoint were determined by their attending investigator to be recovering from their diarrheal episode by the time they submitted their stool sample for CDI testing. In each case, the investigator advised the patient to refrain from antibiotic use and the patients' condition resolved without antibiotic therapy. All three patients were determined to be clinically CDI free at eight weeks. As a result, the clinical cure rate for the study, which we defined as the absence of CDI requiring antibiotic treatment during the eight-week period after SER-109 dosing, was 97%, or 29 of 30 patients.

We also tested a total of 27 patients at Week 8 for C. difficile carriage, where a patient carries the C. difficile bacterium but does not experience symptoms related to C. difficile. Of the 27 patients tested, 24 patients, or 89% of patients, tested negative for C. difficile carriage. Among the three patients who were not tested for C. difficile carriage, one patient did not continue with the study to Week 8 and samples were not collected for two patients at Week 8. In addition, 22 patients continued to participate in the Phase 1b/2 clinical study and did not receive additional antibiotics. Of these patients, 20, or 91% of patients, experienced no recurrence of CDI 24 weeks after treatment.

The results of the SER-109 Phase1b/2 clinical study were published in the Journal of Infectious Diseases (Khanna et al., A Novel Microbiome Therapeutic Increases Gut Microbial Diversity and Prevents Recurrent Clostridium difficile Infection, Journal of Infectious Disease) in February 2016.

We also performed an analysis of the microbiome using next-generation sequencing technology and microbiological analysis to evaluate long-term changes in the microbiome, including the restoration of bacterial diversity in the colon of patients. These studies demonstrated a rapid increase in bacterial diversity and a restructuring of the microbiome towards a healthy state. Upon introduction, SER-109 appears to engraft its bacterial species into the microbiome, with some of these species persisting in the patient's gastrointestinal tract for at least 24 weeks after dosing. In addition, in some patients we noted the repopulation of organisms that were not in SER-109 and had not been detected in the patient prior to treatment. We believe this phenomenon, which we refer to as augmentation, is an important element for restoration of bacterial diversity and repair of dysbiosis. Engraftment and augmentation, as well as the clinical resolution of CDI, were not dependent on the dose of SER-109 administered.

We believe the engraftment and augmentation observed with SER-109 could have important medical implications for treating other infectious agents. For example, in the Phase 1b/2 clinical study, we observed that some patients were not only infected with C. difficile, but were also colonized with other harmful organisms at high levels. Importantly, after SER-109 treatment, levels of these organisms declined by as much as 100,000-fold. For example, we identified multiple patients in the trial with high levels of VRE, which are drug-resistant bacteria that colonize the

gastrointestinal tract and can cause serious bloodstream infections. In patients identified with VRE, the VRE was reduced below the limit of detection of our assays after treatment.

Safety. In Part 1 of the study, 80% of the patients experienced at least one adverse event, all of which were treatment emergent adverse events, or TEAEs. A TEAE was defined as an adverse event that started or worsened at or during the time of or after the date of the first dose of SER-109 through the final follow-up visit. Five, or 33%, of the patients were judged by the investigator to have a TEAE attributable to SER-109 and all were mild or moderate. In Part 2, 100% of the patients experienced at least one adverse event, all of which were TEAEs. Nine, or 60%, of the patients were judged by the investigator to have a TEAE attributable to SER-109 and all were mild or moderate. The most common adverse events were gastrointestinal disorders and diarrhea. The majority of TEAEs were mild in severity and consistent with post-antibiotic recovery from CDI. One patient in Part 2 had a severe adverse event of chest pain, which was not considered related to SER-109. Two patients each in Part 1 and Part 2 had more than one serious adverse event, none of which was considered related to SER-109. There were no deaths in Part 1 or Part 2.

Clinical development plan

In May 2015, we initiated a SER-109 Phase 2 clinical study. We expect initial clinical study results in the middle of 2016. Following the analysis of the data to come from our Phase 2 clinical study, we plan to meet with the FDA to present Phase 2 safety and efficacy results and a proposed protocol for the Phase 3 clinical trial. We are conducting pre-validation studies of our manufacturing process for SER-109, and we expect to obtain sufficient data from these studies for a Phase 3 clinical trial. We plan to initiate the Phase 3 clinical trial in the second half of 2016.

The FDA has indicated that we do not need to conduct further pre-clinical studies of SER-109. We believe this conclusion is the result of several factors, including the following:

- gastrointestinal bacteria are host-specific and animal data would not be more representative than our human clinical data;
- SER-109's favorable safety profile in patients in the Phase 1b/2 clinical study;
- ecobiotic microbiome therapeutics are unlikely to result in systemic exposure because they are not absorbed outside of the gastrointestinal tract;
- engraftment of spores is not dependent on dose based on the range of doses evaluated in our Phase 1b/2 study; and
- SER-109 comprises spores from microbes found in a healthy human gastrointestinal tract. Taken together, we believe these parameters allow for rapid and inexpensive development relative to typical drug discovery and development.

Phase 2 clinical study design

The Phase 2 clinical study is a randomized, double-blinded, placebo-controlled, parallel-group trial with two treatment arms enrolling a total of 87 patients. We plan to enroll eligible patients at approximately 36 sites in the United States. Patients will be randomized 2:1 to receive either a single oral dose of SER-109 in four capsules or a matching placebo in four capsules. Based on the assumptions we have made for the recurrence rate of CDI and assuming we conduct final analyses for a minimum of 78 patients, our Phase 2 clinical study is sufficiently large, with the power of the study over 90%, to demonstrate that SER-109 is superior to placebo. The SER-109 formulation of the inner capsule has been refined to enable production to meet commercial requirements. We believe that the manufacturing and formulation changes have resulted in a more pure form of SER-109 that is comparable in potency to that used in the Phase 1b/2 clinical study based on a pre-clinical mouse C. difficile model.

The Phase 2 clinical study is designed to enroll patients 18 years or older with a documented history of three or more occurrences of CDI in the previous nine months, as compared to 12 months in our Phase 1b/2 clinical study. Additionally, enrolled patients must have been clinically responsive to ten to 21 days of standard of care antibiotics and show no evidence of diarrhea for two or more consecutive days prior to randomization. In contrast, enrolled patients in our Phase 1b/2 clinical study were permitted to be on long-term antibiotic therapy. Inclusion and exclusion criteria for the Phase 2 clinical study are generally similar to our Phase 1b/2 clinical study, but are more restricted in some patient populations. For example, the criteria exclude patients on steroids (≥ 20 mg/d) or on maintenance immunotherapy and those with a history of untreated celiac disease or gluten enteropathy. However, the inclusion and exclusion criteria for the Phase 2 clinical study is less restrictive in other patient populations. For example, the criteria exclude patients with IBS or IBD only if active within the past 24 months, as compared to patients with any history of these diseases in our Phase 1b/2 clinical study, and patients with an absolute neutrophil count, or ANC, less than 500/mm3, as compared to patients with an ANC less than 1000/mm3 in the Phase 1b/2 clinical study.

The primary efficacy objective in the Phase 2 clinical study will be to demonstrate the superiority of SER-109 compared to placebo in the prevention of recurrent CDI in adult patients up to eight weeks after treatment. In this

study, an episode of recurrent CDI will be defined as three or more unformed stools per day over two days with a positive C. difficile stool test and requiring antibiotic treatment. By comparison, our Phase 1b/2 clinical study defined an episode of recurrent CDI as three unformed stools over one day with a positive C. difficile stool test and did not require antibiotic treatment. The decision to treat with antibiotics will be based on the physician's clinical assessment of the patient in accordance with the guidelines set forth in our Phase 2 clinical study protocol. The primary safety objective will be to evaluate the safety of SER-109 in these patients up to 24 weeks after treatment as determined by clinical and laboratory safety assessments. During the follow-up period (Weeks 9-12), patients will be contacted by phone weekly and asked about adverse events and diarrheal symptoms. If diarrheal symptoms meeting the definition of recurrent CDI occur during the follow-up period, patients will be asked to return to the clinic for a clinical evaluation and a C. difficile test. In addition, patients will return to the clinic at Week 12 for safety evaluations. Following the Week 12 visit, patients will be contacted by phone at Weeks 16, 20 and 24 and asked about adverse events and diarrheal symptoms.

We also plan to evaluate secondary objectives including the time to CDI recurrence, if any, in patients who receive SER-109 compared to those who receive placebo, and the proportion of patients experiencing clinical CDI recurrence up to four, 12 and 24 weeks post-treatment in patients who receive SER-109 compared to placebo. In addition, exploratory objectives include comparing the changes in the composition of the gastrointestinal microbiome from baseline to 24 weeks post- treatment using metagenomic analysis and measuring quality of life and health outcomes up to 24 weeks post-treatment.

After all enrolled patients complete the Phase 2 clinical study, which will occur following dosing of each patient, or have discontinued before that time point, an analysis of the efficacy and safety endpoints will be performed. Following the analysis of this data, we plan to meet with the FDA to present Phase 2 safety and efficacy results and a proposed protocol for the Phase 3 clinical trial. We plan to initiate the Phase 3 clinical trial in the second half of 2016.

Open label extension study. Patients in either arm of the Phase 2 clinical study who relapse and experience an episode of recurrent CDI within eight weeks of treatment will be permitted to enroll in an open label extension study in which they will receive a single dose of SER-109. Participation in the open label extension will be conditioned upon the patient's continued satisfaction of the inclusion and exclusion criteria. We believe that providing the open label extension will assist in facilitating enrollment in the Phase 2 clinical study by providing participants the opportunity to ultimately receive SER-109 if they are initially enrolled in the placebo group. In addition, we believe the open label study will provide additional safety data and may provide us with greater understanding of the impact of a second dose of SER-109.

Manufacturing

SER-109 is a purified ecology of spores produced through a process of extraction from a natural human stool source, obtained from qualified, highly screened donors. The donor raw material is collected in a controlled setting, under a protocol that ensures that donors meet qualification criteria.

Donors are required to be in good health, and to possess a medical history and a lifestyle that minimizes the risk of exposure to and transmission of an infectious disease. Donors are tested for infectious agents and screened for gastrointestinal and other health factors. After initial qualification, the donor is eligible to donate for a defined period of time. Donors are monitored for health status changes during the donation period. At the end of the donation period, the qualification assessment is repeated to help ensure the donor has maintained their health status. After successful completion of an exit screening the donations are released from quarantine for use in manufacturing.

We initially process the donor material in our Kendall Square, Cambridge manufacturing facility, and then transfer the process intermediate to a Contract Manufacturing Organization, or CMO, to isolate and concentrate SER-109 for finishing to the oral capsule dosage form. The purified, concentrated Drug Substance is tested for identity, potency and purity, and subsequently formulated into Drug Product where it is again tested for identity, potency, and purity. The final Drug Product dosage form is four hard capsules for oral administration. Steps are specifically built into the process to remove and kill non-spore microbes. We have conducted validation studies demonstrating the ability of the process to inactivate and clear hypothetical extraneous pathogens of concern, and we believe we have sufficient data from these studies to support a Phase 3 clinical trial.

Raw materials, intermediates, drug substance and drug product are tested using cGMP assays developed with our know-how to assess the key quality attributes of identity, potency and purity of the natural product. Identity testing has been developed to assure the presence of specific live spore forms in the product. Potency assays assure the dose of spores, and assess stability of the spores and the product form during storage. Proprietary microbiological purity

assays have been developed to enable testing for microbial contaminants in the presence of the live spore product.

Once ingested, a single dose of SER-109 spores administered to a patient multiply rapidly within the gastrointestinal tract. Therefore, the dosage required to treat a patient is modest. As a result, we believe we can address market demand with a relatively small- scale manufacturing process. Additionally, the need for donors to address anticipated market supply is also modest. If approved, we anticipate that we will be able to produce a sufficient commercial supply of SER- 109 to meet estimated demand in the U.S. using donations from fewer than 20 human donors.

SER-262

We are developing SER-262, which is a synthetic fermented, multi-strain Ecobiotic microbiome therapeutic intended to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI. We are designing SER-262 to increase and improve diversity in the colonic microbiome after antibiotics following CDI. The results of our Phase 1b/2 clinical study of SER-109 provided multiple insights that employed in designing the spore ecology used in SER-262, which consists of a subset of bacteria found

in SER-109. Pre-clinical studies of SER-262 have demonstrated that it is comparable in efficacy to SER-109 in the mouse model of CDI..

As part of our selection of SER-262 we screened multiple candidates for efficacy in animal models using SER-109 as a reference compound. SER-262 provided significant protection against CDI with reduced mortality, minimum weight loss and clinical score measures of efficacy. Strains in SER-262 have met initial bioprocess specifications for spore titer and yield, and each organism has been characterized by whole genome sequencing and a battery of in vitro tests and characterizations.

The results of some of these pre-clinical studies are depicted in the diagrams below.

We have discussed our pre-clinical data and intended Phase 1b study protocol with FDA and intend to initiate a SER-262 clinical study in the middle of 2016. Each of the strains used in our pre-clinical studies were purified from a qualified donor who participated in the SER-109 Phase 1b/2 clinical study. Given our ability to grow the spores in bacterial fermenters, we will not require any additional donations from human donors for purposes of manufacturing SER-262.

SER-262 represents the continued evolution of our platform and capabilities, validating our ability to extend our technology to new indications. SER-262, unlike SER-109, is made in bacterial fermenters and in a rational in vitro design similar to a fixed dose combination of small or large molecules. We intend to use this approach going forward for future Ecobiotic microbiome therapeutics, which will eliminate the need for ongoing human donors in the CMC process. There are several advantages to using a synthetic approach to developing microbiome therapeutics. Synthetically derived product candidates can be manufactured in a reliable, reproducible manner, with extremely well-defined characteristics. Based on our metagenomics expertise, vast proprietary bacterial library, and advanced manufacturing capabilities, we are able to specifically design synthetically produced microbiome therapies for specific target indications. Importantly, our unique capabilities provide Seres with a significant competitive advantage in developing synthetically produced microbiome therapies.

Manufacturing

To manufacture SER-262, bacterial components for formulation are fermented and purified as spores. The bacteria originate from cell banks that have been manufactured starting from proprietary research strain banks. Research strain banks have been made by clonal isolation and multiple rounds of streaking for purity, followed by banking and testing for identity and purity. The strains are cultured in controlled fermentations to meet projected initial clinical testing needs. The intended processes have been piloted to demonstrate the Phase 1 production process, and the cGMP campaign for production of supplies has been initiated. cGMP Drug Product processing is similar to SER-109 for initial proof-of-concept clinical trial materials, with the addition of a blending step to combine the individually fermented drug substances. Drug Substance and Drug Product will be tested for identity, purity, and potency Optimization of the fermentation and purification processes, and the dosage form are ongoing to refine manufacturing processes for future needs.

SER-287

Recent published third-party research reported changes in the microbiome in a cohort of patients with IBD, including ulcerative colitis, compared to healthy individuals. The changes include higher levels of Enterobacteriaceae and lower levels of Clostridiales. The changes in these organisms are a form of dysbiosis, and we believe that if we can repopulate keystone organisms and functional pathways we could restore the microbiome thereby treating ulcerative colitis. Ulcerative colitis is a serious chronic condition affecting approximately 700,000 individuals in the United States. The disease results in inflammation of the colon and rectum and can result in debilitating symptoms, including abdominal pain, bowel urgency and diarrhea.

Based on this research and our experience with SER-109, we believe that we can use a complex spore ecology to restore the underlying dysbiosis of ulcerative colitis. SER-109 is comprised of organisms in the class of Clostridiales, which engraft after treatment with SER-109. SER-109 has also been shown to reduce the colonization of Enterobacteriaceae in CDI patients. We developed SER-287 to treat ulcerative colitis using data generated in our studies of SER-109.

We initiated our Phase 1b study in December 2015 and are enrolling subjects with mild to moderate ulcerative colitis to evaluate the safety and efficacy of SER-287 added to standard of care treatment. The study will examine the safety and tolerability, effect on composition of the intestinal microbiome, the engraftment of SER-287 bacteria into the intestinal microbiome, and the clinical response, complete remission and endoscopic improvement in subjects following treatment with SER-287 compared to placebo.

Phase 1b clinical study design

The broad objectives of the SER-287 Phase 1b clinical study are to determine the safety and tolerability of SER-287, and microbiome dynamics, in patients with active mild-to-moderate ulcerative colitis.

The Phase 1b clinical study is a multicenter, randomized, double-blind, placebo-controlled multiple dose study utilizing weekly or daily dosing with SER-287 conducted in 55 adult subjects with mild-to-moderate ulcerative colitis. We plan to enroll eligible subjects at approximately 20 sites in the United States. The Phase 1b clinical study is designed to enroll adults 18 years of age and older who have mild-to-moderate ulcerative colitis as defined by a total modified Mayo score between 4 and 10, inclusive, with a modified Mayo endoscopic subscore ≥ 1.

Patients will be randomized to one of four study arms:

- Pre-treatment with placebo for 6 days, followed by weekly dosing of SER-287 for 8 weeks
- Pre-treatment with placebo for 6 days, followed by daily dosing with placebo for 8 weeks
- Pre-treatment with vancomycin for 6 days, followed by daily dosing of SER-287 for 8 weeks
- Pre-treatment with vancomycin for 6 days, followed by weekly dosing of SER-287 for 8 weeks

The primary objectives of the study are to evaluate the safety and tolerability of SER-287 compared to placebo; to compare the baseline composition of the intestinal microbiome to the composition at 8 weeks post-initiation of SER-287 or placebo; and to determine the engraftment of SER-287 bacteria into the intestinal microbial community in each of the SER-287 arms compared to the placebo arm.

The secondary objectives of the study are to determine the proportion of subjects in each of the treatment arms who at eight weeks post-initiation of treatment achieve a clinical response, complete remission, and endoscopic improvement; to assess changes in serum and fecal biomarkers from baseline throughout treatment; to determine the complement of

metabolic pathways from stool, urine and blood in each of the treatment arms from baseline throughout treatment; and to compare the changes in exploratory biomarkers from mucosal biopsies, stool and oral swabs in each of the treatment arms from baseline through eight weeks

This study will provide a safety profile of SER-287 compared to placebo for the ulcerative colitis population, describe the changes in the microbiome as a result of treatment with SER-287 and provide potential predictive biomarkers for future studies. Ulcerative colitis is characterized by a decrease in microbial diversity and richness, with a lower prevalence of spore-forming organisms within the phylum Firmicutes. Preliminary data suggest that microbial interventions can affect clinical outcomes in ulcerative colitis, and this study will evaluate whether the ecology of bacterial spores in SER-287 can correct the dysbiosis in ulcerative colitis, increase microbial diversity and safely lead to a clinical response in ulcerative colitis patients with mild-to-moderate disease.

Other Product Candidates and Products in Discovery

SER-155

We have an active pre-clinical program to discover and develop Ecobiotic microbiome therapeutics for other infectious diseases. The Phase 1b/2 clinical study of SER-109 provided initial evidence suggesting that Ecobiotic microbiome therapeutics have the potential to eliminate colonization by potential microbial pathogens, such as VRE and Gram-negative Enterobacteriaceae. Enterobacteriaceae, such as Klebsiella, Morganella and Proteus. These may be present at low levels in the healthy colon, but like C. difficile, they can overgrow after antibiotic use. Enterobacteriaceae can include multidrug resistant organisms, or MDROs, that represent significant public health concerns. For example, carbapenem resistant Enterobacteriaceae, or CRE, is a significant problem in the United States and has been identified as an urgent priority by the Centers for Disease Control. VRE, CRE and other MDROs colonize the gastrointestinal tract after antibiotic use and can spread through contact with patients and healthcare workers both in institutional and in community settings.

We are currently designing and developing SER-155, an Ecobiotic microbiome therapeutic that is expected to have activity against Gram-positive and Gram-negative enteric bacterial pathogens. We expect to develop SER-155 for the prevention of transplant-related mortality in recipients of allogeneic hematopoietic stem cell transplant (HSCT) due to invasive infection and graft versus host disease (GvHD). The selection of patient population will be based on pre-clinical data, and the assessment of clinical development plan, regulatory path and market opportunities. We plan to conduct studies in animal models as well as conduct further in vitro characterization of individual strains, in order to define and nominate a composition for clinical development.

Sales and Marketing

In January 2016 we hired Wael Hashad as Chief Commercial Officer and Executive Vice President. In this newly created role, Mr. Hashad will be responsible for all activities related to the anticipated commercialization of our products in development. If SER-109 is approved in the United States, we plan to commercialize it with our own focused specialty sales force. We believe we can effectively commercialize SER-109 with a commercial team of 100 or fewer sales representatives that will target gastrointestinal and infectious disease physicians, which are the two primary groups of physicians who treat multiple recurrent CDI patients.

In January 2016 we entered into an agreement with NHS for the development and commercialization outside of the United States and Canada of our product candidates in development for CDI and IBD, including ulcerative colitis and Crohn’s disease. The agreement will support the development of our portfolio of products for CDI and IBD in markets outside of the United States and Canada and provide financial support for our ongoing research and development.

Manufacturing

The production of live bacterial products is highly specialized. Owing to their hardiness and environmental persistence, production of spore-forming organisms poses unique considerations for product, personnel and facility protection. Manufacturing activities with spores are subject to specialized regulations. We believe that many of the challenges associated with manufacturing bacterial combinations are overcome by the low dose requirements of our product. For example, we expect that a typical commercial fermentation will yield on the order of hundreds or thousands of doses per liter depending on the product and its composition. Additionally, because a given total dose is split between several strains, the per-strain requirements for production may be even lower. As a result, we believe the high productivity relative to the dose level will enable production scales for both clinical and commercial supply to be

modest.

We have developed a supply chain for producing and testing materials to ensure the availability of future clinical trial supplies. Our development processes are designed to ensure that the raw materials, process technologies and analytical tests we use are scalable and transferable to a cGMP manufacturing environment. These include the following core elements:

- Fermentation. We are using that microscale screening to optimize culture of the bacterial strains of interest in our current and foreseeable product candidates. These screens can identify the fermentation platform that is best-suited for optimization and scale- up of the strains. Small-scale fermentation systems (0.1 L to 20 L) enable the optimization of a wide variety of culture conditions and have been demonstrated to be scalable to commercial fermentation processes and enable technology transfer to clinical and final manufacturing scales. We employ platform fermentation processes as starting points for cGMP production processes, and develop strain specific processes as required. To develop master cell banks, working cell banks, and bulk drug substance for commercial product, we are using bacterial strains originating from a unique research cell bank precursor, so we expect the research cell banks and final drug product should be genetically and physiologically similar.

- Purification. Similar to fermentation, we believe small-scale purification operations are available for assessing large-scale cGMP manufacturing of live cells, and to quickly assess downstream process yield, quality and robustness. For our oral products, purification is typically less complex than for parenteral biologics such as monoclonal antibodies that must purify away very similar components from the culturing process. Separation of microbes from soluble fermentation broth components is much simpler.
- Formulation. Our Ecobiotic microbiome therapeutics are combinations of live bacteria and can be administered by a number of methods and by different routes. The primary goal in developing formulation is to deliver the bacteria to the intended location in a condition where they are able to replicate and correct dysbiosis. Formulation development generally uses approved excipients and preservatives, and will include screening of liquid, solid, and suspension formulations to maximize the opportunity for extended stability with minimal cold-chain requirements.
- Analytical. We intend to address quality control requirements for our Ecobiotic microbiome therapeutics using proprietary microbiological and molecular sequence-based testing schemes. We have available and are further developing quality control and in-process analytical tools that can quantitatively measure the composition of spore, vegetative microbe and spore/vegetative combinations, which we believe enable a wide variety of drug products to be manufactured. Throughout the bioprocess and formulation development platform we use and will expand on high- throughput quantitative analytics to assess the identity, potency and purity of the final product.

We currently have a small scale pilot manufacturing facility at our Cambridge Kendall Square location where we conduct process development, scale-up activities and a portion of the cGMP manufacture of Ecobiotic microbiome therapeutics to support Phase 1 clinical supplies. We are expanding capacity with construction of a larger cGMP manufacturing facility at our new headquarters, with the goal to perform both Drug Substance and Drug Product manufacturing for Phase 1 and 2 clinical development. We intend to establish further manufacturing facilities that will serve late-phase clinical and commercial supply for our product candidates. We may do this by expanding our current and planned facilities, or by purchasing or building additional facilities.

Intellectual Property

We strive to protect the proprietary technology that is important to our business, including seeking and, if granted, maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other aspects of inventions that are commercially important to the development of our business. We also utilize regulatory exclusivity as well as trade secrets to protect aspects of our business.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of treatment, methods of manufacture and methods for patient selection created or identified from our ongoing development of our product candidates. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce any patents that we may obtain, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position and, in the future, may rely on or leverage in-licensing opportunities. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent may be challenged in courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or at all, whether the claims of any patent applications, should they issue, will cover our product candidates, or whether the claims of any issued

patents will provide sufficient protection from competitors or otherwise provide any competitive advantage.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and because publication of discoveries in the scientific or patent literature often lags behind actual discoveries and patent application filings, we cannot be certain of the priority of inventions covered by pending patent applications. Accordingly, we may not have been the first to invent the subject matter disclosed in some of our patent applications or the first to file patent applications covering such subject matter, and we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention.

Our patent portfolio includes patent applications in the early stages of prosecution and four issued U.S. patents. For our pending Patent Cooperation, or PCT, applications, we anticipate determining, in advance of the applicable deadlines, whether to pursue these applications and if so will pursue them in the United States and selected ex-U.S. jurisdictions. We believe that issued claims will provide protection for SER-109, SER-262, SER-287 and SER-155.

Our patent estate leverages both offensive and defensive strategies. As of February 5, 2016, we owned a total of thirteen patent application families that include Patent Cooperation Treaty, or PCT, applications and/or U.S. patent applications and ex-US patent applications. Some of these families are briefly described below. Four of the patent application families that include only U.S. provisional applications that will not themselves be examined and for which the deadline to file PCT applications and/or U.S. non-provisional applications has not yet expired. The pending patent applications as of February 5, 2016 in six of the patent application families in our portfolio are described briefly below. We expect to pursue additional applications in these families over time.

- A family related to binary combinations of microbes that includes the following issued and pending applications: (i) an issued U.S. patent, which claims therapeutic compositions that include selected binary combinations of microbes; (ii) an issued U.S. patent, which claims methods of using such compositions to treat or prevent CDI; (iii) a continuation U.S. patent application and (iv) national stage applications based on the PCT application in 14 ex-U.S. jurisdictions. Patents issuing from or based on these applications, if any, are expected to expire in 2033, assuming all required maintenance fees are paid and absent any applicable patent term extension or patent term adjustment. We expect this patent application family to provide patent protection for SER-109, SER-262, SER-287 and SER-155.
- A family related to combinations of bacterial spores that includes the following issued and pending applications: (i) two issued U.S. patents and one U.S. application that claim certain methods of treatment of gastrointestinal diseases, including Crohn's disease and colitis, using combinations of bacterial spores and (ii) national stage applications based on the PCT application in 12 ex-U.S. jurisdictions claiming similar methods, as well as related compositions. Patents issuing from or based on these applications, if any, are expected to expire in 2034, assuming all required maintenance fees are paid and absent any applicable patent term extension or patent term adjustment. We expect this patent application family to provide patent protection for SER-109, SER-262, SER-287 and SER-155.
- A family that includes a pending U.S. and a European national stage application based on a PCT application related to compositions of matter and methods for new combinations of microbes for treating gastrointestinal diseases. Patents based on these applications, if granted, are expected to expire in 2034, assuming all required maintenance fees are paid and absent any applicable patent term extension or patent term adjustment.
- A family that includes pending national stage applications in the U.S. and Europe, related to quality control of Ecobiotic products and characterization methods. Patents based on these applications, if granted, are expected to expire in 2034, assuming all required maintenance fees are paid and absent any applicable patent term extension or patent term adjustment.
- A family that includes pending national stage applications in the U.S. and 6 ex-U.S. jurisdictions, related to methods of restructuring of a host microbiome using microbial populations identified using our network-based discovery platforms. Patents based on these applications, if granted, are expected to expire in 2034, assuming all required maintenance fees are paid, and absent any applicable patent term extension or patent term adjustment.
- A family that includes a pending PCT application related to compositions of matter and methods of treating disorders with compositions that include, for example, ternary combinations of microbes. The time period for electing to pursue U.S. and foreign patent protection by filing national stage applications in individual jurisdictions based on this PCT application has not yet expired, and we will need to decide whether and where to pursue U.S. and ex-U.S. protection before expiration of the applicable deadlines. If we do pursue protection in one or more jurisdictions, patents based on this application, if granted, are expected to expire in 2034, assuming all required maintenance fees are paid and absent any applicable patent term extension or patent term adjustment.

Patent term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional, patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development

and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of such an FDA-approved drug, an FDA- approved method of treatment using the drug and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or fourteen years from the date of the FDA approval of the drug, and a patent cannot be extended more than once or for more than a single product. During the period of extension, if granted, the scope of exclusivity is limited to the approved product for approved uses. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our product candidates receive FDA approval, we expect to apply, if appropriate, for patent term extension on patents covering those product candidates, their methods of use and/or methods of manufacture.

Trade secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically utilize trade secrets to protect aspects of our business. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements provide that all confidential information developed or made known during the course of an individual or entities' relationship with us must be kept confidential during and after the relationship. These agreements also provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Competition

The development and commercialization of new drug and biologic products is highly competitive and is characterized by rapid and substantial technological development and product innovations. 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. We are aware of a number of large pharmaceutical and biotechnology companies, as well as smaller, early-stage companies, that are pursuing the development of products, including microbiome therapeutics, for the prevention of CDI, IBD and other disease indications we are targeting. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others may be based on entirely different approaches. For example, FMT is a procedure that is currently used for recurrent CDI and has resulted in high cure rates for recurrent CDI and our competitors and physicians may continue to seek to standardize and implement this procedure. 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, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and 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, clinical, manufacturing 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.

The key competitive factors affecting the success of SER-109, SER-287 and any other product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price, the level of 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, 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 lower cost products.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs and biologics such as those we are developing. We, along with our contract manufacturers, will be required to navigate the various pre-clinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval for our product candidates. The process of obtaining regulatory approvals and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug and Cosmetic Act, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our product candidates are subject to regulation by the FDA as biologics. Biologics require the submission of a biologics license application, or BLA, and approval by the FDA before being marketed in the United States. None of our product candidates has been approved by the FDA for marketing in the United States, and we currently have no BLAs pending. If we fail to comply with applicable FDA or other requirements at any time during product development, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, suspension or revocation of approved applications, warning letters, product recalls, product seizures, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

The process required by the FDA before our biologic product candidates may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests and animal studies performed in accordance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before clinical trials in the United States may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication, conducted in accordance with the FDA's good clinical practice, or GCP, regulations;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP regulations; and
- FDA review and approval of the BLA prior to any commercial marketing, sale or shipment of the product.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Pre-clinical and Clinical Trials

Once a product candidate is identified for development, it enters the pre-clinical testing stage. Pre-clinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which must be conducted in accordance with GLP requirements. The results of the pre-clinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol must be submitted to the FDA as part of the IND. An independent institutional review board, or IRB, for each investigator site proposing to participate in a clinical trial must also review and approve the clinical trial before it can begin at that site, and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP requirements, including requirements for informed consent.

For purposes of BLA approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

- Phase 1 — Phase 1 clinical trials involve initial introduction of the investigational product into healthy human subjects or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2 — Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.
- Phase 3 — Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval. Such post-approval clinical trials are typically referred to as Phase 4 clinical trials.

Although most clinical research performed in the United States in support of a BLA must be authorized in advance by the FDA, under the IND regulations and procedures described above, there are certain circumstances under which clinical trials can be conducted without submission of an IND. For example, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. Similarly, the FDA may exercise enforcement discretion to permit sponsors to conduct certain types of clinical investigations without an IND. Pursuant to the FDA guidance document "Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies" (July 2013), the FDA currently exercises enforcement discretion regarding the IND requirements for the use of FMT to treat CDI not responsive to standard therapies, provided that the treating physician obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products. The FDA provided confirmation that it intends to exercise enforcement discretion with respect to our Phase 1b/2 clinical study of SER-109,and accordingly, we did not conduct this trial under an IND. However, the guidance document states that the FDA will continue to work with any sponsors who wish to submit INDs for this use of FMT, and we intend to conduct all future clinical studies of SER-109, including our Phase 2 clinical study and our planned Phase 3 clinical trial, under an IND.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing

the biologic in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality 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 product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and FDA Review

The results of pre-clinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the biologic, are submitted to the FDA in the form of a BLA requesting approval to market the biologic for one or more specified indications. The submission of a BLA requires payment of a substantial user fee unless a waiver is granted. However, an orphan-designated product, such as our SER-109, is not subject to an application user fee unless the human drug application includes an indication for other than a rare disease or condition. Each BLA submitted to the FDA is reviewed

for administrative completeness and reviewability within 60 days of the FDA's receipt of the application. If the BLA is found to be complete, the FDA will file the BLA, triggering a full review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission.

Once a BLA has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. However, the review process is often significantly extended by FDA requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA has a goal of reviewing BLAs within ten months of the 60-day filing date for standard review or six months for priority review, but the overall timeframe is often extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether the biological product is safe, pure and potent and whether the facility or facilities in which it is manufactured meet standards designed to assure the product's continued safety, purity and potency. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will inspect the facility or the facilities at which the biologic product is manufactured, and will not approve the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance with GCP requirements, and will not approve the biologic unless compliance with such requirements is satisfactory.

The FDA may deny approval of a BLA if the applicable statutory and regulatory criteria are not satisfied, or it may require additional pre-clinical or clinical data. Even if such data are submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than sponsors. Once the FDA approves a BLA, such approval defines the indicated uses for which the biologic may be marketed. The FDA may also require implementation of a Risk Evaluation and Mitigation Strategy, or REMS, which can include a medication guide, communication plan, or elements to assure safe use, such as restricted distribution methods, physician training, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling claims or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the market. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing based on the results of these post-marketing studies.

The biologic testing and approval processes encompasses significant risk, and requires substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our product candidates for the treatment of a disease or condition, the results may not be satisfactory to the FDA. Pre-clinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing our product candidates. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of our products. After approval, certain changes to the approved biologic, such as adding new indications, manufacturing changes or additional labeling claims, are subject to further FDA review and approval. Depending on the nature of the change proposed, a BLA supplement must be filed and approved before the change may be implemented. For many proposed post-approval changes to a BLA, the FDA has up to 180 days to review the application. As with new BLAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

Expedited Development and Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life- threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Accelerated Approval, and the purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. SER-109 has obtained Breakthrough Therapy, as well as Orphan Drug, designations.

A new drug or biologic is eligible for fast track designation if it is intended to treat a serious or life- threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during pre-clinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as Priority Review, discussed below. In addition, a new drug or biologic may be eligible for breakthrough therapy designation if it is intended 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.

Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review process, including Priority Review designation and accelerated approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. The FDA aims to review applications for new products designated for priority review within six months, compared to ten months under standard review. Additionally, products intended to treat serious or life-threatening diseases or conditions may receive accelerated approval. Products are eligible for accelerated approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which is reasonably likely to predict an effect on 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. Accelerated Approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. In addition, the FDA currently requires, as a condition for accelerated approval, pre-approval of all promotional materials intended for dissemination or publication within 120 days following marketing approval, which could adversely impact the timing of commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Accelerated Approval do not change the standards for approval but may expedite the development or review process. We have received Breakthrough Therapy designation for SER-109, and we may apply for one or more of the FDA's expedited programs for our other product candidates. The FDA may disagree that our product candidates satisfy the criteria for such programs, such programs may fail to result in expedited development or review timelines, or the FDA may ultimately refuse to approve our product candidates despite their inclusion in any expedited programs. In addition, if the Breakthrough Therapy designation for SER-109 is no longer supported by subsequent data, FDA may rescind the designation.

Post-Approval Requirements

Approved biologics that are manufactured or distributed in the United States are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. There also are continuing, annual user fee requirements for products and the establishments at which such products are manufactured, as well as new application fees for certain supplemental applications.

Any biologics manufactured or distributed by us or our contract manufactures pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Manufacturers and their subcontractors 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 ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply

with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution or withdraw approval of the BLA for that product.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Physicians may prescribe legally available biologics for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Biosimilars and Regulatory Exclusivity

We believe that any of our product candidates approved under a BLA should qualify for a 12-year period of exclusivity against biosimilar competition currently permitted by the Biologics Price Competition and Innovation Act, or BPCIA. Specifically, as part of the Patient Protection and Affordable Care Act enacted in 2010, as amended by the Health Care and Education Affordability Reconciliation Act, collectively the Affordable Care Act, the BPCIA established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The new abbreviated regulatory pathway provides legal authority for the FDA to review and approve biosimilar biologics based on their similarity to an existing brand product, referred to as a reference product, including the possible designation of a biosimilar as interchangeable with a brand product. Under the BPCIA 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. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological drug products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning is subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes that operate to limit the scope or length of exclusivity afforded by the BPCIA could have a material adverse effect on the future commercial prospects for our biological products. In addition, the period of exclusivity provided by the BPCIA only operates against third parties seeking approval via the abbreviated pathway, but would not prevent third parties from pursuing approval via the traditional approval pathway. In addition, foreign regulatory authorities may also provide for exclusivity periods for approved biological products. For example, biological products in the EU may be eligible for at least a ten-year period of exclusivity.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a 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 making the product available in the United States for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting a BLA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. Further, if a designated orphan product receives marketing approval for an indication broader than the rare disease or condition for which it received orphan designation, it may not be entitled to orphan exclusivity.

In August 2015, the FDA granted orphan drug designation to SER-109.

We may seek orphan designation for one or more of our product candidates, but the FDA may disagree with our analysis of the prevalence of a disease or condition or other criteria for designation and refuse to grant orphan status. We cannot guarantee that we will obtain designation or approval for any product candidate, or that we will be able to secure orphan product exclusivity if we do obtain approval.

Government Regulation Outside of the United States

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, manufacturing, commercial sales and distribution of our products.

For instance, in the EEA (comprised of the 28 EU Member States plus Iceland, Liechtenstein and Norway) medicinal products must be authorized for marketing by using either the centralized authorization procedure or national authorization procedures.

Centralized procedure—Under the centralized procedure, following the opining of the EMA's Committee for Medicinal Products for Human Use, or, CHMP, the European Commission issues a single marketing authorization valid across the EEA. The centralized procedure is compulsory for human medicines derived from biotechnology processes advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases, and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned contains a new active substance not yet authorized in the EEA, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EEA. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA 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 assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops.

National authorization procedures—There are also two other possible routes to authorize medicinal products in several countries, which are available for products that fall outside the scope of the centralized procedure:

- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In the EEA, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period

prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The criteria for designating an "orphan medicinal product" in the EEA are similar in principle to those in the United States. In the EEA a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. 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. During this ten year orphan market exclusivity period, 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 EU for pediatric studies. The ten 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 (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Other Healthcare Laws

Although we currently do not have any products on the market, if our product candidates are approved and we begin commercialization, we will be subject to healthcare regulation and enforcement by the federal government and the states in which we conduct our business. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits the offer, receipt, or payment of remuneration in exchange for or to induce the referral of patients or the use of products or services that would be paid for in whole or part by Medicare, Medicaid or other federal healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts and free or reduced price items and services. The government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham research or consulting and other financial arrangements with physicians. Further, 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. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act (discussed below). Many states have similar laws that apply to their state healthcare programs as well as private payors.

The False Claims Act, or FCA, imposes liability on persons who, among other things, present or cause to be presented false or fraudulent claims for payment by a federal health care program. The FCA has been used to prosecute persons submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. Actions under the FCA 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 FCA can result in significant monetary penalties and treble damages. The federal government is using the FCA, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi–billion dollar settlements under the FCA in addition to individual criminal convictions under applicable criminal statutes. In addition, companies have been forced to implement extensive corrective action plans, and have often become subject to consent decrees or corporate

integrity agreements, severely restricting the manner in which they conduct their business. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposed new reporting requirements on certain drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug must submit reports by the 90th day of each subsequent calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

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. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "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 effect, thus complicating compliance efforts.

The shifting commercial compliance environment and the need to build and maintain robust systems to comply with different compliance and/or reporting requirements in multiple jurisdictions increase the possibility that a healthcare company may violate one or more of the requirements. 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, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In both domestic and foreign markets, sales and reimbursement of any approved products will depend, in part, on the extent to which third-party payors, such as government health programs, commercial insurance and managed healthcare organizations provide coverage, and establish adequate reimbursement levels for, such products. Third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. Third-party payors may limit, or hinder, 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. Additionally, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products, as well as provide rebates and discounts which may impact the net selling price of our products. If third-party payors do not consider our products to be cost-effective compared to other therapies, the payors may not cover our products as a benefit under their plans or, if they do, the level of reimbursement may not be sufficient to allow us to sell our products on a profitable basis.

The containment of healthcare costs also has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results.

Outside the United States, ensuring adequate coverage and payment for our products will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other

available therapies. Conducting such a clinical trial could be expensive and result in delays in our commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved healthcare products. Recent budgetary pressures in many countries are also causing governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates. If budget pressures continue, governments may implement additional cost-containment measures. Cost-control initiatives could decrease the price we might establish for products that we may develop or sell, which would result in lower product revenues or royalties payable to us. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

Healthcare Reform

In the United States, there have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biological products, government control and other changes to the healthcare system. It is uncertain what legislative proposals will be adopted or what actions federal, state or private payors for medical goods and services may take in

response to any healthcare reform proposals or legislation. We cannot predict the effect medical or healthcare reforms may have on our business, and no assurance can be given that any such reforms will not have a material adverse effect.

By way of example, in March 2010, the Affordable Care Act was signed into law, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among other things, the Affordable Care Act:

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of ''average manufacturer price,'' or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- extended Medicaid drug rebates, previously due only on fee-for-service utilization, to Medicaid managed care utilization, and created an alternate rebate formula for new formulations of certain existing products that is intended to increase the amount of rebates due on those drugs;
- expanded the types of entities eligible for the 340B drug discount program that mandates discounts to certain hospitals, community centers and other qualifying providers. With the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, because 340B pricing is determined based on AMP and Medicaid drug rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discounts to increase; and
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, 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 years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals. Adoption of other new legislation at the federal or state level could further limit reimbursement for pharmaceuticals, including our product candidates if approved.

As of December 31, 2015, we had 86 full-time permanent employees. Thirteen employees work in administration and operations and seventy-three work in research and development.

Our Corporate Information

We were incorporated in the State of Delaware in 2010 under the name Newco LS21, Inc. In October 2011, we changed our name to Seres Health, Inc., and in May 2015, we changed our name to Seres Therapeutics, Inc. Our principal executive offices are located at 215 First Street, Cambridge, Massachusetts 02142 and our telephone number is (617) 945-9626. Our website address is www.serestherapeutics.com. The information contained in, or accessible through, our website does not constitute a part of this annual report on Form 10-K.

Item 1A. Risk Factors

Our business faces significant risks and uncertainties. Accordingly, in evaluating our business, you should carefully consider the risk factors discussed below, as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition.". The occurrence of any of the events or developments described below or elsewhere in this report could harm our business, financial condition, results of operations or growth prospects.

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 $6.1 million for the year ended December 31, 2013, $16.7 million for the year ended December 31, 2014 and $54.8 million for the year ended December 31, 2015, respectively. As of December 31, 2015, we had an accumulated deficit of $82.6 million. To date, we have financed our operations through the initial public offering of our common stock, private placements of our preferred stock, and the issuance of convertible promissory notes and borrowings under a loan and security agreement with Comerica Bank, or the loan and security agreement. We have devoted substantially all of our financial resources and efforts to developing our microbiome therapeutics platform, identifying potential product candidates and conducting pre-clinical studies and clinical trials. We are in the early stages of development of our product candidates, which we call Ecobiotic microbiome therapeutics, and we have not completed development of any Ecobiotic microbiome therapeutics or other drugs or biologics. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- conduct our Phase 2 clinical study of SER-109, our lead product candidate, and potentially advance to Phase 3 clinical studies;
- conduct our Phase 1 clinical study of SER-287;
- continue the research and development of our other product candidates, including completing pre-clinical studies and commencing clinical trials for SER-262 and SER-155;
- seek to enhance our microbiome therapeutics platform 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 manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- 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 operation as 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 pre-clinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. 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 revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product and biological 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 the European Medicines Agency, or EMA, 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 even continue our operations.

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 Phase 2 clinical study of SER-109 and our Phase 1 clinical study of SER-287, and continue to research, develop and initiate clinical trials of SER-262 and SER-155 and 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. Furthermore, we have incurred and expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing 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 expect that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements well into 2018. 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 Phase 2 clinical study of SER-109 and our Phase 1b clinical study of SER-287, as well as future clinical studies for these candidates;
- the cost of manufacturing clinical supplies of our product candidates;
- the scope, progress, results and costs of pre-clinical development, laboratory testing and clinical trials for our other product candidates, including SER-262 and SER-155;
- 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.

Since our inception in October 2010, we have devoted substantially all of our resources to developing SER-109 and SER-287, researching SER-262, 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 two of our product candidates, SER-109 and SER-287, are still in pre-clinical development. We have completed our Phase 1b/2 clinical study of SER-109, our lead product candidate, but have not completed any other clinical trials for this or any other product candidate. We have not yet demonstrated our ability to successfully complete any Phase 2 clinical study 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 future success or viability may not be as accurate as they could be if we had a longer operating history.

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates

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

We are using our microbiome therapeutics platform to develop Ecobiotic microbiome therapeutics, with an initial focus on developing SER-109 for the prevention of further recurrences of CDI in patients suffering from recurrent CDI and SER-287 for the treatment of ulcerative colitis. While we believe our pre-clinical and Phase 1b/2 clinical data to date has validated our platform to a degree, we are at an early stage of development and our platform has not yet, and may never lead to, approvable or marketable drugs. We are developing additional product candidates that we intend to be used to prevent non-Clostridium difficile infection and to treat inflammatory and metabolic diseases. We may have problems applying our technologies to these other areas, and our new product candidates may not be as effective in preventing infection and disease 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 their 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 pre-clinical 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 our own, commercial manufacturing capabilities;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- entering into new collaborations throughout the development process as appropriate, from pre- clinical studies through to commercialization;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- 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 a continued acceptable safety profile of the products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology.

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

Our product candidates are based on microbiome therapeutics, which is an unproven approach to therapeutic intervention.

All of our product candidates are based on microbiome therapy, a therapeutic approach that is designed to treat disease by restoring the function of a dysbiotic microbiome. We have not, nor to our knowledge has any other company, received regulatory approval for a therapeutic based on this approach. We cannot be certain that our approach will lead to the development of approvable or marketable products. In addition, our Ecobiotic microbiome therapeutics may have different effectiveness rates in various indications and in different geographical areas. Finally, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of products based on microbiome therapeutics, which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our product candidates.

Our microbiome therapeutics platform relies on third parties for biological materials, including human stool. Some biological materials have not always met our expectations or requirements, and any disruption in the supply of these biological materials could materially adversely affect our business. For example, if any supplied biological materials are contaminated with disease organisms, we would not be able to use such biological materials. Although we have control processes and screening procedures, biological materials are susceptible to damage and contamination and may contain active pathogens. Improper storage of these materials, by us or any third-party suppliers, may require us to destroy some of our raw materials or products, which could delay the development or commercialization of our product.

Clinical drug development involves a risky, 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.

We dosed the first patient in a Phase 2 clinical study of our lead product, SER-109, in May 2015. In December 2015, we initiated a Phase 1b clinical trial evaluating SER-287 in mild-to-moderate ulcerative colitis. Our other product candidates are in pre-clinical 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 pre-clinical 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 is uncertain as to outcome. A failed clinical trial can occur at any stage of testing. The outcome of pre-clinical 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. For example, in anticipation of our Phase 2 clinical study of SER-109, we have refined the formulation of the inner capsule and changed the manufacturing process that we expect to use for commercial production. This formulation has not previously been clinically tested. The Phase 2 clinical study is the first clinical trial using this formulation and we cannot assure you that the results of this new formulation will be consistent with those experienced in the Phase 1b/2 clinical study of SER-109. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks.

In addition, we cannot be certain as to what type and how many clinical trials the FDA, or other regulators, will require us to conduct before we may successfully gain approval to market SER-109 or any of our other product candidates. 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. In the course of our discussions with the FDA, the FDA has indicated that we may be required to conduct more than one Phase 3 clinical trial of SER-109 in order to gain approval. Additional clinical trials could cause us to incur significant development costs, delay or prevent the commercialization of SER-109 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 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 clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may demonstrate undesirable side effects or produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- 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;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- 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 anticipate; and
- regarding trials managed by 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;
- lose the support of current or any future collaborators, requiring us to bear more of the burden of development of certain compounds;
- 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 we intend or desire;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;
- be subject to increased pricing pressure ; or
- have the product removed from the market after obtaining marketing approval.

We completed our Phase 1b/2 clinical study of SER-109 in 2014 and dosed the first patient in a Phase 2 clinical study for this product candidate in May 2015. Although most clinical research performed in the United States must be authorized in advance by the FDA under its investigational new drug application, or IND, regulations, we did not conduct our Phase 1b/2 clinical study under an IND pursuant to the FDA’s exercise of enforcement discretion with regard to IND requirements for use of fecal microbiota for transplantation to treat CDI not responsive to standard therapies. Although the FDA provided confirmation that it intends to exercise enforcement discretion with respect to our Phase 1b/2 clinical study of SER-109, it stated that continued clinical evaluation of SER-109 will require an IND. In April 2015, the FDA authorized the conduct of our Phase 2 clinical study of SER-109 under an IND. We intend to conduct all future clinical studies of SER-109 under this IND. Unlike with SER-109, we expect that the FDA will require an IND before we initiate clinical testing of our other product candidates and may also require us to conduct more extensive pre-clinical tests prior to the start of clinical trials than were required for SER-109.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our pre-clinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant pre- clinical 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. We are developing our lead product candidate, SER-109, to prevent further recurrences of CDI in patients suffering from recurrent CDI. We estimate the addressable population of patients with recurrent CDI to be between 85,000 and 110,000 patients per year in the United States, and accordingly, there is a limited number of patients from which to draw for clinical studies.

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;
- the efforts to facilitate timely enrollment in clinical trials;
- our payments for conducting clinical trials;
- the patient referral practices of physicians;
- the burden, or perceived burden, of the clinical study;
- 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 would cause the value of our company 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 or will not be able to do so as soon as anticipated, 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, storage, approval, advertising, promotion, 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 in any jurisdiction will prevent us from commercializing the product candidate in that jurisdiction, and may affect our plans for commercialization in other jurisdictions as well. 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 pre-clinical 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 or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, risky and may take many years. The scope and amount of clinical data required to obtain marketing approvals can vary substantially from jurisdiction to jurisdiction, and it may be difficult to predict whether a particular regulatory body will require additional or different studies than those conducted by a sponsor, especially for novel product candidates such as our Ecobiotic microbiome therapeutics. The FDA or foreign regulatory authorities may delay, limit, or deny approval to market our product candidates for many reasons, including: our inability to demonstrate that the clinical benefits of our product candidates outweigh any safety or other perceived risks; the regulatory authority's disagreement with the interpretation of data from nonclinical or clinical studies; the regulatory agency's requirement that we conduct additional pre-clinical studies and clinical trials; changes in marketing approval policies during the development period;

changes in or the enactment of additional statutes or regulations, or changes in regulatory review process for each submitted product application; or the regulatory authority's failure to approve the manufacturing processes or third-party manufacturers with which we contract. Regulatory authorities have substantial discretion in the approval process and may refuse to accept a marketing application as deficient. In addition, varying interpretations of the data obtained from pre-clinical 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. Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized.

Furthermore, our product candidates may not receive marketing approval even if they achieve their specified endpoints in clinical trials. Clinical data is often susceptible to varying interpretations and many companies that have believed that their products performed satisfactorily in clinical trials have nonetheless failed to obtain regulatory agency approval for their products. The FDA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from nonclinical and clinical studies. Upon the FDA's review of data from any pivotal trial, it may request that the sponsor conduct additional analyses of the data and, if it believes the data are not satisfactory, could advise the sponsor to delay filing a marketing application.

Even if we eventually complete clinical testing and receive approval of a biologics license application, or BLA, or foreign marketing authorization for one of our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA or the applicable foreign regulatory agency may also approve our therapeutic candidates for a more limited indication and/or a narrower patient population than we originally request, and the FDA, or applicable foreign regulatory agency, may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our therapeutic candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of our therapeutic candidates and would materially adversely impact our business and prospects.

The development of therapeutic products targeting the underlying biology of the human microbiome is an emerging field, and it is possible that the FDA and other regulatory authorities could issue regulations or new policies in the future affecting our Ecobiotic microbiome 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.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek Fast Track designation for some of our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA Fast Track designation. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during pre-clinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. The FDA has broad discretion whether or not to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Fast Track designation does not assure ultimate approval by the FDA. The FDA may withdraw Fast Track

designation if it believes that the designation is no longer supported by data from our clinical development program.

A Breakthrough Therapy designation by the FDA for our product candidates may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have received Breakthrough Therapy designation for SER-109, and we may seek a Breakthrough Therapy designation for our other product candidates. A Breakthrough Therapy is defined as a drug or biologic that is intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed in early clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA are also eligible for rolling review of the associated marketing application, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as priority review, where the agency aims to act on the application within eight months.

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, and the FDA has only recently released additional guidance as to the criteria it uses in designating drugs as breakthrough therapies. As a result, we cannot be sure that our evaluation 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 conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, not all products designated as breakthrough therapies ultimately will be shown to have the substantial improvement over available therapies suggested by the preliminary clinical evidence at the time of designation. As a result, if the Breakthrough Therapy designation for SER-109 or any future designation we receive is no longer supported by subsequent data, the FDA may rescind the designation.

We may seek orphan drug designation for some of our product candidates, but may not be able to obtain it.We have obtained orphan drug designation for SER-109 for recurrent C. difficile infection and may seek orphan drug designation and exclusivity for some of our future product candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. In the United States, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is defined as a disease or condition that affects fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug or biologic for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure a sufficient quantity of the drug or biologic to meet the needs of patients with the rare disease or condition.

Orphan drug exclusivity for a product 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 in that it is shown to be safer, more effective or makes a major contribution to patient care.

Risks Related to our Dependence on Third Parties and Manufacturing

The Collaboration and License Agreement, or the License Agreement, with Nestec Ltd., or NHS, is important to our business. If we or NHS fail to adequately perform under the License Agreement, or if we or NHS terminate the License Agreement, the development and commercialization of our CDI and IBD product candidates, including SER-109 and SER-287, would be delayed or terminated and our business would be adversely affected

The License Agreement may be terminated:

- by NHS in the event of serious safety issues related to SER-109, SER-262, SER-287, SER-301 or other specific products added under the License Agreement, or, collectively, the NHS Collaboration Products;
- by us if NHS challenges the validity or enforceability of any of our licensed patents; and
- by either NHS or us in the event of the other party's uncured material breach or insolvency.

Upon termination of the License Agreement, all licenses granted to NHS by us will terminate, and all rights in and to the NHS Collaboration Products held by NHS will revert to us. If we commit a material breach of the License Agreement, NHS may elect not to terminate the License Agreement but instead apply specified adjustments to its payment obligations and other terms and conditions of the License Agreement. If NHS were to make such adjustments, the funding from and benefits of the License Agreement could be diminished, which could adversely affect our financial condition. Unless the License Agreement is terminated by us for NHS' uncured material breach, upon termination of the License Agreement, NHS will be eligible to receive post-termination royalties from us until NHS has recouped certain development costs related to the NHS Collaboration Products and specified percentages of any milestone payments paid to us under the License Agreement prior to termination, which could have a material adverse effect on our business.

Termination of the License Agreement could cause significant delays in our product development and commercialization efforts that could prevent us from commercializing our CDI and IBD product candidates, including SER-109 and SER-287, outside of

the United States and Canada, without first expanding our internal capabilities or entering into another agreement with a third party. Any alternative collaboration or license could also be on less favorable terms to us. In addition, under the License Agreement, NHS agreed to provide funding for certain clinical development activities. If the License Agreement were terminated, we may need to refund those payments and seek additional financing to support the research and development of any terminated products or discontinue any terminated products, which could have a material adverse effect on our business.

Under the License Agreement, we are dependent upon NHS to successfully commercialize any NHS Collaboration Products, including SER-109 and SER-287, outside of the United States and Canada. We cannot directly control NHS' commercialization activities or the resources it allocates to our product candidates. Our interests and NHS' interests may differ or conflict from time to time, or we may disagree with NHS' level of effort or resource allocation. NHS may internally prioritize our product candidates differently than we do or it may not allocate sufficient resources to effectively or optimally commercialize them. If these events were to occur, our business would be 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 failing to meet deadlines for the completion of such trials.

We expect to continue to rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct and manage our clinical trials.

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 practices, 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 with which we must comply. 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 and may not be able to, or may be delayed in our efforts to, successfully commercialize 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 our products, producing additional losses and depriving us of potential product revenue.

We rely on third parties for the manufacture of our product candidates for pre-clinical and clinical testing and expect to continue to do so for the foreseeable future. This 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 rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for pre-clinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on 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:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of manufacturing agreements by the third-party manufacturers;
- failure to manufacture our product according to our specifications;

- failure to manufacture our product according to our schedule or at all;
- misappropriation or disclosure of our proprietary information, including our trade secrets and know-how; 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 processes, 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. The contract manufacturer we rely on to produce SER-109 and SER-287 has never produced a FDA-approved therapeutic. If our contract manufacturer is unable to comply with cGMP regulation or if the FDA does not approve their facility upon a pre-approval inspection, our therapeutic candidates 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. Except for a backup facility in California, 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 SER-109 product. 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 anticipated future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts.

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 Cambridge location where we conduct process development, scale-up activities and a portion of the manufacture of Ecobiotic microbiome therapeutics. 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 meet cGMP. We do not have any manufacturing facilities that meet the FDA’s cGMP requirements for the production of any product candidates used in humans.

We may establish a manufacturing facility for our product candidates for production at a commercial scale. 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. We expect our new headquarters in Cambridge, MA to expand our existing clinical supply manufacturing capabilities. 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 facility, 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, hospitals, 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. For example, current CDI treatment involves the use of antibiotics that are well established in the medical community or the use of fecal microbiota transplantation, or FMT, and physicians may continue to rely on these treatments. If our product candidates receive approval but do not achieve an adequate level of

acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our approved 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 products 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 products together with other medications;
- interactions of our products with other medicines patients are taking; and
- inability of certain types of patients to take our product.

We currently have a limited 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 have limited sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product 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 products 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.

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

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 is highly competitive and is characterized by rapid and substantial technological development and product innovations. 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. We are aware of a number of large pharmaceutical and biotechnology companies, as well as smaller, early-stage companies, that are pursuing the development of products, including microbiome therapeutics, for the prevention of CDI and other disease indications we are targeting. 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, FMT is a procedure that has resulted in high cure rates for recurrent CDI and our competitors and physicians may continue to seek to standardize and implement this procedure. 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, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement and 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 and reimbursement policies, any of which would harm our business.

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and 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 impact reimbursement levels.

Obtaining and maintaining adequate reimbursement for our products may be difficult. 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, drugs. 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 drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. 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, and the royalties resulting from the sales of those products may also be adversely impacted.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that a drug 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 drugs, 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 drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost treatment approaches and may be incorporated into existing payments for other services. Net prices for drugs 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 drugs 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 drug 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 drug before it can be reimbursed. 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;
- 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 $3.0 million in product liability insurance coverage in the aggregate, with a per occurrence limit of $3.0 million, 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.

We may face competition from biosimilars, which may have a material adverse impact 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, or BCPIA, enacted in 2010 as part of the Patient Protection and Affordable Care Act, 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. 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. 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.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. In each of his proposed budgets for fiscal years 2013 through 2015, President Obama has 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." It is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity. The BCPIA is complex and only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact is subject to uncertainty. The FDA has issued several guidance documents to date discussing the biosimilar pathway, and the FDA approved the first biosimilar under the BCPIA in March 2015. However, several issues still remain unclear with respect to the FDA's final implementation of the BCPIA, and such FDA implementation could have a material adverse effect on the future commercial prospects for our product candidates.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

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

In order to market and sell our products in the European Union, or EU, and many other jurisdictions, we or our collaborators must 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 be approved for reimbursement

before the product 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 products in any market.

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 unanticipated 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 specific conditions of approval, including a requirement to implement a risk evaluation and mitigation strategy, or REMS, which could include requirements for a medication guide, communication plan, or restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, 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 drugs 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 unanticipated 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 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 similar EU requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with 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.

Our relationships with customers, physicians and third-party payors will 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 governmental healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors, physicians 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 for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons 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 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 federal False Claims Act (described below);
- the federal False Claims Act imposes criminal and civil penalties, including 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, imposes criminal and civil liability for executing 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 these statutes or specific intent to violate them to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members; manufacturers are required to submit reports to the government by the 90th day of each calendar year;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, 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 and may 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 that govern 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.

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. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements.

Efforts to ensure that our business arrangements with third parties will 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 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 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, and the curtailment or restructuring of our operations.

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.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The MMA expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs. In addition, the MMA authorized Medicare Part D prescription drug plans to limit the number of drugs that will be covered in any therapeutic class in their formularies. The MMA's cost reduction initiatives and other provisions could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in Medicare reimbursement may result in a similar reduction in payments from private payors. Similar regulations or reimbursement policies may be enacted in international markets which could similarly impact our business.

More recently, in 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, 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 Affordable Care Act of importance to our potential product candidates are the following:

- establishment of a new pathway for approval of lower-cost biosimilars to compete with biologic products, such as those we are developing;
- 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;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti- Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
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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 Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, 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 years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on

April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria 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 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 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.

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

In some countries, particularly the countries of the EU, 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. 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 negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various EU member states and parallel distribution or arbitrage between low-priced and high- priced member states, 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. If coverage and reimbursement of our products 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 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 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 chemicals and biological materials such as human stool. 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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our Intellectual Property

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

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 state 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, financial condition and operating results.

If, in the future, we obtain licenses from third parties, 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, if we do obtain necessary licenses, we will likely have obligations under those 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.

Our patent portfolio is in the early stages of prosecution. We currently have four issued U.S. patents. Although we have numerous patent applications pending, substantive prosecution has begun in only a small number of those applications. We cannot provide any assurances that any of our 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. For example, we are pursuing claims to therapeutic, binary compositions of certain bacterial populations. Any claims that may issue may provide coverage for such binary compositions and/or their use. However, such claims would not prevent a third party from commercializing alternative compositions that do not include both of the bacterial populations claimed in pending applications, potential applications or patents that have or may issue. There can be no assurance that any such alternative composition will not be equally effective. Further, given that our SER-109 product candidate is a complex composition with some variation from lot-to-lot and that, likewise, third-party compositions may have similar

complexity and variability, it is possible that a patent claim may provide coverage for some but not all lots 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 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 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 which 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 United States 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 products 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.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by any existing patent and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe or design around our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued, will be found to ultimately be valid and enforceable;
- third parties will not compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we will be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents or proprietary rights of others.

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.

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

In addition to seeking patents for some of our technology and product candidates, we also utilize 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.

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

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, only 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 will require us to be cognizant going forward 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 United States 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 United States Congress, or the USPTO, may change the standards of patentability and any such changes could have a negative impact on our business.

A number of recent cases decided by the Supreme Court have involved questions of when claims reciting abstract ideas, laws of nature, natural phenomena and/or natural products are eligible for a patent, regardless of whether the claimed subject matter is

otherwise novel and inventive. These cases include Association for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 12-398 (2013) or Myriad; Alice Corp. v. CLS Bank International, 573 U.S. 13-298 (2014); and Mayo Collaborative Services v. Prometheus Laboratories, Inc., or Prometheus, 566 U.S. 10-1150 (2012). In response to these cases, the USPTO has issued guidance to the examining corps.

The full impact of these decisions is not yet known. The Myriad decision, issued on June 13, 2013, is the most recent Supreme Court decision to address patent eligibility of natural products. Our current product candidates include natural products, therefore, this decision and its interpretation by the courts and the USPTO may impact prosecution, defense and enforcement of our patent portfolio. In Myriad, the Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA, or cDNA, molecules, which are not genomic sequences, may be patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the Myriad and Prometheus decisions. The guidance did not limit the application of Myriad to DNA but, rather, applied the decision broadly to other natural products, which may include our product candidates. The March 4, 2014 memorandum and the USPTO's interpretation of the cases and announced examination rubric received widespread criticism from stakeholders during a public comment period and was superseded by interim guidance published on December 15, 2014. Additional guidance was published in July 2015 (July 2015 Update: Subject Matter Eligibility). The USPTO's interpretation of the case law and new guidelines for examination may influence, possibly adversely, prosecution and defense of certain types of claims in our portfolio.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by 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.

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, products or use of our products do not infringe third-party patents.

We are aware of numerous patents and pending applications owned by third parties 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 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 products or the use of our products. We are aware of several pending patent applications containing one or more claims that could be construed to cover some of our product candidates or technology, should those claims issue in their original form or in the form presently being pursued. In addition, we are aware of a third-party patent family that includes issued and allowed patents, including in the United States, with claims that, if valid and enforceable, could be construed to cover some of our product candidates or their methods of use.

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 products 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 products 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 these 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 products. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. 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;
- 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.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

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 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 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 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 a material 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.

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 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 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 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. 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 candidates, the relevant statutory deadlines have not yet expired. Therefore, for each of the patent families that we believe provide coverage for our lead product candidates, we will need to decide whether and where to pursue protection outside the United States. 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, even if we do elect to pursue patent rights outside the United States, 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 that in the United States. These products may compete with our products 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 products, 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.

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 Roger Pomerantz, our President and Chief Executive Officer and Chairman of the Board of Directors, as well as the other principal members of our management, scientific and clinical team, including Eric Shaff, our Chief Financial Officer and Executive Vice President, David Cook, our Chief Scientific Officer and Executive Vice President of Research & Development, John Aunins, our Chief Technology Officer and Executive Vice President of Bioprocess & Manufacturing, Michele Trucksis, our Chief Medical Officer and Executive Vice President, Wael Hashad, our Chief Commercial Officer, and Executive Vice President, and Matthew Henn, our Head of Drug Discovery & Bioinformatics and Senior Vice President. Although we have entered into employment agreements with 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 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 products. 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 operational 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 anticipated 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 anticipated 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 internationally could materially adversely affect our business.

We currently have limited international operations, but our business strategy incorporates potentially expanding internationally if any of our product candidates receive regulatory approval. We currently plan to rely on collaborators, including NHS, to commercialize any approved products outside of the United States. Doing business 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;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;

- limits in 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 products and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions;
- certain expenses including, among others, expenses for travel, translation and insurance; 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 U.S. Foreign Corrupt Practices Act, or 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.

Our business and operations would suffer in the event of information technology and other 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.

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

We may acquire other businesses, products 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 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;
- unanticipated 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 anticipated 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

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

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 price you paid for your common stock. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or anticipated 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 any future collaborations;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and may 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 anticipated 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.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 70.2% of our outstanding voting stock. As a result, if these stockholders were to 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 and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or

- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

A significant portion of our total outstanding shares are eligible to be sold into the market, 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. Approximately 30.5 million shares of our common stock recently became eligible to be sold into the market, unless held by one of our affiliates, in which case the resale of those securities is subject to volume limitations under Rule 144 of the Securities Act. Moreover, holders of an aggregate of approximately 22.9 million shares of our common stock as of the completion of the initial public offering of our common stock on July 1, 2015 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 have also registered and intend to continue 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.

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 that term is used 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 the initial public offering of our common stock. 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;
- 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 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 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 continue to incur increased costs as a result of being a public company, and our management will continue to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we have incurred and will continue to 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 Select 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 devote and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and 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 maintain 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.

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 and 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 that 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 issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. 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 clinical studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail 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 amended 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 amended and restated bylaws 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:

- 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 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. Furthermore, our restated certificate of incorporation 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 actions brought against us by stockholders. 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 and officers. 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.

Because we do not anticipate 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. 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.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Research and Offices

Our corporate headquarters are located in Cambridge, Massachusetts, where we currently sublease approximately 7,461 square feet of office space under a sublease that expires in May 2016. We also maintain a research and development facility in Cambridge, Massachusetts, where we lease approximately 13,568 square feet of space for

office and laboratory facilities under a lease that expires in January 2018 and approximately 7,484 square feet under a lease that expires in April 2020.

We have entered into a lease for 83,396 square feet of office, laboratory and pilot manufacturing space at in Cambridge, Massachusetts. The lease term is expected to commence in March 2016 and end in November 2023, and we expect to move our corporate headquarters to this location in mid-2016.

Clinical Manufacturing

We currently conduct part of our manufacturing operations in our leased laboratory facilities in Cambridge, Massachusetts. We believe our current laboratory facilities and contract relationships are sufficient to meet our current bioprocess development and

manufacturing needs. During the fourth quarter of 2015, we entered into a lease for 83,396 square feet of office, laboratory and pilot manufacturing space in Cambridge, Massachusetts, that will also house our corporate headquarters. We expect the pilot facility will represent an important addition to our existing manufacturing network by broadening our capabilities in bioprocess development and manufacturing, in particular, the production of synthetic microbiome candidates. We expect to utilize our new manufacturing facility to prepare for commercialization of SER-109, SER-262, SER-287, SER-155. Other product candidates may be brought into the facility for economies of operation, or may remain external with contract manufacturing organizations, depending on business dynamics and development needs.

We plan to control the production of SER-109 under current good manufacturing practices by making strategic investments in manufacturing, which may include collaborations with third parties, the design and renovation of existing facilities and the construction of additional new facilities.

Item 3. Legal Proceedings

We are not party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

Executive Officers of the Registrant

Roger J. Pomerantz, M.D., has served as our President and Chief Executive Officer since June 2014 and as Chairman of our board of directors since November 2013. Since July 2014, Dr. Pomerantz has been a Senior Partner at Flagship Ventures, an early-stage venture capital firm. From January 2011 to September 2013, Dr. Pomerantz was Worldwide Head of Licensing and Acquisitions and Senior Vice President at Merck & Co., Inc., or Merck, a pharmaceutical company, where he oversaw licensing and acquisitions for Merck Research Laboratories, the research and development division of Merck. From February 2010 to February 2013, Dr. Pomerantz served as Global Head of Infectious Diseases and Senior Vice President at Merck, where he oversaw pharmaceutical development and discovery of antibiotics, antivirals, antifungals and antiparasitic agents. Prior to Merck, Dr. Pomerantz was Global Head of Infectious Diseases for the pharmaceutical division of Johnson & Johnson, Inc., a multinational medical device, consumer goods and pharmaceutical corporation, where he was responsible for anti-infective agents worldwide. He joined Johnson & Johnson, Inc. in August 2005 as President of Tibotec Pharmaceuticals, Inc., now Janssen Therapeutics and a subsidiary of Johnson & Johnson, Inc., a pharmaceutical company focused on the treatment of infectious diseases. Dr. Pomerantz has developed nine approved infectious disease drugs for diseases including HIV, HCV and tuberculosis. He also serves on the board of directors of Contrafect Corporation. Dr. Pomerantz received his B.A. in Biochemistry from The Johns Hopkins University and his M.D. from The Johns Hopkins School of Medicine. We believe Dr. Pomerantz's extensive academic and clinical experience, as well as his knowledge of the pharmaceutical industry, qualifies him to serve on our board of directors.

John G. Aunins, Ph.D., has served as our Chief Technology Officer and Executive Vice President of Bioprocess Development since December 2012. Prior to joining our company, Dr. Aunins served on our Scientific Advisory

Board from February 2012 to December 2012. From April 1989 to November 2011, Dr. Aunins served in various roles at Merck, most recently as Executive Science Director. At Merck, Dr. Aunins led process and product development teams for six licensed vaccines and multiple vaccine candidates. He is a Fellow of the American Institute for Medical and Biological Engineering and an adjunct Full Professor at the Instituto de Tecnologia Quimica e Biologica in Oeiras, Portugal. Dr. Aunins received his B.S. from the University of Kansas and his Ph.D. in Chemical Engineering from the Massachusetts Institute of Technology.

David N. Cook, Ph.D., has served as our Chief Scientific Officer and Executive Vice President of Research & Development since October 2012. From February 2010 to October 2012, Dr. Cook was the Chief Operating Officer at the International AIDS Vaccine Initiative, a global not-for-profit, research and development organization focused on the development of a safe and accessible vaccine for HIV. As Chief Operating Officer, Dr. Cook acted as the head of operations, overseeing seven international offices and research facilities. Dr. Cook received his A.B. from Harvard College and his Ph.D. in Chemistry from the University of California, Berkeley.

Eric D. Shaff has served as our Chief Financial Officer and Executive Vice President since November 2014. From January 2012 to November 2014, Mr. Shaff was Vice President of Corporate Finance for Momenta Pharmaceuticals, a biotechnology company, where he helped manage Momenta’s accounting, finance, planning, and procurement functions, as well as contributing to Momenta’s investor relations efforts. From June 2004 to December 2011, Mr. Shaff held a number of corporate development and finance positions with Genzyme Corporation, a biotechnology company, most recently as Vice President of Finance/Controller for the

Personalized Genetic Health division. Mr. Shaff received his B.A. from the University of Pennsylvania and his MBA from Cornell University.

Michele Trucksis, Ph.D., M.D., has served as our Chief Medical Officer and Executive Vice President since January 2015. Dr. Trucksis was an Associate Clinical Professor at Harvard Medical School from January 2005 to April 2015. From December 2006 to December 2014, Dr. Trucksis held various positions of increasing seniority at Merck Research Laboratories, the research and development division of Merck. Most recently, from June 2014 to December 2014, Dr. Trucksis served as Executive Director, Team Leader & Clinical Lead, Antifungals and Antibacterials where she was responsible for medical, clinical and global product development and strategy. From July 2011 to June 2014, Dr. Trucksis was Project Leader, Antifungals and Antibacterials, and from December 2006 to July 2011, she was Director in Clinical Pharmacology. Dr. Trucksis received her B.S. in Medical Technology from Youngstown State University, her Ph.D. in Biochemistry from Kent State University and her M.D. from Case Western Reserve University School of Medicine.

Wael Hashad has served as our Chief Commercial Officer since January 2016. He has over 20 years of experience as a commercial leader and has held senior marketing and general management positions in the pharmaceutical and biotechnology industry. Prior to joining Seres, from July 2013 to September 2015, he served as Vice President and General Manager for Middle East and Africa at Amgen, Inc., a pharmaceutical company, where he lead a team of more than 200 to expand markets, launch new products and grow existing products. Prior to that he served as Vice President – Regional Commercial Head for Japan, China and Asia Pacific at Amgen, from October 2012 to June 2013, where he expanded commercial opportunities through strategic partnerships and implementation of go-to-market strategies. From August 2011 to June 2013, Mr. Hashad was Vice President – Head of Global Marketing for General Medicine at Amgen, where he optimized the launch of Repatha (Evolocumab). Prior to Amgen, Mr. Hashad worked at Boehringer Ingelheim, a pharmaceutical company, from April 2009 to August 2011, as Vice President – US Cardiovascular and Metabolic Disorders and at Eli Lilly, a pharmaceutical company, from 1989 to 2009, where he held various roles. At Boehringer Ingelheim and Eli Lilly, Mr. Hashad launched several products in the U.S., most notably Pradaxa® and Cymbalta®. Mr. Hashad earned his B.Sc. in Pharmacy and Pharmaceutical Sciences from the University of Cairo and his MBA from the University of Akron.

Directors of the Registrant

Noubar B. Afeyan, Ph.D., has served as a member of our board of directors since October 2010. Since 1999, Dr. Afeyan has served as the Managing Partner and Chief Executive Officer of Flagship Ventures, an early-stage venture capital firm that he co-founded. Dr. Afeyan is serving or has served on the board of directors of several public and private companies, including BG Medicine, Inc., BIND Therapeutics, Inc., Eleven Biotherapeutics, Inc., Helicos Biosciences, Moderna Therapeutics, Inc. and Pronutria Biosciences, Inc. Dr. Afeyan received a B.S. from McGill University and a Ph.D. in Biochemical Engineering from the Massachusetts Institute of Technology. We believe Dr. Afeyan is qualified to serve on our board of directors because of his extensive investment experience and his knowledge of the biotechnology industry.

Dennis A. Ausiello, M.D., has served as a member of our board of directors since April 2015. Dr. Ausiello serves as the Director of the Center for Assessment Technology and Continuous Health (CATCH), Jackson Distinguished Professor of Clinical Medicine at Harvard Medical School and Physician-in-Chief Emeritus at Massachusetts General Hospital. From 1996 to April 2013, Dr. Ausiello served as the Chief of Medicine at Massachusetts General Hospital. Dr. Ausiello is a member of the Institute of Medicine of the National Academy of Sciences and a fellow of the American Academy of Arts and Sciences. Dr. Ausiello has also served on the board of directors of Pfizer Inc. since December 2006 and Alnylam Pharmaceuticals since April 2012, each a pharmaceutical company. Dr. Ausiello received his undergraduate degree from Harvard College and an M.D. from the University of Pennsylvania. We believe that Dr. Ausiello is qualified to serve on our board of directors because of his extensive experience as a physician and as a director of pharmaceutical companies.

Grégory Behar has served as a member of our board of directors since December 2014. Mr. Behar has served as Chief Executive Officer of Nestlé Health Science S.A., a health sciences company, since October 2014. From July 2011 to July 2014, Mr. Behar was President and Chief Executive Officer of Boehringer Ingelheim Pharmaceuticals Inc. (USA), a pharmaceutical company. From 2010 to July 2011, Mr. Behar was Corporate Vice President Region NECAR (North European Union, Canada and Australasia) for Boehringer-Ingelheim GmbH, a pharmaceutical company. Mr. Behar received his B.S. from the University of California, Los Angeles, a M.S. in Mechanical Engineering and Manufacturing from EPFL in Switzerland and an MBA from INSEAD in France. We believe that Mr. Behar is qualified to serve on our board of directors because of his extensive business experience in the health sciences and pharmaceutical industries.

Werner Cautreels, Ph.D., has served as a member of our board of directors since March 2013. Dr. Cautreels has served as President and Chief Executive Officer of Selecta Biosciences, a biotechnology company, since June 2010. From May 1998 to June 2010, Dr. Cautreels worked for Solvay Pharmaceuticals, the pharmaceutical division of the Solvay Group, which was acquired by Abbot Laboratories. Since 2009, Dr. Cautreels has served on the board of directors of Galapagos NV, a biotechnology company. Dr.

Cautreels received a B.S. and M.S. and a doctorate in Chemistry from the University of Antwerp and an eMBA from Harvard Business School. We believe Dr. Cautreels is qualified to serve on our board of directors because of his extensive experience in the biotechnology industry.

Peter Barton Hutt has served as a member of our board of directors since May 2013. Mr. Hutt is senior counsel at Covington & Burling LLP, specializing in food and drug law. Mr. Hutt has served as a member of the board of directors of Q Therapeutics, Inc. since 2002, Xoma Corporation since 2005, Concert Pharmaceuticals since 2006, BIND Therapeutics, Inc. since 2008 DBV Technologies since 2009 and Flex Pharma, Inc. since 2014. Mr. Hutt previously served on the board of directors of Momenta Pharmaceuticals, Inc., Celera Corporation, which was acquired by Quest Diagnostics in 2011, and ISTA Pharmaceuticals, which was acquired by Bausch & Lomb in 2012. Mr. Hutt received a B.A. from Yale University, an LL.B. from Harvard Law School and an LL.M. from the New York University School of Law. We believe that Mr. Hutt is qualified to serve on our board of directors because of his experience serving as a director of biotechnology companies and his legal and regulatory knowledge.

Richard N. Kender has served as a member of our board of directors since October 2014. From October 1978 to September 2013, Mr. Kender held positions in a variety of corporate areas at Merck, most recently serving as Senior Vice President of Business Development and Corporate Licensing. Mr. Kender serves on the board of directors of INC Research Holdings, Inc., a contract research organization, Poxel and Abide Therapeutics. Mr. Kender received a B.S. from Villanova University and an MBA from Fairleigh Dickinson University. We believe Mr. Kender is qualified to serve on our board of directors because of his extensive business experience and his knowledge of the pharmaceutical industry.

Lorence H. Kim, M.D., has served as a member of our board of directors since October 2014. Since April 2014, Dr. Kim has been the Chief Financial Officer of Moderna Therapeutics, a biotechnology company. From July 2000 to April 2014, Dr. Kim held a number of positions at Goldman, Sachs & Co., an investment bank, most recently as Managing Director and Co-Head of Biotechnology Investment Banking. Dr. Kim received an A.B. from Harvard University, an MBA in Healthcare Management from the Wharton School of the University of Pennsylvania and an M.D. from the University of Pennsylvania’s School of Medicine. We believe Dr. Kim is qualified to serve on our board of directors because of his finance experience and knowledge of the biotechnology industry.

Kurt C. Graves has served on our Board of Directors since November 2015. Mr. Graves has been the Chairman, President and Chief Executive Officer of Intarcia Therapeutics, a biotechnology company, since April 2012. Mr. Graves served as Executive Chairman of Biolex Therapeutics, a biotechnology company, from November 2010 to March 2012, and served as Executive Chairman of Intarcia Therapeutics from August 2010 to April 2012. Previously, he served as Executive Vice President, Chief Commercial Officer and Head of Strategic Development at Vertex Pharmaceuticals Inc. from July 2007 to October 2009. Prior to joining Vertex, Mr. Graves held various leadership positions at Novartis pharmaceuticals from 1999 to June 2007. He was also the first Chief Marketing Officer for the Pharmaceuticals division from September 2003 to June 2007. He currently serves as a director of Intarcia Therapeutics, Radius Health, Pulmatrix Therapeutics and Achillion Pharmaceuticals. Mr. Graves received a B.S. in Biology from Hillsdale College. We believe Mr. Graves is qualified to serve as a member of our Board of Directors because of his extensive experience in the life sciences industry, membership on various boards of directors and his leadership and management experience

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock has been traded on the Nasdaq Global Select Market under the symbol "MCRB" since our initial public offering on June 26, 2015. Prior to this time, there was no public market for our common stock. The following table shows the high and low sale prices per share of our common stock as reported on the Nasdaq Global Select Market for the periods indicated:

	High	Low
2015		
Second Quarter 2015 (beginning June 26, 2015)	$51.40	$28.11
Third Quarter 2015	$52.00	$26.95
Fourth Quarter 2015	$44.51	$25.00

On March 7, 2016, the last reported sale price for our common stock on the Nasdaq Global Select Market was $29.60 per share.

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on our common stock between June 26, 2015 (the date of our initial public offering) and December 31, 2015, with the cumulative total return of (a) the Nasdaq Biotechnology Index and (b) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 on June 26, 2015 in our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and assumes the reinvestment of dividends, if any. The graph assumes our closing sales price on June 26, 2015 of $51.40 per share as the initial value of our common stock and not the initial offering price to the public of $18.00 per share.

Holders

As of March 7, 2016, there were approximately 33 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

Use of Proceeds from Registered Securities

On July 1, 2015, we completed the initial public offering of our common stock and issued and sold 8,545,138 shares of our common stock at a public offering price of $18.00 per share, including 1,114,583 shares of our common stock pursuant to the underwriters' full exercise of their option to purchase additional shares of our common stock. We received aggregate net proceeds of

approximately $139.3 million after deducting underwriting discounts and commissions of $10.8 million and offering expenses of $3.7 million.

The offer and sale of all of the shares in the offering was registered under the Securities Act of 1933, as amended, pursuant to a registration statement on Form S-1 (File No. 333-204484), which was declared effective by the SEC on June 25, 2015, and a registration statement on Form S-1MEF (File No. 333-205238), which was automatically effective upon filing with the SEC on June 25, 2015. On September 17, 2015, we made a payment of $1.8 million to Comerica Bank to satisfy all amounts owed under our loan and security agreement. The payoff amount was comprised of $1.7 million of outstanding principal under the loan and security agreement and $0.1 million of final payment fees and accrued interest. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 26, 2015.

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

There were no repurchases of shares of common stock made during the quarter ended December 31, 2015.

Item 6. Selected Consolidated Financial Data

The following selected consolidated financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” our consolidated financial statements and related notes, and other financial information included in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2015, 2014 and 2013 and the consolidated balance sheet data as of December 31, 2015 and 2014 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The consolidated statement of operations data for the year ended December 31, 2012 and the consolidated balance sheet data as of December 31, 2013 and 2012 are derived from our audited consolidated financial statements that are not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results that should be expected in the future.

	Year Ended December 31,			
	2015	2014	2013	2012
	(in thousands, except per share data)			
Consolidated Statement of Operations Data:				
Revenue	$—	$—	$—	$—
Operating expenses:				
Research and development	38,095	10,718	4,805	2,077
General and administrative	16,761	4,364	1,247	956
Total operating expenses	54,856	15,082	6,052	3,033
Loss from operations	(54,856)	(15,082)	(6,052)	(3,033)
Other income (expense):				
Interest income	638	—	—	—
Interest expense	(555)	(209)	(42)	(93)
Revaluation of preferred stock warrant liability	(7)	(1,418)	(8)	—

Total other income (expense), net	76	(1,627)	(50)	(93)
Net loss	(54,780)	(16,709)	(6,102)	(3,126)
Accretion of convertible preferred stock to redemption value	—	(1,291)	(875)	(276)
Net loss attributable to common stockholders	$(54,780)	$(18,000)	$(6,977)	$(3,402)
Net loss per share attributable to common stockholders, basic and diluted[1]	$(2.33)	$(2.67)	$(1.09)	$(0.59)

(1) See Note 11 to our consolidated financial statements appearing at the end of this annual report on Form 10-K for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

	As of December 31,			
	2015	2014	2013	2012
	(in thousands)			
Consolidated Balance Sheet Data:				
Cash and cash equivalents	$73,933	$114,185	$1,654	$6,215
Investments	131,149	—	—	—
Working capital[(1)]	196,690	109,140	649	6,067
Total assets	216,900	117,345	2,125	6,538
Preferred stock warrant liability	—	1,582	164	—
Long-term debt, net of discount, including current portion	—	2,504	838	—
Convertible preferred stock[(2)]	—	136,077	11,583	10,708
Total stockholders' equity (deficit)	205,394	(26,721)	(11,116)	(4,348)

(1) We define working capital as current assets less current liabilities.

(2) Convertible preferred stock was converted into our common stock upon the listing of our common stock on NASDAQ on June 26, 2015. See Note 8 to our consolidated financial statements appearing at the end of this annual report on Form 10-K for further details.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of financial condition and results of operations together with Item 6 "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in Item 1A. Risk Factors.

Overview

We are a microbiome therapeutics platform company developing a novel class of biological drugs, which are designed to treat disease by restoring the function of a dysbiotic microbiome. Our lead product candidate, SER-109, is designed to prevent further recurrences of Clostridium difficile infection, or CDI, a debilitating infection of the colon, by treating the dysbiosis of the colonic microbiome and, if approved by the U.S. Food and Drug Administration, or FDA, could be a first-in-field drug. Using our microbiome therapeutics platform, we are developing additional product candidates, including SER-262 to prevent an initial recurrence of primary CDI, SER-287 to treat inflammatory bowel disease, or IBD, including ulcerative colitis and SER-155 to treat enteric bacterial pathogens. We are also conducting research on metabolic diseases, such as early-stage, non-insulin dependent diabetes; non-alcoholic steatohepatitis; obesity and metabolic syndrome; other inflammatory diseases, such as Crohn's disease; cancer chemotherapy and immune suppression; rare genetic diseases; and immune-oncology related applications.

Since our inception in October 2010, we have devoted substantially all of our resources to developing SER-109, researching SER-262 and SER-287, building our intellectual property portfolio, developing our supply chain, business planning, raising capital and providing general and administrative support for these operations. From our inception through June 30, 2015, we had financed our operations through private placements of our convertible preferred stock, the issuance of convertible promissory notes and borrowings under a loan and security agreement with Comerica Bank, or the loan and security agreement. Through June 30, 2015, we had received gross proceeds of $137.0 million from such transactions.

On July 1, 2015, we completed an initial public offering, or IPO, of our common stock, and issued and sold 8.5 million shares of common stock at a public offering price of $18.00 per share, resulting in net proceeds of approximately $139.3 million after deducting underwriting discounts and commissions and offering expenses. Upon the listing of our common stock on The NASDAQ Global Select Market, or NASDAQ, on June 26, 2015, all outstanding shares of our convertible preferred stock automatically converted into 22.9 million shares of our common stock. The shares issued upon closing of the IPO included 1.1 million shares of our common stock, pursuant to the underwriters' full exercise of their option to purchase additional shares of common stock.

As of December 31, 2015 we had repaid all amounts of the total $3.0 million borrowed under the loan and security agreement.

We are a development stage company and have not generated any revenue. All of our product candidates other than SER-109 and SER-287 are still in pre-clinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Since our inception, we have incurred significant operating losses. Our net loss was $6.1 million for the year ended December 31, 2013, $16.7 million for the year ended December 31, 2014 and $54.8

million for the year ended December 31, 2015. As of December 31, 2015, we had an accumulated deficit of $82.6 million.

We expect that our expenses will increase substantially in connection with our ongoing activities, particularly as we:

- advance the clinical development of SER-109 for the prevention of further recurrences of CDI in patients suffering from recurrent CDI, through a Phase 2 clinical study and beyond;
- initiate clinical development of SER-262 to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI;
- continue the Phase 1b clinical study of SER-287 for the treatment of ulcerative colitis;
- conduct research and continue pre-clinical development of additional Ecobiotic microbiome therapeutics, including SER-155 for the treatment of enteric bacterial pathogens;
- make strategic investments in manufacturing capabilities, including potentially planning and building a small-scale commercial manufacturing facility;

- maintain our current intellectual property portfolio and opportunistically acquire complementary intellectual property; and
- seek to obtain regulatory approvals for our product candidates.

In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company.

As a result, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

In January 2016 we entered into a Collaboration and License Agreement, or the License Agreement, with Nestec Ltd., or NHS, for the development and commercialization of certain of our product candidates in development for the treatment and management of CDI and IBD, including ulcerative colitis and Crohn's disease. The License Agreement will support the development of our portfolio of products for CDI and IBD in markets outside of the United States and Canada, or the Licensed Territory, and is expected to provide substantial financial support for our ongoing research and development. We have retained full commercial rights to our entire portfolio of product candidates with respect to the United States and Canada, where we plan to build our own commercial organization.

Under the License Agreement, we granted to NHS an exclusive, royalty-bearing license to develop and commercialize, in the Licensed Territory, certain products based on our microbiome technology that are being developed for the treatment of CDI and IBD, including SER-109, SER-262, SER-287 and SER-301, or, collectively, the NHS Collaboration Products. We also granted to Nestlé a non-exclusive license to export, develop and make NHS Collaboration Products in the licensed fields worldwide solely for commercialization in the licensed fields and in the Licensed Territory.

In exchange for the license, NHS is obligated to pay the Company an upfront cash payment of $120 million, which the Company received in February 2016. NHS has also agreed to pay the Company tiered royalties, at percentages ranging from the high single digits to high teens, of net sales of NHS Collaboration Products in the Licensed Territory. Additionally, NHS has agreed to pay the Company up to $660 million for the achievement of certain development and regulatory milestones and up to an aggregate of $1.125 billion for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products. We expect to receive a total of $30 million in milestone payments in 2016 associated with the planned initiation of a Phase 1b study for SER-262 in CDI and the anticipated initiation of the Phase 3 clinical trial for SER-109 in CDI. The full potential value of the up-front payment and milestone payments payable by NHS is over $1.9 billion, assuming all products receive regulatory approval and are successfully commercialized. NHS is also obligated to pay some of the costs related to our clinical trials. See "—Liquidity and Capital Resources."

We expect that our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements well into 2018. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future.

Operating Expenses

Our operating expenses since inception have consisted primarily of research and development activities and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, which include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, pre-clinical activities and clinical trials on our behalf as well as contract manufacturing organizations, or CMOs, that manufacture drug products for use in our pre-clinical and clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel in our research and development functions;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the cost of laboratory supplies and acquiring, developing and manufacturing pre-clinical study and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

Our primary focus of research and development since inception has been on our microbiome therapeutics platform and the subsequent development of SER-109, SER-287 and SER-262. Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to investigators, consultants and CROs in connection with our pre- clinical studies and clinical trials and regulatory fees. We do not allocate employee-related costs and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under development and, as such, are classified as costs of our microbiome therapeutics platform research, along with external costs directly related to our microbiome therapeutics platform.

The table below summarizes our research and development expenses incurred on our platform and by product development program.

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Microbiome therapeutics platform	$20,603	$7,584	$3,424
SER-109	13,828	3,122	729
SER-262	1,549	12	652
SER-287	2,115	—	—
Total research and development expenses	$38,095	$10,718	$4,805

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we advance the clinical development of SER-287 and initiate clinical trials for certain product candidates, including SER-262, continue to discover and develop additional product candidates, including SER-155, and pursue later stages of clinical development of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs.

Other Income (Expense), Net

Interest Income. Interest income consists of interest earned on our cash, cash equivalents and investments.

Interest Expense. Interest expense consists of interest expense incurred on our debt. During the years ended December 31, 2015, 2014 and 2013, interest expense consisted of interest at the stated rate on borrowings under our loan and security agreement, amortization of deferred financing costs and interest expense related to the accretion of debt discount associated with (1) the fair value of preferred stock warrant we issued in connection with the loan and security agreement and (2) a final payment due at maturity.

Revaluation of Preferred Stock Warrant Liability. Revaluation of preferred stock warrant liability consists of the net gain or loss associated with the change in the fair value of our preferred stock warrant liability. In connection with the loan and security agreement, we issued a warrant for the purchase of our Series A-2 convertible preferred stock, which we believe is a financial instrument that may have required a transfer of assets because of the redemption feature of the underlying stock. Therefore, we classified this warrant as a liability that we re-measured to fair value at each reporting period, and we recorded the changes in the fair value as a component of other income (expense), net. Upon the listing of our common stock on the NASDAQ on June 26, 2015, the preferred stock warrant became a warrant to purchase common stock. The Company performed the final mark to market adjustment on the preferred stock warrant using the fair value of the underlying common shares of $18.00 per share on June 26, 2015 and recorded the change in fair value in other income (expense), net in the consolidated statement of operations and comprehensive loss. The preferred stock warrant liability was then reclassified to additional paid-in-capital as it became a warrant to purchase common stock.

Income Taxes

Since our inception in 2010, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2015, we had federal and state net operating loss carryforwards of $65.4 million and $64.3 million, respectively, both of which begin to expire in 2031. As of December 31, 2015, we also had federal and state research and development tax credit carryforwards of $3.0 million and $1.3 million, respectively, which begin to expire in 2031 and 2027, respectively.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles, or GAAP, in the United States of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an

ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

Accrued Research and Development 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 open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research services on our behalf and clinical trials;
- investigative sites or other providers in connection with clinical trials;

- vendors in connection with pre-clinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of pre-clinical and clinical supplies.

We base our expenses related to pre-clinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs that conduct and manage clinical trials 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. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated 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 or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, 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 us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

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.

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. Use of this model requires that we make assumptions as to the volatility of our common stock, the expected term 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. Because we lack company-specific historical and implied volatility information, we estimate our expected volatility based on the historical volatility of a group of publicly traded peer companies. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. We use the simplified method prescribed by Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term of options granted to employees and directors. We base the expected term of options granted to consultants and non-employees on the contractual term of the options. We determine the risk-free interest rate by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

The assumptions we used to determine the fair value of stock options granted to employees and directors are as follows, presented on a weighted average basis:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.80%	1.83%	1.27%
Expected term (in years)	6.0	6.0	6.0
Expected volatility	81.4%	83.5%	85.9%
Expected dividend yield	0 %	0 %	0 %

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment.

We recognize compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures.

The following table summarizes the classification of our stock-based compensation expenses recognized in our consolidated statements of operations:

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Research and development	$5,297	$1,068	$177
General and administrative	4,397	1,000	32
	$9,694	$2,068	$209

Fair value of stock options

Prior to our IPO, the estimated fair value of our common stock was determined contemporaneously by our board of directors based on valuation estimates provided by management and prepared in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, or AICPA Practice Aid, as well as independent third-party valuations. Our contemporaneous valuations of our common stock were based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which we sold shares of preferred stock, the superior rights and preferences of securities senior to our common stock at the time of each grant and the likelihood of achieving a liquidity event such as an IPO. Consequently, after the IPO the fair value of the shares of common stock underlying the stock options is the closing price on the option grant date.

Valuation of Warrant to Purchase Convertible Preferred Stock

We classified a warrant to purchase shares of our Series A-2 convertible preferred stock as a liability on our balance sheets as this warrant is a free-standing financial instrument that may require us to transfer assets upon exercise. The warrant was initially recorded at fair value on date of grant, and it was subsequently remeasured to fair value at each balance sheet date. Changes in fair value of this warrant were recognized as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss.

We used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the preferred stock warrant. We assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying Series A-2 convertible preferred stock, the remaining contractual term of the warrant, risk-free interest rate, 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 our most recent sales of our convertible preferred stock, results obtained from third-party valuations and additional factors that we deemed relevant. We have historically been a private company and lack company-specific historical and implied volatility information of our stock. Therefore, we estimated expected stock volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrant. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrant. We estimated a 0% dividend yield based on the expected dividend yield and the fact that we have never paid or declared dividends.

Upon the listing of our common stock on the NASDAQ on June 26, 2015, the preferred stock warrant became a warrant to purchase common stock. We performed the final mark to market adjustment on the preferred stock warrant using the fair value of the underlying common shares of $18.00 per share on June 26, 2015 and recorded the change in fair value in other income (expense), net in the consolidated statement of operations and comprehensive loss. The preferred stock warrant liability was then reclassified to additional paid-in-capital as it became a warrant to purchase common stock.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an ‘‘emerging growth company’’ such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to ‘‘opt out’’ of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for the years ended December 31, 2014 and 2015:

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Revenue	$—	$—	$—
Operating expenses:			
Research and development	$38,095	$10,718	$27,377
General and administrative	16,761	4,364	12,397
Total operating expenses	54,856	15,082	39,774
Loss from operations	(54,856)	(15,082)	(39,774)
Other income (expense):			
Interest income	638	—	638
Interest expense	(555)	(209)	(346)
Revaluation of preferred stock warrant liability	(7)	(1,418)	1,411
Total other income (expense), net	76	(1,627)	1,703
Net loss	$(54,780)	$(16,709)	$(38,071)

Research and Development Expenses

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Microbiome therapeutics platform	$20,603	$7,584	$13,019
SER-109	13,828	3,122	10,706
SER-262	1,549	12	1,537
SER-287	2,115	—	2,115
Total research and development expenses	$38,095	$10,718	$27,377

Research and development expenses were $38.1 million for the year ended December 31, 2015, compared to $10.7 million for the year ended December 31, 2014. The increase of $27.4 million was due primarily to the following:

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an increase of $13.0 million in research expenses related to our microbiome therapeutics platform, due primarily to higher payroll and consultant costs of $10.0 million, which included an increase in stock-based compensation expense of $4.2 million, due primarily to an increase in employee headcount, an increase in laboratory consumables and supply costs of $1.2 million, facility- related costs of $1.4 million and travel costs of $0.4 million;

- an increase of $10.7 million in expenses related to our SER-109 program, due primarily to higher clinical trial costs of $6.0 million, higher bioprocess development costs of $3.0 million, higher laboratory consumables and supply costs of $1.2 million and higher sequencing costs of $0.5 million;
- an increase of $1.5 million in expenses of our SER-262 program in connection with various pre- clinical, development and clinical activities related to the program; and
- an increase of $2.1 million in expenses of our SER-287 program in connection with various pre- clinical, development, and clinical activities related to the program.

We expect that our research and development expenses will continue to increase in the foreseeable future as we advance the clinical development of SER-287 and initiate clinical trials for certain product candidates, including SER-262, continue to discover and develop additional product candidates, including SER-155, and pursue later stages of clinical development of our product candidates.

General and Administrative Expenses

	Year Ended December 31,		
	2015	2014	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$8,371	$2,047	$6,324
Professional fees	5,894	1,785	4,109
Facility-related and other	2,496	532	1,964
Total general and administrative expenses	$16,761	$4,364	$12,397

General and administrative expenses were $16.8 million for the year ended December 31, 2015, compared to $4.4 million for the year ended December 31, 2014. The increase of $12.4 million was primarily due to an increase in personnel related costs of $6.3 million, which included an increase of $3.4 million in stock-based compensation, an increase in professional fees of $4.1 million and an increase in facility-related and other costs of $2.0 million. Personnel related costs increased primarily due to the hiring of additional employees from December 31, 2014 to December 31, 2015 to support corporate operations and business development activities. The increase in professional fees was due to an increase in accounting, audit and legal fees as a result of operating as a public company including $0.5 million in costs in connection with the collaboration agreement with Nestlé . The increase in facility-related and other costs was primarily due to an increase in office-related expenses and rent expense resulting from our new facility for research and development that commenced in February 2015.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2015 was an income of $0.1 million, compared to an expense of $1.6 million for the year ended December 31, 2014. The $1.7 million increase in other income, net was primarily due to gains recorded to adjust the fair value of our preferred stock warrant liability due to a decrease in the fair value of the underlying Series A-2 convertible preferred stock over that period.

In connection with the extinguishment of the loan and security agreement, we recorded a loss on extinguishment of $0.1 million, which has been recorded as interest expense in the year ended December 31, 2015.

Comparison of Years Ended December 31, 2014 and 2013

The following table summarizes our results of operations for the years ended December 31, 2014 and 2013:

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		

Revenue	$—	$—	$—
Operating expenses:			
Research and development	10,718	4,805	5,913
General and administrative	4,364	1,247	3,117
Total operating expenses	15,082	6,052	9,030
Loss from operations	(15,082)	(6,052)	(9,030)
Other income (expense):			
Interest income (expense), net	(209)	(42)	(167)
Revaluation of preferred stock warrant liability	(1,418)	(8)	(1,410)
Total other income (expense), net	(1,627)	(50)	(1,577)
Net loss	$(16,709)	$(6,102)	$(10,607)

Research and Development Expenses

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		
Microbiome therapeutics platform	$7,584	$3,424	$4,160
SER-109	3,122	729	2,393
SER-262	12	652	(640)
Total research and development expenses	$10,718	$4,805	$5,913

Research and development expenses were $10.7 million for the year ended December 31, 2014, compared to $4.8 million for the year ended December 31, 2013. The increase of $5.9 million was due primarily to the following:

- an increase of $4.2 million in research expenses related to our microbiome therapeutics platform, due primarily to higher payroll and consultant costs of $2.1 million, which included an increase in stock-based compensation expense of $0.9 million; an increase in laboratory supply costs of $0.7 million; an increase in facility-related costs of $0.5 million; and an increase in licensing costs of $0.3 million;
- an increase of $2.4 million in expenses related to our SER-109 program, due primarily to higher clinical trial costs of $2.1 million and higher contract manufacturing costs of $0.4 million, partially offset by lower animal studies costs; and
- a decrease of $0.6 million in expenses of our SER-262 program due to our shifted focus to SER-109 and our microbiome therapeutics platform research.

General and Administrative Expenses

	Year Ended December 31,		
	2014	2013	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$2,047	$419	$1,628
Professional fees	1,785	691	1,094
Facility-related and other	532	137	395
Total general and administrative expenses	$4,364	$1,247	$3,117

General and administrative expenses were $4.4 million for the year ended December 31, 2014, compared to $1.2 million for the year ended December 31, 2013. The increase of $3.2 million was primarily due to an increase in personnel related costs of $1.6 million, which included an increase of $1.0 million in stock-based compensation, an increase in professional fees of $1.1 million and an increase in facility-related and other costs of $0.4 million. Personnel related costs increased primarily due to the hiring of 11 new employees to support corporate operations and

business development activities, including the hiring of our Chief Executive Officer in June 2014 and our Chief Financial Officer in November 2014. The increase in professional fees was due to an increase in accounting, audit and legal fees as a result of ongoing business activities. The increase in facility-related and other costs was primarily due to an increase in rent expense resulting from exercising an option of our lease to increase the rentable square footage.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2014 was an expense of $1.6 million, compared to an expense of $0.1 million for the year ended December 31, 2013. During the year ended December 31, 2014, there was an increase of $0.2 million in interest expense incurred on borrowings under our loan and security agreement, as compared to the year ended December 31, 2013. In addition, the revaluation of preferred stock warrant liability for the year ended December 31, 2014 consisted of a $1.4 million loss to adjust the fair value of our preferred stock warrant liability due primarily to an increase in the fair value of the underlying Series A-2 convertible preferred stock over that period. This preferred stock warrant liability relates to a warrant we issued in September 2013 in connection with entering into the loan and security agreement.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred recurring net losses. We anticipate that we will continue to incur losses for at least the next several years. 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 obtain from additional financings, public offerings, research funding, collaborations, contract and grant revenue or other sources.

From our inception through June 30, 2015, we had financed our operations through private placements of our convertible preferred stock, the issuance of convertible promissory notes and borrowings under the loan and security agreement. Through June 30, 2015, we had received gross proceeds of $137.0 million from such transactions and we had repaid $1.0 million of the total $3.0 million borrowed under the loan and security agreement.

On July 1, 2015, we completed the initial public offering of our common stock, or IPO, and issued and sold 8.5 million shares of our common stock at a public offering price of $18.00 per share, resulting in net proceeds of approximately $139.3 million after deducting underwriting discounts and commissions and estimated offering expenses. The shares issued upon closing of the IPO included 1.1 million shares of our common stock, which were sold pursuant to the underwriters' full exercise of their option to purchase additional shares of our common stock. Upon the listing of our common stock on NASDAQ on June 26, 2015, all outstanding shares of our convertible preferred stock automatically converted into 22.9 million shares of our common stock. On September 17, 2015, we made a payment of $1.8 million to Comerica to satisfy all amounts owed under the loan and security agreement. The extinguishment amount was comprised of $1.7 million of outstanding principal and $0.1 million of final payment fees and accrued interest. Upon payment, Comerica released us of all security interests held in our assets, except for the cash collateral securing our corporate cards and standby letters of credit, and terminated all loan documents related to the loan and security agreement (other than any indemnification obligations and other provisions which survive termination).

In connection with the extinguishment of the loan and security agreement, we recorded a loss on extinguishment of $0.1 million, which has been recorded as interest expense in the year ended December 31, 2015.

In January 2016 we entered into the License Agreement with NHS, for the development and commercialization of certain of our product candidates in development for the treatment and management of CDI and IBD, including ulcerative colitis and Crohn's disease. The License Agreement will support the development of our portfolio of products for CDI and IBD in the Licensed Territory, and is expected to provide substantial financial support for our ongoing research and development. We have retained full commercial rights to our entire portfolio of product candidates with respect to the United States and Canada, where we plan to build our own commercial organization.

Under the License Agreement, we granted to NHS an exclusive, royalty-bearing license to develop and commercialize, in the Licensed Territory, certain products based on our microbiome technology that are being developed for the treatment of CDI and IBD, including SER-109, SER-262, SER-287 and SER-301, or, collectively, the NHS Collaboration Products. Upon mutual agreement, one or more other products based on our microbiome technology for CDI or IBD may be added to the License Agreement in lieu of or in addition to the then-existing NHS Collaboration Products. NHS' exclusive license in the Licensed Territory to develop and commercialize NHS Collaboration Products extends to any indications for which the parties agree to develop such products. We also granted to NHS a non-exclusive license to export, develop and make NHS Collaboration Products in the licensed fields worldwide solely for commercialization in the licensed fields and in the Licensed Territory. Additionally, the rights to develop and commercialize a given Collaboration Product in certain non-EU countries within the Licensed

Territory may revert to us if NHS either elects not to pursue commercialization of such Collaboration Product in such country, or fails to meet certain agreed upon milestones for commercialization of such Collaboration Product in such country. If the licensed rights in any country revert to us in this way, then we would pay to NHS a royalty in the mid-single digits on net sales of such Collaboration Product in such country.

In exchange for the license, NHS is obligated to pay the Company an upfront cash payment of $120 million, which the Company received in February 2016. NHS has also agreed to pay the Company tiered royalties, at percentages ranging from the high single digits to high teens, of net sales of NHS Collaboration Products in the Licensed Territory. Additionally, NHS has agreed to pay the Company up to $660 million for the achievement of certain development and regulatory milestones and up to an aggregate of $1.125 billion for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products. We expect to receive a total of $30 million in milestone payments in 2016 associated with the planned initiation of a Phase 1b study for SER-262 in CDI and the anticipated initiation of the Phase 3 clinical trial for SER-109 in CDI. The full potential value of the up-front payment and milestone payments payable by NHS is over $1.9 billion, assuming all products receive regulatory approval and are successfully commercialized.

For the development of NHS Collaboration Products for IBD under a global development plan, we are obligated to pay the costs of clinical trials of such products up to and including Phase 2 clinical trials, and 67% of the costs for Phase 3 and other clinical trials of such products, with NHS bearing the remaining 33% of such costs. For other clinical development of NHS Collaboration Products for IBD, we will pay the costs of such activities to support approval in the United States and Canada, and NHS will bear the cost of such activities to support approval of NHS Collaboration Products in the Licensed Territory.

With respect to development of NHS Collaboration Products for CDI under a global development plan, we agreed to pay all costs of an ongoing Phase 2 clinical trial for SER-109 and of Phase 3 clinical trials for SER-109. We agreed to bear all costs of conducting any Phase 1 or Phase 2 clinical trials under a global development plan for NHS Collaboration Products other than SER-109 for CDI. We agreed to pay 67% and NHS agreed to pay 33% of other costs of Phase 3 clinical trials conducted for NHS Collaboration Products other than SER-109 for CDI under a global development plan. For other clinical development of NHS Collaboration Products for CDI, we agreed to pay costs of such development activities to support approval in the United States and Canada, and NHS agreed to bear the cost of such activities to support approval of NHS Collaboration Products in the Licensed Territory.

As of December 31, 2015, we had cash, cash equivalents and investments totaling $205.1 million and an accumulated deficit of $82.6 million.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Cash used in operating activities	$(40,844)	$(10,358)	$(5,321)
Cash used in investing activities	$(137,133)	(1,103)	(184)
Cash provided by financing activities	$137,725	123,992	944
Net increase (decrease) in cash and cash equivalents	$(40,252)	$112,531	$(4,561)

Operating Activities. During the year ended December 31, 2015, operating activities used $40.8 million of cash, primarily resulting from our net loss of $54.8 million and cash provided by changes in our operating assets and liabilities of $3.1 million, partially offset by non-cash charges of $10.8 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2015 consisted of a $2.5 million increase in prepaid expenses and other current assets, a $2.7 million increase in accounts payable and a $2.9 million increase in accrued expenses and other current liabilities. The increases in our accounts payable and accrued expenses were due to the timing of payments, an increase in payroll related costs and an increase in amounts accrued for clinical trial and contracted manufacturing expenses. The increase in prepaid expenses and other current assets was due primarily to prepayments made for clinical trial activities.

During the year ended December 31, 2014, operating activities used $10.4 million of cash, primarily resulting from our net loss of $16.7 million, partially offset by non-cash charges of $4.1 million and by cash provided by changes in our operating assets and liabilities of $2.3 million. Net cash provided by changes in our operating assets and liabilities

during the year ended December 31, 2014 consisted primarily of a $0.8 million increase in accounts payable and a $1.5 million increase in accrued expenses and other current liabilities. The increase in accounts payable was due to an overall increase in our development activities, primarily driven by expenditures in connection with advancing the development of SER-109. The increase in accrued expenses and other current liabilities was due to an increase in accruals for development and manufacturing costs related to SER-109; payroll and payroll-related costs due primarily to bonuses; legal and audit-related professional fees; and facility- related costs.

During the year ended December 31, 2013, operating activities used $5.3 million of cash, resulting from our net loss of $6.1 million, partially offset by non-cash charges of $0.3 million and from cash provided by changes in our operating assets and liabilities of $0.5 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2013 consisted primarily of a $0.3 million increase in accounts payable and a $0.2 million increase in accrued expenses and other current liabilities. The increase in accounts payable was due to the timing of vendor invoicing and payments. The increase in accrued expenses and other current liabilities was primarily due to an increase in our accruals for consultant fees.

Investing Activities. During the year ended December 31, 2015, we used $137.1 million of cash in investing activities, consisting of purchases of investments of $267.8 million, purchases of property and equipment of $4.4 million, and an increase in our restricted cash balance of $1.4 million; these increases were offset by maturities of investments of $136.4 million.

During the year ended December 31, 2014, we used $1.1 million of cash in investing activities, primarily consisting of purchases of property and equipment of $1.0 million.

During the years ended December 31, 2013, we used $0.2 million of cash in investing activities, primarily for purchases of property and equipment.

Financing Activities. During the year ended December 31, 2015, net cash provided by financing activities was $137.7 million as a result of proceeds from the issuance of common stock in connection with our IPO of $143.0 million and proceeds of $0.3 million in connection with the exercise of options and warrants to purchase our common stock. These increases were partially offset by principal repayments of $2.6 million of borrowings under our loan and security agreement and payments of costs in connection with the IPO of $2.9 million.

During the year ended December 31, 2014, net cash provided by financing activities was $124.0 million as a result of net proceeds of $123.2 million received from our sale of Series B, Series C, Series D and Series D-1 convertible preferred stock and $2.0 million from borrowings under our loan and security agreement. These amounts were partially offset by principal repayments of $0.4 million of borrowings under our loan and security agreement and payments of IPO costs of $0.8 million.

During the year ended December 31, 2013, net cash provided by financing activities was $0.9 million as a result of net proceeds of $0.9 million borrowings under our loan and security agreement.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing development activities related to SER-109, which is still in clinical development, and our follow-on therapeutics and other programs. In addition we expect to continue to incur additional costs associated with operating as a public company. We anticipate that our expenses will increase substantially if and as we:

- conduct our Phase 2 clinical study of SER-109, our lead product candidate, and potentially advance to Phase 3 clinical studies;
- conduct our Phase 1 clinical study of SER-287;
- continue the research and development of our other product candidates, including commencing clinical trials for SER-262;
- seek to enhance our microbiome therapeutics platform and discover and develop additional product candidates, including SER-155;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- 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;

- 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; and
- perform our obligations under the collaboration agreement with Nestlé.

We expect that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into 2018. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of SER-109 or our follow-on programs, we are unable to estimate the amounts of increased capital outlays and operating

expenses associated with completing the research and development of our product candidates. Our future capital requirements for SER-109 or our other programs will depend on many factors, including:

- the progress and results of our Phase 2 clinical study of SER-109;
- the progress and results of our Phase 1 clinical study of SER-287;
- the cost of manufacturing clinical supplies of our product candidates;
- the scope, progress, results and costs of pre-clinical development, laboratory testing and clinical trials for our other product candidates, including SER-262 and SER-155;
- 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, although we currently have no commitments or agreements to complete any such transactions.

Identifying potential product candidates and conducting pre-clinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Additional debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interest.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, in addition to the collaboration with Nestlé, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, 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 programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2015 and the effect such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
		1 Year			More Than
	Total	Less Than	1 - 3 Years	4 - 5 Years	5 Years
	(in thousands)				
Operating lease commitments[1]	$3,637	$1,274	$1,805	$ 558	$ —
Total	$3,637	$1,274	$1,805	$ 558	$ —

Amounts in the table reflect payments due for (i) our laboratory and office space in Cambridge, Massachusetts under an operating lease agreement that expires on January 31, 2018, (ii) our sublease for office space in Cambridge, Massachusetts, with a term expiring

in May 2016, and (iii) our lease for office and laboratory space in Cambridge, Massachusetts with a term expiring April 2020. The table does not include our lease for office, laboratory and pilot manufacturing space at 200 Sidney Street in Cambridge, Massachusetts with a term commencing in March 2016 and expiring in November 2023. Amounts due under this lease total $41.8 million, with $0.9 million due in less than 1 year, $11.2 million due in 1-3 years, $11.9 million due in 4-5 years and $17.8 million due in more than 5 years. These amounts are not included within the table above as our lease for the Sidney Street facility had not commenced as of December 31, 2015.

We enter into contracts in the normal course of business with CROs for clinical trials, pre-clinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non- cancelable obligations under these agreements are not material.

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 in the rules and regulations of the Securities and Exchange Commission.

Recently Issued and Adopted Accounting Pronouncements

For a discussion of recent accounting standards see Note 2, Summary of Significant Accounting Policies, to our consolidated financial statements included in this report.

Item 7A. Quantitative and Qualitative Disclosures about Market Risks

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2015, our cash, cash equivalents and investments consisted of cash, money market accounts and investments in corporate bonds and commercial paper with remaining maturities of less than one year. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, an immediate 10% change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”)), as of the end of the period covered by this Annual Report on Form 10-K. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

Our board of directors has adopted a Code of Business Conduct and Ethics applicable to all officers, directors and employees, which is available on our website at www.serestherapeutics.com in the “Investors & Media” section under “Corporate Governance.” We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics, as well as NASDAQ’s requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address and location specified above.

The information in response to this item is contained in part under the caption “Executive Officers of the Registrant” at the end of Part I of this Annual Report on Form 10-K. The remainder of the response to this item is contained in the Proxy Statement for our Annual Meeting of Stockholders scheduled to be held on June 15, 2016 and is incorporated herein by reference.

Item 11. Executive Compensation

The information required to be disclosed by this item is contained in the Proxy Statement for our Annual Meeting of Stockholders scheduled to be held on June 15, 2016 and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required to be disclosed by this item is contained in the Proxy Statement for our Annual Meeting of Stockholders scheduled to be held on June 15, 2016 and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required to be disclosed by this item is contained in the Proxy Statement for our Annual Meeting of Stockholders scheduled to be held on June 15, 2016 and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required to be disclosed by this item is contained in the Proxy Statement for our Annual Meeting of Stockholders scheduled to be held on June 15, 2016 and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statements and Schedules

(a)(1) Financial Statements.

See the “Index to Consolidated Financial Statements” on page F-1 below for the list of financial statements filed as part of this report.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto set forth below beginning on page F-1.

(a)(3) Exhibits.

See the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this Annual Report on Form 10-K.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of

Seres Therapeutics, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Seres Therapeutics, Inc. and its subsidiaries at December 31, 2015 and 2014, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2015 in conformity with accounting principles generally accepted in the United States of America. 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 of these statements 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. An audit 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.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts

March 14, 2016

SERES THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31,	
	2015	2014
Assets		
Current assets:		
Cash and cash equivalents	$73,933	$114,185
Investments	131,149	—
Prepaid expenses and other current assets	2,528	58
Total current assets	207,610	114,243
Property and equipment, net	7,751	1,264
Restricted cash	1,539	139
Deferred offering costs	—	1,684
Deferred financing costs	—	15
Total assets	$216,900	$117,345
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$5,397	$2,166
Accrued expenses and other current liabilities	5,523	1,737
Notes payable; current portion	—	1,200
Total current liabilities	10,920	