Seres Therapeutics, Inc.
Form 10-K
March 08, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2017

OR

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.)

200 Sidney Street – 4th Floor

Cambridge, Massachusetts	02139
(Address of Principal Executive Offices)	(Zip Code)

(617) 945-9626

(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act

Title of each class	Name of each exchange on which registered
Common stock, par value $0.001 per share	The Nasdaq Global Select Market

Securities Registered pursuant to Section 12(g) of the Act: None

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

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 No

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 No

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 No

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.

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

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
Emerging growth company		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to section 13(a) of the Exchange Act.

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

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, 2017, was $229,703,925.

As of March 2, 2018, there were 40,648,356 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 2018 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. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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. 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 important factors that could cause actual results to differ materially from those in the forward-looking statements, including the 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 clinical-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 U.S. Food and Drug Administration 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.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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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 drug candidates 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 microbial ecologies in the human body.

The human microbiome is one of the richest and most diverse ecosystems on earth, with a population of more than 40 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 or following gastrointestinal infection. These changes in composition may result in the loss of key microbes, resulting in a state of dysbiosis. 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 various indications, including: infectious diseases, metabolic diseases, and inflammatory and immune diseases, including immuno-oncology.

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 therapeutic candidates, which are derived from our microbiome therapeutics platform, are rationally-designed ecological compositions, consisting of discrete combinations of beneficial microorganisms with functional properties that provide the ability to re-establish keystone features of a functional microbiome in settings of disease. There are currently no therapeutics approved by the U.S. Food and Drug Administration, or the FDA, 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 microbiological and functional 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 then studied in clinical trials. We apply a comparative genomic systems biology framework that leverages proprietary computational, microbiological and screening capabilities to design lead candidates targeted at these microbiological and functional deficiencies. We are able to apply this framework and experience to clinical data sets from published studies and those generated with our collaborators, as well as to the proprietary clinical data set we have generated through our clinical trials. We believe we can utilize our knowledge and data to design Ecobiotic microbiome therapeutics to treat various medical conditions. We also have advanced capabilities in the production and formulation of colonic bacteria as well as 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, manufacturing and formulation of Ecobiotic microbiome therapeutic candidates, 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 rapidly and durably repair dysbiosis in the colonic microbiome in the setting of recurrent Clostridium difficile infection, or 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 can express toxins leading to debilitating diarrhea in infected individuals, but can also lead to more severe outcomes, such as inflammation of the colon (colitis), 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. Based on an epidemiological study conducted by the CDC, the incidence of CDI in the United States, based on a positive toxin or molecular assay in patients who did not have a positive result in the previous eight weeks, was estimated

to be 453,000 (95% confidence interval, 397,100 to 508,500) (Lessa et. al., Burden of Clostridium difficile Infection in the United States, New England J. of Medicine, 2015). 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 CDI recurrence, we believe it is this dysbiosis of the microbiome, not the presence of C. difficile, which is the proximal cause of disease. Published data suggests that the risk of recurrence is approximately 25% after the primary CDI, 40% after a first recurrence and approximately 60% for those experiencing two or more recurrences.

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. If approved by the FDA, SER-109 could be a first-in-field oral microbiome drug. In June 2017 we initiated a Phase 3 clinical study of SER-109 in approximately 320 patients with multiply recurrent CDI. The new study is designed to evaluate patients for 24 weeks with the primary endpoint of comparing the C. difficile recurrence rate in subjects who receive SER-109 verses placebo at up to eight weeks after dosing.

We progressed our drug discovery and development platforms with the initiation in July 2016 of a Phase 1b dose-escalating study for SER-262, the first clinical, rationally designed ecology of spore forming bacteria designed to be used following antibiotic treatment for primary CDI to prevent an initial recurrence of CDI. We believe there are several advantages to using a rationally designed approach to developing microbiome therapeutics, such as scaling-up manufacturing of rationally designed product candidates to meet global demand in a reliable and reproducible manner, with well-defined characteristics. Based on our metagenomics expertise, proprietary in silico algorithms, extensive proprietary bacterial library, and advanced manufacturing capabilities, we believe we can rationally design microbiome therapeutic candidates for specific target indications. We believe these capabilities provide us with a competitive advantage in developing microbiome therapeutics. SER-262, available in oral capsule form, is derived from a manufacturing process that does not require human donor material. SER-262 contains a consortium of 12 bacterial strains in spore form constructed from strains from our microbiome strain library via in vitro fermentation.

The Phase 1b clinical study is a 24-week, randomized, placebo-controlled, dose-escalation trial. The study was initially designed to evaluate a single dose administration of SER-262 at ascending spore doses ranging from 1×10^4 to 1×10^8 Spore Colony Forming Units, or SCFU, with each dosing cohort comprised of 10 subjects treated with SER-262 and two subjects administered placebo. Following analysis of prior SER-109 clinical studies that suggest higher doses of microbiome therapeutics may be important to rapidly address dysbiosis and provide increased efficacy, in mid-2017 we added additional multiple-dose cohorts to the Phase 1b study of $1x10^6$, $1x10^7$ and $1x10^8$ SCFU per day of SER-262, for a three-day period.

The primary endpoints of the study are to evaluate the safety and tolerability of SER-262 and to compare the CDI recurrence rate between the SER-262 and placebo groups at up to eight weeks post-dosing. A secondary endpoint is the analysis of the SER-262 bacterial strain engraftment in patient microbiomes. As of now, we have received unblinded clinical data on all but the final 1×10^8 multiple dose cohort, which continues to enroll subjects. No drug-related serious adverse events were observed in these first seven cohorts. No relevant differences were observed in the relative risk of recurrence rates in patients administered SER-262 as compared to placebo. However, this small, first-in-human, Phase 1b study was not powered to detect a statistically significant difference in recurrence rates compared to placebo. A small group of placebo patients were included in this study and, in that group, no recurrences were observed. In addition, there was a measurable difference in recurrence rates in patients treated with Vancomycin and SER-262, as compared to those treated with Metronidazole and SER-262 (4% versus 31%, respectively). This difference was statistically significant with a p value of 0.0049. The medical literature suggests a recurrence rate of about 25% in patients treated with vancomycin for primary CDI.

Microbiome analysis has been conducted on the first five, lowest dose cohorts to assess drug pharmacokinetics. We detected a majority of SER-262 strains in patients receiving SER-262; detection of strains was variable across subjects. Partial engraftment of strains was also a characteristic in our SER-109 clinical studies, and has been reported in fecal microbiota treatment, or FMT of CDI. Engraftment of SER-262 strains was associated with broader changes in the microbiome composition. Microbiome profile differences, based on the antibiotics that were used to treat each patient's CDI, were also demonstrated. Vancomycin led to more rapid and more robust engraftment of SER-262 strains as compared to Metronidazole. More detailed microbiome and metabolomic analyses remain ongoing. These SER-262 proprietary data, the first ever obtained from a rationally-designed microbiome development candidate, will be used to inform the further development of SER-262 and our other therapeutic candidates.

The clinical development of SER-287 to treat ulcerative colitis, or UC is supported by preclinical studies in multiple animal models of colitis which provide evidence that SER-287 administration results in reduced pathology. Published clinical reports furthermore suggest that modulation of the microbiome through repetitive FMT may lead to meaningful clinical response in certain UC patients. We initiated our Phase 1b clinical study for our IBD drug candidate, SER-287, in December 2015 and enrolled subjects with active mild to moderate UC, a form of IBD, 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 enrolled 58 subjects with active mild-to-moderate UC, who are failing current therapies.

On October 2, 2017, we announced positive topline results from our Phase 1b clinical trial of SER-287 in patients with UC. The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study enrolled patients with active mild-to-moderate UC, with Total Modified Mayo scores of 4 to 10. The study enrolled 58 patients at 20 sites across the United States. Study subjects exhibited pre-study disease activity despite use of current therapies in a majority of subjects, which included 5-amino-salacylic acid, low dose corticosteroids, or immunomodulatory therapy. An evaluation of SER-287 safety and tolerability was a primary study endpoint. Study results demonstrated no imbalance in adverse events in SER-287-treated patients as compared to patients treated with placebo. There were no drug related serious adverse events.

Analyses of study patients' microbiome data, a co-primary study endpoint of the trial, demonstrated that SER-287 induced dose-dependent engraftment of SER-287-derived bacterial species into the colonic microbiome of the patients treated with SER-287. Patients administered vancomycin pre-treatment followed by daily administration of SER-287 had the highest level of SER-287 engraftment, which was statistically significant. This patient cohort corresponded with the study arm where the most significant clinical benefits were observed, including clinical remission and endoscopic improvement. Differences in the composition of the microbiome post treatment were also associated with clinical remission. Bacterial engraftment signatures were durable throughout the dosing period of the trial and were also observed at four weeks post administration of the final SER-287 dose. The SER-287 Phase 1b study microbiome data support the previously reported clinical results.

We are also designing and developing SER-401, for use with checkpoint inhibitors, or CPIs in patients with solid tumors to enhance efficacy and improve survival. CPIs are used to block mechanisms used by cancer to evade detection and destruction by the immune system. In 2015, studies showed that CPI efficacy in mouse models was dependent on the composition of the microbiome. That work was extended to humans in November 2017 when additional studies showed that human subjects who respond to CPI treatment have a different microbiome composition than non-responders. One of these reports was from a group led by Dr. Jennifer Wargo of MD Anderson Cancer Center, or MD Anderson. In November 2017, we announced a collaboration with MD Anderson and the Parker Institute for Cancer Immunotherapy, or the Parker Institute, to evaluate the potential of SER-401 to improve the outcomes of cancer patients treated with currently-available immunotherapy. MD Anderson granted us an exclusive option, with pre-defined financial terms, to license intellectual property rights from them related to the use of bacteria in combination with CPIs.

We are also designing and developing SER-301, a rationally designed Ecobiotic microbiome therapeutic candidate for the treatment of IBD. The design is being driven by insights into the microbiome and metabolomic data gained from the Phase 1b study of SER-287 as well as insights from FMT for UC conducted by our academic collaborators. The SER-301 program also benefits from what we learn about rationally designed Ecobiotic microbiome therapeutic development in our SER-262 program.

We are also designing and developing SER-155, a rationally designed product candidate to prevent infections and improve gastrointestinal barrier function (including the consequences of graft versus host disease, or GvHD) in patients following allogeneic hematopoietic stem cell transplants, or allo-HSCT, or solid organ transplants. This preclinical program is based on published clinical evidence from our collaborators at Memorial Sloan Kettering Cancer Center showing that allo-HSCT patients with reduced microbiome diversity are far more likely to die due to infection and/or lethal GvHD. In November 2017, we were awarded a grant from Combating Antibiotic-Resistant Bacteria Accelerator, or CARB-X, to support continued preclinical research and early development work for SER-155. The CARB-X grant provides us with up to $2.5 million of research funding with potential for an additional $3.1 million upon completion of milestones.

We are also researching Ecobiotic microbiome therapeutics for the treatment of metabolic diseases, such as early-stage, non-insulin dependent diabetes, non-alcoholic steatohepatitis, or 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 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 Pioneering, the innovation foundry of Flagship Ventures. Through Flagship Pioneering's 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 ten FDA-approved infectious disease drugs in his career. Our management team has extensive experience in microbial ecology, microbiology and live biologicals, with over 25 years of experience 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 the commercialization of vaccine products, which have analogous manufacturing processes to that of Ecobiotic microbiome therapeutics.

Our Strategy

Our goal is to remain the leading biopharmaceutical company developing and commercializing microbiome therapeutics to address significant unmet medical needs. We intend to focus in the near term on the highest priority clinical programs which we believe will optimally advance our pipeline: SER-287 for UC; SER-109 for recurrent CDI; and the SER-401 immuno-oncology program. The critical components of our strategy include:

- Continuing clinical development of SER-287 for the treatment of UC. 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 FMT may lead to meaningful clinical response in certain UC patients. In December 2015, we initiated a Phase 1b clinical trial evaluating SER 287 in patients with mild to moderate UC. In October 2017, we announced positive topline results from our Phase 1b clinical trial of SER-287 in patients with UC. The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study enrolled patients with active mild-to-moderate UC, with Total Modified Mayo scores of 4 to 10. The study enrolled 58 patients at 20 sites across the United States. Study subjects exhibited pre-study disease activity despite use of current therapies in a majority of subjects, which

included 5-amino-salacylic acid, low dose corticosteroids, or immunomodulatory therapy. In addition, SER-287 has been awarded Orphan Drug Designation for pediatric UC. We are currently in discussions with the FDA on the design of our next clinical study of SER-287.

- 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. In our randomized, double-blind, placebo controlled Phase 2 clinical study, 44% of subjects (26 of 59) who received SER-109 experienced a recurrence at the 8 week endpoint compared to 53% of subjects (16 of 30) who received placebo, a result that was not statistically significant. Based on a detailed analysis of clinical, microbiome and CMC factors that may have contributed to the outcome of this study, as well as a comparison to our earlier Phase 1b/2 clinical study and following discussions with the FDA, a new SER-109 clinical study in approximately 320 patients with multiply recurrent CDI was initiated in June 2017. Study participants will be randomized 1:1 between SER-109 and placebo and will receive a total dose that is approximately 10-fold higher than in the Phase 2 study, administered over three consecutive days.
- Developing SER-401 for use with CPIs in patients with solid tumors. We are designing and developing SER-401, for administration in combination with CPI treatment to increase efficacy in patients with solid tumors. The design is being driven by insights from our collaborators at MD Anderson and recent published data in a number of high profile scientific journals from other international research groups that suggest that the microbiome may impact patients' response to CPI treatment. Together with our collaborators, we plan to initiate a Phase 1b multicenter study in metastatic melanoma patients as part of our collaboration with MD Anderson and the Parker Institute this year.
- 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 bacteria that are a subset of the bacterial ecology comprising SER-109, however, SER-262 is not derived from human stool and, in contrast, is rationally designed based on in vitro and in vivo screening data and made in bacterial fermenters. Pre-clinical studies of SER-262 have demonstrated efficacy in a mouse model of CDI, similar to pre-clinical studies of SER-109. In July 2016, we initiated a randomized, placebo-controlled dose escalation Phase 1b study. The study is expected to enroll up to 96 patients who have experienced a first episode of CDI. The primary endpoints of the study are to evaluate the safety and tolerability of SER-262 in subjects with primary CDI and compare the CDI recurrence rate between the SER-262 dosing cohorts and the pooled placebo group at up to eight weeks after dosing. As of now, we have received unblinded clinical data on all but the final 1 x 10^8 multiple dose cohort, which continues to enroll subjects. No drug-related serious adverse events were observed in these first seven cohorts. No relevant differences were observed in the relative risk of recurrence rates in patients administered SER-262 as compared to placebo. However, this small, first-in-human, Phase 1b study was not powered to detect a statistically significant difference in recurrence rates compared to placebo. A small group of placebo patients were included in this study and, in that group, no recurrences were observed. In addition, there was a measurable difference in recurrence rates in patients treated with Vancomycin and SER-262, as compared to those treated with Metronidazole and SER-262 (4% versus 31%, respectively). This difference was statistically significant with a p value of 0.0049. The medical literature suggests a recurrence rate of about 25% in patients treated solely with vancomycin for primary CDI. Microbiome analysis has been conducted on the first five, lowest dose cohorts to assess drug pharmacokinetics. We detected a majority of SER-262 strains in patients receiving SER-262; detection of strains was variable across subjects. Partial engraftment of strains was also a characteristic in our SER-109 clinical studies, and has been reported in FMT of CDI. Engraftment of SER-262 strains was associated with broader changes in the microbiome composition. Microbiome profile differences, based on the antibiotics that were used to treat each patient's CDI, were also demonstrated. Vancomycin led to more rapid and more robust engraftment of SER-262 strains as compared to Metronidazole. More detailed microbiome and metabolomic analyses remain ongoing. These SER-262 proprietary data, the first ever obtained from a rationally-designed microbiome development candidate, will be used to inform the further development of SER-262 and our other therapeutic candidates.
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Developing SER-301 for the treatment of IBD. We are designing and developing SER-301, a rationally designed Ecobiotic microbiome therapeutic candidate for the treatment of IBD. The design is driven by insights from FMT and will leverage information from SER-287, including changes to the microbiome in patients with UC

- Developing SER-155 for the prevention of transplant-related mortality. We are designing and developing SER-155, a rationally designed Ecobiotic microbiome therapeutic candidate for the prevention of transplant-related mortality (due to infection and GvHD) in allo-HSCT recipients. The design is driven by insights from our collaborators at Memorial Sloan Kettering Cancer Center into the microbiome composition of patients following allo-HSCT. Some of the costs of preclinical development of SER-155 are being supported by a grant from the CARB-X, a joint program funded by BARDA and the Wellcome Trust.
- 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 design treatments for 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, if approved, directly in the United States and Canada and with collaborators outside of North America. In January 2016, we entered into a strategic collaboration with NHS for microbiome-based CDI and IBD 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 and Canada with a highly focused and specialized sales force of less than 100 individuals. To the extent we are able to commercialize SER-109 in the United States, we will leverage that experience 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. Ecobiotic microbiome therapeutic manufacturing will require capabilities that are distinct from other biologic drugs. We have made 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 therapeutic candidates. 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 microbial ecologies 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 microbial ecologies in the human body, the colonic microbiome is one of the most diverse microbial communities with up to 100 billion to one trillion cells per milliliter. 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 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 metagenomic sequencing technologies to analyze 5,000 samples, representing more than 3.5 terabases of genome sequence data, to identify specific genetic sequences found only in bacteria. HMP researchers estimate that 500 to 1,000 unique bacterial 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, or NAFLD/NASH; allergies; autoimmune disease; inflammatory diseases, such as UC, Crohn's disease and pouchitis; and cancer, including immune-oncology related applications. Examples of some studies include:

- 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. Seres has shown that SER-262, it's clinical consortium of human-derived bacterial species formulated as spores, can protect mice from disease in a Clostridium difficile infection model.

- A placebo-controlled, randomized, blinded clinical study published in Gastroenterology in 2015 showed that repetitive FMT delivered via enema weekly for 6 weeks could induce clinical remissions in 24% of patients with active UC compared to 5% receiving placebo (Moayyedi et al., Gastroenterology, 2015). This study utilized endoscopy, a direct visualization of the colon, before and after treatment to assess the efficacy of FMT, thus demonstrating the role of the microbiome in treating active UC. A subsequent randomized, placebo controlled, blinded study of FMT delivered via enema 5 days per week for 8 weeks demonstrated similar clinical remission rates: 27% receiving FMT and 8% receiving placebo (Paramsothy et al., Lancet, 2017). We announced top-line clinical data from its Phase 1b clinical trial for SER-287 in October 2017. In patient with mild-to-moderate UC, those receiving a vancomycin pre-treatment followed by a daily oral dose of SER-287 for 8 weeks achieved a 40% rate of clinical remission compared to 0% for placebo. This analysis followed the Intent-to-Treat "worst case" analysis used for drug registration studies in which missing data is counted as failure.
- Data from cancer patients undergoing allo-HSCT show the influence of the microbiome on patient survival. An observational study of allo-HSCT patients following allo-HSCT demonstrated that 3-year survival in patients with a low diversity microbiome was 36% whereas survival in patients with a medium to high diversity microbiome was ≥60%. Excess mortality in the low diversity subset was driven by deaths due to infection and GvHD, not the underlying cancer itself (Taur et al, Blood, 2014). A follow up from the same researchers looked at allo-HSCT patients receiving transplants who are at highest risk of GvHD and showed a greater than 5-fold increase in mortality was correlated with microbiome composition. (Jenq et al., Biol of Blood and Marrow Transplant, 2015).
- Two studies in mouse cancer models, both published in Science in 2015, demonstrated that the anti-tumor response to immunel checkpoint inhibitors could be enhanced by altering the microbiome (Velizou et al., Science 2015; Slvan et al., Science 2015). More recently, independent groups from MD Anderson, the Institute Gustave Roussy in Paris, France, and the University of Chicago have published data from human studies showing that cancer patients who successfully respond to immune checkpoint inhibitors tend to have a distinct microbiome from patients who do not respond. Moreover, when human fecal samples from responding and non-responding patients are transferred into mice, these have been shown to exhibit the same response to checkpoint inhibitors in tumor model experiments as their human donors (Golpalakrishnan et al, Science, 2017; Routy et al, Science, 2017; Matson et al, Science, 2018). Taken together, these results suggest that microbiome therapies might improve the 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 have developed the leading microbiome therapeutics platform, which we believe enables us to significantly reduce the time typically required to advance therapeutics to the clinic, and ultimately, to the market. We use reverse translation, the practice of starting with microbiome data from healthy volunteers and patients to understand the role of the microbiome in disease, and use that data in our design and development programs.

Our microbiome therapeutics platform combines two approaches. Our donor-derived platform has two product candidates, SER-109 and SER-287. In this setting, we target indications where we believe a deficiency in the spore-forming bacterial population is likely to cause or contribute to disease, such as recurrent CDI and IBD. Our donor-derived product candidates have been rapidly translated into clinical studies in patients. Our rationally-designed platform produces ecological compositions that consist of discrete combinations of beneficial microorganisms, selected from our strain library to have functional properties relevant to the underlying cause of disease.

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 therapeutic candidates. We compare healthy, normal colonic microbiomes to those in an unhealthy dysbiotic state, revealing the ecological and functional differences. We then develop our Ecobiotic microbiome therapeutic candidates to target these differences. Our clinical data from the SER-109 and SER-287 programs, and microbiome data generated with external collaborators, serve to instruct us on how the introduction of certain keystone microbes can restore a dysbiotic colonic microbiome.

We have developed a proprietary suite of bioinformatics and computational tools, which facilitate our insights into the human microbiome. Using whole metagenomic shotgun sequencing, and our proprietary, curated, reference database of novel bacterial

genomes, our algorithms enable us to track changes in the microbiome at the level of individual bacterial strains. We have also developed tools integrating metabolomics data (the small molecules made by the microbiome) with genomic data (the collection of bacteria defined by sequencing) to understand the functions related groups of organisms contribute to the state of disease or health.

Our proprietary strain library of over 35,000 bacterial isolates from healthy donors and patients enables us to translate computational insights into defined compositions. It includes the majority of the National Institute of Health's Human Microbiome Project's "most wanted" and many novel species not described in other databases or the scientific literature. Using proprietary assays, we characterize the functional capabilities of the bacteria in our strain library, based on both metabolomics and how the bacteria interact with human colonic epithelial cells and the human immune system. We also seek to understand how these microbes improve colonic barrier health and how colonic barrier health impacts immune responses.

We select bacteria from our library with specific predicted properties using novel algorithms for functional design and grow the compositions in the lab to be tested both in vitro and in animal models. Our animal models include using "humanized" mice that possess only bacteria derived from humans, which we developed to minimize confounding variables presented by murine microbes. This data is analyzed and used to optimize the next round of screening; introducing new bacterial strains and optimizing existing strains until we identify a composition for clinical testing.

Finally, we manufacture the bacterial composition under current Good Manufacturing Practices, or cGMP, which are required by FDA and European regulators. We believe our manufacturing is successful because we are uniquely positioned to interpret and implement regulations given our development position and we have proprietary data enabling us to better understand the biology of human commensal bacteria. We have optimized fermentation conditions to generate spores and enhance bacterial yields in anaerobic fermentation and have in-house capabilities to formulate both spores and live bacteria. Our manufacturing facility in Cambridge, Massachusetts is uniquely fit-for-purpose and is highly differentiated compared to the offerings of commercial contract research organizations. We address quality control requirements for our Ecobiotic microbiome therapeutic candidates using proprietary microbiological and qualified sequence-based testing schemes, including high-throughput quantitative analytics to assess the identity, potency and purity of the final product.

Taken together, our platform, spanning drug discovery, pre-clinical translation, and novel manufacturing and quality control approaches, has enabled a field leading pipeline across a range of therapeutics areas.

Disease Overview and Our Product Pipeline

We believe our Ecobiotic microbiome therapeutic candidates 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 has been designated as a Breakthrough Therapy and an Orphan Drug by the FDA. Based on feedback received from the FDA, we have initiated a new Phase 3 SER-109 clinical study in approximately 320 patients with multiply recurrent CDI. SER-262 is an Ecobiotic drug candidate under development for treatment of dysbiosis following primary CDI, in order to prevent recurrence, and is currently in a Phase 1b study in the United States. SER-287 is under development for the treatment of active mild-to-moderate UC and has completed a Phase 1b study in the United States. SER-287 has been designated an Orphan Drug for pediatric UC by the FDA. We are designing SER-301, a rationally-designed Ecobiotic microbiome therapeutic candidate, for the treatment of IBD, SER-401 for combination therapy with immune checkpoint inhibitors in cancer, and SER-155, a designed Ecobiotic microbiome therapeutic candidate, for the prevention of transplant-related mortality (due to infection and GvHD) following allo-HSCT or liver transplant. We are also researching potential Ecobiotic microbiome therapeutic candidates for the treatment of metabolic disorders, such as early-stage, non-insulin dependent diabetes , 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.

CDI Overview and Product Candidates

Clostridium difficile Infection

C. difficile is a Gram-positive, toxin-producing, spore forming bacterium that may cause debilitating diarrhea in infected individuals, but can also lead to more severe outcomes, such as inflammation of the colon (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 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 including cells of the immune system, 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 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). 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. 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 (Higa & Kelly, New Drugs and Strategies for Management of Clostridium difficile Colitis, J. of Intensive Care Medicine, 2013). Based on an epidemiological study conducted by the CDC, the incidence of C. difficile infection in the United States, based on a positive toxin or molecular assay in patients who did not have a positive result in the previous 8 weeks, was estimated to be 453,000 (95% confidence interval [CI], 397,100 to 508,500) (Lessa et. al., Burden of Clostridium difficile Infection in the United States, New England J. of Medicine, 2015).

Current and developing treatment alternatives and their limitations

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

Antibiotics. According to the Infectious Disease Society of America, or IDSA, guidelines, the current standard of care for primary CDI is to treat with antibiotics, such as fidaxomicin or vancomycin. Metronidazole is only recommended for mild disease or where access to other drugs is limited. In addition, while fidaxomicin is recommended to treat primary CDI, it does not have a label claim to reduce or prevent CDI recurrence. No antibiotic therapeutics are currently approved for treatment of recurrent CDI.

Recurrent CDI, defined as the presence of diarrhea and a positive C. difficile stool assay within two to eight weeks following the initial episode, is not well addressed by any of the available antibiotics. When a patient has recurred two or more times after the initial occurrence, CDI recurrence rates are greater than 60% and the probability of additional recurrences increases with successive cycles. 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, resulting in increased risk of future CDI. 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, supports 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 that, as currently practiced by clinical centers in the U.S., it may be unable to gain such approval since the product, to our knowledge, cannot be characterized according to current regulatory requirements for identity, potency, purity and safety and has not been tested in rigorous, placebo controlled, randomized and blinded clinical studies. Commercial providers of FMT must meet FDA regulatory requirements for a biologics license and must produce FMT material using cGMP.

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. The European Food Safety Authority has 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. Bezlotoxumab a fully human monoclonal antibody directed against C. difficile toxin B was approved in the United States in October, 2016 and in Europe in 2017 for the treatment of CDI. The antibody demonstrated 10% absolute risk reduction in preventing recurrence of CDI. Antibodies bind 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. Bezlotoxumab requires intravenous infusion.

Vaccines. The efficacy of vaccines in treating CDI in humans currently remains under investigation. In addition, it is difficult to define and access 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 an ecology of bacteria in spore form enriched from fecal donations obtained from healthy screened donors. SER-109 consists of an average of approximately 50 bacterial species and is designed to reduce 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, 87% of patients (26 of 30) met the predefined endpoint and 97% (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. A subsequent randomized, double-blind, placebo controlled Phase 2 clinical study was conducted in 89 subjects to evaluate the safety, tolerability and efficacy of SER-109 in adults with recurrent CDI. In that study, 44% of subjects (26 out of 59) who received SER-109 experienced a recurrence at the 8-week endpoint compared to 53% of subjects (16 out of 30) who received placebo, a result that did not show a statistically significant difference between the two treatment arms. SER-109 was generally safe and well tolerated in both the Phase 1b/2 and Phase 2 clinical studies. In each study 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 administration after completion of antibiotics. Four capsules of SER-109 is comprised of about 30 million SCFU that are delivered in four oral capsules. The spores in SER-109 are intended to germinate in the gastrointestinal tract and compete for the same nutrients required by C. difficile.

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. Part 1 of the study evaluated a single dose of SER-109 administered orally in 30 capsules over two days, with a dose that varied between 3×10^7 and 2×10^{10}. Part 2 of the study evaluated a single dose of SER-109 administered orally in a range of one to 7 capsules over one day. 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.

Phase 1b/2 clinical study results. 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 a positive C. difficile stool test) during the eight weeks after initiating therapy. Twenty-six of 30 patients, or 87% of patients, in the Phase 1b/2 clinical study achieved the primary efficacy endpoint, consisting 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. Of the patients who did not meet the primary efficacy endpoint, one had a recurrence of CDI on Day 5 and did not receive a second treatment with SER-109 and the three other patients were determined by their attending investigator to be recovering from their diarrheal episode by the time they submitted their stool sample for CDI testing. The 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. SER-109 was well tolerated. The most common adverse events were diarrhea, nausea, and abdominal pain. The majority of treatment-emergent adverse events, or TEAEs, were mild in severity and consistent with post-antibiotic recovery from CDI.

Phase 2 clinical study design. The Phase 2 clinical study was a randomized, double-blinded, placebo-controlled, parallel-group two arm trial that enrolled a total of 89 patients with a history of multiply-recurrent CDI, defined as 3 or more CDI episodes within 9 months. Subjects were randomized at a 2:1 ratio with 59 subjects receiving SER-109 and 30 subjects receiving placebo. SER-109 was administered orally as a single dose of $1x10^8$ bacterial spores, following the completion of antibiotic treatment for CDI. The study was conducted at 36 centers across the United States. The primary endpoint was the absence of recurrence of C. difficile positive diarrhea requiring antibiotic treatment up to 8 weeks following treatment with SER-109 or placebo.

Phase 2 clinical study results. The predefined study primary efficacy endpoint was the relative risk of CDI recurrence up to 8 weeks after treatment with SER-109 compared to treatment with placebo. CDI recurrence was defined as diarrhea for 2 or more consecutive days, a positive CDI test, and the requirement for antibiotic treatment. Based on 8-week data, CDI recurrence occurred in 44% of subjects (26 of 59) who received SER-109, compared to 53% of subjects (16 of 30) who received placebo. The relative risk of CDI recurrence for the placebo population compared to the SER-109 population was not statistically significant.

The most commonly reported adverse events in both the SER-109 and placebo arms were in the gastrointestinal category, and were diarrhea (25% vs 14%), abdominal pain (22% vs 14%), flatulence (12% vs 3%), and nausea (10% vs 10%), for SER-109 and Placebo, respectively. No drug-related serious adverse events were observed. The SER-109 analyses were shared with the FDA. Based on feedback received from the FDA, a new Phase 3 SER-109 clinical study in approximately 320 patients with multiply recurrent C. difficile infection. Study participants are randomized 1:1 between SER-109 and placebo and will receive a total dose that is approximately 10-fold higher than in the Phase 2 study, administered over three consecutive days. Diagnosis of C. difficile infection for both study entry and for endpoint analysis will be confirmed by C. difficile cytotoxin assay, compared to the first Phase 2, where most patients were diagnosed by polymerase chain reaction, or PCR. The primary endpoint will compare the C. difficile recurrence rate in subjects who receive SER-109 verses placebo at up to eight weeks after dosing. The FDA has agreed that this new trial may qualify as a pivotal study with achievement of a persuasive clinical effect and addressing FDA requirements, including clinical and statistical factors, an adequately sized safety database, and certain CMC parameters.

Analysis of Phase 1b/2 and Phase 2 clinical study results In our Phase 2 clinical study, the study's primary endpoint of reducing the relative risk of CDI recurrence at up to 8 weeks after treatment was not achieved. In order to understand the difference in outcome between Phase 1b/2 and Phase 2 clinical studies, we conducted an analysis of the available clinical, microbiome and CMC data. This root-cause investigation looked at the clinical trial population, study conduct, and diagnostic testing used for study inclusion and endpoint analysis, assessed clinical specimens for genomic and metabolomic biomarkers that might give insight into SER-109 efficacy and potency, reviewed manufacturing procedures and processes, performed retrospective analysis using high-resolution whole metagenomics sequencing of Phase 1b/2 clinical study stool samples, and reviewed analytical methods, that may have differed between the Phase 1b/2 and Phase 2 clinical studies. We have now identified key factors that we believe contributed to the Phase 2 clinical study results, including issues related to both the accurate diagnosis of C. difficile recurrent infection, and potential suboptimal dosing of certain subjects in the trial.

The key factors include:

- The diagnostic test for entry may not have differentiated subjects with active CDI disease from those with other disease but who had C. difficile carriage (e.g., irritable bowel syndrome)
- The diagnostic test for CDI recurrence during the study (the primary endpoint) overestimated recurrences, as PCR was the most common test performed.
- The difference in recurrence rates by age in the placebo arm was confounded by the small number of placebo subjects (30) and the likely inclusion of subjects with irritable bowel syndrome rather than recurrent CDI, or RCDI
- The safety profile of SER-109, which includes diarrhea in the first week following dosing, led to SER-109 subjects presenting for evaluation of recurrence at a time when they were likely to be colonized with C. difficile leading to mistaken diagnosis of RCDI
- The dose and dosing regimen used in the study may not have been optimal in the Phase 2 clinical study based upon an assessment of the microbiome response using whole metagenomics shotgun sequencing.

We performed an analysis of the microbiome of our Phase 2 clinical study and a reanalysis of our Phase 1b/2 clinical study using whole metagenomics shotgun sequencing and microbiological analysis to evaluate long-term changes in the microbiome, including the restoration of bacterial diversity in the colon of patients. This 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. We did not observe any dose-dependent effect on engraftment, augmentation, or the clinical resolution of CDI in the Phase 1b/2 clinical study.

Phase 3 clinical study design. In June 2017 we initiated a Phase 3 clinical study of SER-109 in approximately 320 patients with multiply recurrent C. difficile infection. Study participants are randomized 1:1 between SER-109 and placebo. Diagnosis of C. difficile infection for both study entry and for endpoint analysis utilize a C. difficile cytotoxin assay, compared to the Phase 2 clinical study, where most patients were diagnosed by PCR. Patients in the SER-109 arm will receive a total SER-109 dose, administered over three days, approximately 10-fold higher than the dose used in the Phase 2 clinical study. The new study will evaluate patients for 24 weeks and the primary endpoint will compare the C. difficile recurrence rate in subjects who receive SER-109 verses placebo at up to eight

weeks after dosing. CDI recurrence is defined as diarrhea (>3 UBMs/day for 2 or more consecutive days), a positive CDI toxin test, and the decision by the primary investigator that antibiotic treatment is warranted. The study will be conducted at approximately 100 sites in the United States and Canada.

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 appropriate qualification criteria.

Donors are required to be in good health, and to possess a medical history 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. 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, donations are released for use in manufacturing.

We initially process the donor material in our 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 drug substance is tested for identity, potency and purity, and subsequently formulated into drug product where it is again tested for identity, potency, purity, and pharmaceutical properties in our Cambridge facility. 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 ongoing and proposed clinical trials.

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 product. Identity testing has been developed to assure the presence of specific live spore forms in the product. Potency assays assure the intended dose of spores, and assess stability of the spores during storage. Stability of the dosage form is also confirmed. Proprietary microbiological purity assays have been developed to enable testing for microbial contaminants in the presence of the live spore product.

We believe we can address market demand with a relatively small-scale manufacturing process. If approved, we anticipate that we will be able to produce a sufficient commercial supply of SER-109 to meet estimated demand in the United States using donations from a modest number of donors.

SER-262

We are developing SER-262, which is a rationally designed, multi-strain Ecobiotic microbiome therapeutic intended to be used following antibiotic treatment of primary CDI to prevent an initial recurrence of CDI. We have designed SER-262 to increase and improve diversity in the colonic microbiome after antibiotics treatment of primary CDI. The results of our Phase 1b/2 clinical study of SER-109 provided multiple insights 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 efficacy in mouse models of CDI similar to those observed in pre-clinical studies of SER-109.

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.

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 may eliminate the need for ongoing human donors in the CMC process. There are several advantages to using a rationally designed approach to developing microbiome therapeutics. Rationally designed product candidates can be manufactured in a reliable and reproducible manner, with extremely well-defined characteristics. Based on our metagenomics expertise, proprietary in silico algorithms, extensive proprietary bacterial library, and advanced manufacturing capabilities, we believe we can rationally design produced microbiome therapeutic candidates for specific target indications. We believe, our capabilities provide us with a competitive advantage in developing microbiome therapies.

We progressed our drug discovery and development platforms with the initiation in July 2016 of a Phase 1b dose-escalating study for SER-262, the first clinical, rationally designed ecology of spore forming bacteria designed to be used following antibiotic treatment for primary CDI to prevent an initial recurrence of CDI. We believe there are several advantages to using a rationally designed approach to developing microbiome therapeutics, such as scaling up manufacturing of rationally designed product candidates

to meet global demand in a reliable and reproducible manner, with well-defined characteristics. Based on our metagenomics expertise, proprietary in silico algorithms, extensive proprietary bacterial library, and advanced manufacturing capabilities, we believe we can rationally design microbiome therapeutic candidates for specific target indications. We believe these capabilities provide us with a competitive advantage in developing microbiome therapeutics. SER-262, available in oral capsule form, is derived from a manufacturing process that does not require human donor material. SER-262 contains a consortium of 12 bacterial strains in spore form constructed from strains from our microbiome strain library via in vitro fermentation.

The Phase 1b clinical study is a 24-week, randomized, placebo-controlled, dose-escalation trial. The present study was initially designed to evaluate a single dose administration of SER-262 at ascending spore doses ranging from $1x10^4$ to $1x10^8$ SCFU, with each dosing cohort comprised of 10 subjects treated with SER-262 and two subjects administered placebo. Following analysis of prior SER-109 clinical studies that suggest higher doses of microbiome therapeutics may be important to rapidly address dysbiosis and provide increased efficacy, in mid-2017 we added additional multiple-dose cohorts to the Phase 1b study of $1x10^6$, $1x10^7$ and $1x10^8$ SCFU per day SER-262, for a three-day period.

The primary endpoints of the study are to evaluate the safety and tolerability of SER-262 and to compare the CDI recurrence rate between the SER-262 and placebo groups at up to eight weeks post-dosing. A secondary endpoint is the analysis of the SER-262 bacterial strain engraftment in patient microbiomes. As of now, we have received unblinded clinical data on all but the final 1 x 10^8 multiple dose cohort, which continues to enroll subjects. No drug-related serious adverse events were observed in these first seven cohorts. No relevant differences were observed in the relative risk of recurrence rates in patients administered SER-262 as compared to placebo. However, this small, first-in-human, Phase 1b study was not powered to detect a statistically significant difference in recurrence rates compared to placebo. A small group of placebo patients were included in this study and, in that group, no recurrences were observed. In addition, there was a measurable difference in recurrence rates in patients treated with Vancomycin and SER-262, as compared to those treated with Metronidazole and SER-262 (4% versus 31%, respectively). This difference was statistically significant with a p value of 0.0049. The medical literature suggests a recurrence rate of about 25% in patients treated with vancomycin for primary CDI.

Microbiome analysis has been conducted on the first five, lowest dose cohorts to assess drug pharmacokinetics. We detected a majority of SER-262 strains in patients receiving SER-262; detection of strains was variable across subjects. Partial engraftment of strains was also a characteristic in our SER-109 clinical studies, and has been reported in FMT of CDI. Engraftment of SER-262 strains was associated with broader changes in the microbiome composition. Microbiome profile differences, based on the antibiotics that were used to treat each patient's CDI, were also demonstrated. Vancomycin led to more rapid and more robust engraftment of SER-262 strains as compared to Metronidazole. More detailed microbiome and metabolomic analyses remain ongoing. These SER-262 proprietary data, the first ever obtained from a rationally-designed microbiome development candidate, will be used to inform the further development of SER-262 and our other therapeutic candidates.

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 from stool originating from healthy, medically screened donors, followed by banking and testing for identity and purity. The strains are cultured in controlled fermentations to meet clinical study needs. cGMP material has been produced for the SER-262 Phase 1b clinical study. 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 are tested for identity, purity, and potency, and the material is placed on stability studies to support clinical storage and use. Optimization of the fermentation and purification processes, and the dosage form are ongoing to refine manufacturing processes for future studies and commercial needs.

Ulcerative Colitis and SER-287

UC is a relapsing-remitting chronic inflammatory disorder affecting the mucosal surface of the colon, leading to episodes of bloody diarrhea, urgency and mucosal inflammation (Danese and Fiocchi, 2011), which generally begins in young adulthood and endures for life. As the disease mostly affects young and middle-aged individuals, a time of peak reproductive and economic productivity, thus, the disease leads to decreased quality of life in those affected by the condition, high morbidity, and significant health economic burden. (Ghosh and Mitchell, 2007; Kappelman et al., 2008; Rubin et al., 2014; Theede et al., 2015) The incidence of UC is rising worldwide and the prevalence of the disease is highest in the United States, Canada, and Europe. In the United States alone, the prevalence of UC in adults is estimated to be 263 per 100,000, while in the pediatric population (age <20 years), prevalence of the disease is estimated to be 33.9 per 100,000. (Kappelman et al., 2013)

Ulcerative colitis is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. The severity of symptoms, diarrhea associated with blood and abdominal pain, may range from mild disease to severe disease with more than 10 stools per day with severe cramps and continuous bleeding. The severity, extent, and duration of disease are also risk factors for developing colon cancer, which occurs at a rate as high as 0.5-1.0% per year, an important complication given the young age at which

the disease strikes. Patients with ulcerative colitis also experience increased risk of Clostridium difficile infection and primary sclerosing cholangitis, compared to the general population.

The pathogenesis of UC is unclear but thought to arise from an aberrant immune response to a change in the colonic luminal environment in a genetically susceptible individual. The key features of UC include diffuse mucosal inflammation in a continuous pattern starting distally in the rectum to more proximal disease in the left colon to pancolitis.

Symptoms of UC include rectal bleeding, tenesmus, increased stool frequency, urgency, incontinence, fever, fatigue and malaise, which negatively impact quality of life, physical and mental health and productivity. A subset of patients has extra-intestinal manifestations ranging from iron deficiency anemia to primary sclerosing cholangitis with implications for increased morbidity. In pediatric patients, the symptoms of UC have a more damaging impact, as they affect children's growth and lead to delayed puberty. These patients also suffer from weight loss, anemia and joint symptoms and current therapy itself adversely impacts normal growth and development. (Kelsen et al., 2008) Treatment of UC with corticosteroids and immunosuppressive agents adds further medical complications to these vulnerable patients including corticosteroid toxicity and increased risk of invasive infections and malignancy. Both environmental and genetic factors contribute to the etiology of the disease. Environmental factors may induce an ongoing immune response and inflammation in the genetically predisposed host. Efforts to identify specific environmental factors has implicated commensal bacteria or their products as key determinants of the inflammatory response in UC patients (Xavier et al., 2007). Thus, we believe SER-287 likely targets an "underlying cause" of UC rather than its symptoms.

Current and developing treatment alternatives and their limitations

Currently, patients with UC require life-long therapy. The goals of medical therapy are to induce and maintain clinical and endoscopic remission. Endoscopic remission is recognized as a key treatment goal since it better predicts short- and long-term clinical outcomes than symptomatic improvement alone. Attainment of these goals is generally associated with improved quality of life and decreased need for corticosteroids, and lower risk of hospitalization, colectomy, and colon cancer.

Although the etiology of UC is not fully understood, much progress has been made in the understanding of pathogenesis. Under homeostatic conditions, there is a balance between pro-inflammatory and anti-inflammatory cytokine signals mediated by epithelial and immune cells in the gastrointestinal tract. However, UC is characterized by dysregulated mucosal immune responses and translocation of inflammatory mediators of microbiological origin across a disrupted gastrointestinal barrier that may cause or perpetuate inflammation leading to chronic inflammatory disease. Migration of innate and adaptive immune cells into gut mucosal tissues is potentiated by locally produced cytokines and chemokines, and by the expression of integrins that enhance cellular trafficking into the gut lamina propria. Inhibition of the immune response, via antibodies and proteins that sequester pro-inflammatory cytokines or block the function of integrins, has been an important target of UC drug development over the past decade.

Current management of UC includes medications that decrease general inflammation (e.g., 5-aminosalicylate derivatives, corticosteroids) or dampen specific components of the host immune response (e.g., immunomodulators, inhibitors of tumor necrosis factor, anti-integrin antibodies).

For mild-to-moderate disease, the 5-aminosalicylic acid (5-ASA) derivatives are the standard of care for both induction and remission. 5-ASA derivatives achieve clinical remission in only 25-40% of patients during induction and approximately one-third of responders have disease flares during the first year of maintenance therapy, necessitating additional treatment interventions such as corticosteroids and immunomodulators (6-mercaptopurine, methotrexate, azathioprine). Corticosteroids are not recommended by guideline panels for chronic therapy since these drugs are ineffective for maintaining remission and are associated with significant adverse events. Patients taking thiopurines require ongoing monitoring for hepatotoxicity, myelosuppression, and opportunistic infections, as well as

counseling on the potential risk of lymphoma.

Current medical therapies for the treatment of UC suppress the immune system rather than reducing the triggers of immune activation. There remains an unmet need for safer agents with novel non-immunosuppressive mechanisms of action. Moreover, alternative therapy is needed for patients with mild-to-moderate UC who experience frequent flares or are intolerant to the aminosalicylate class of medication or where there are safety concerns relating to the use of immunomodulator or steroid therapy.

SER-287

Given the dysbiosis seen in UC patients, studies have explored the use of FMT to treat UC. (Angelberger et al., 2013; Colman and Rubin, 2014; Kump et al., 2013; Kunde et al., 2013; Moayyedi et al., 2015; Rossen et al., 2015; Paramsothy et al., 2017) Early reports of enhanced clinical remission and endoscopic improvement with repetitive FMT compared to placebo motivated the preclinical development and clinical testing of SER-287. SER-287 is composed of the spore-forming fraction of the intestinal microbiota that is underrepresented in UC patients. We initiated our Phase 1b clinical study in December 2015 in subjects with mild-to-moderate UC to evaluate the safety and efficacy of SER-287 added to standard of care treatment. The primary endpoints of the study were to evaluate the safety and tolerability of SER-287, compare the change in the microbiome composition versus placebo and determine engraftment of SER-287 bacteria following SER-287 treatment. The study evaluated clinical response, complete remission, and endoscopic improvement, as well as metabolomic and immunological findings.

In October 2017, we announced positive topline results from our Phase 1b clinical trial of SER-287 in patients with UC. The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study enrolled patients with active mild-to-moderate UC, with Total modified Mayo scores of 4 to 10. The study enrolled 58 patients at 20 sites across the United States. Study subjects exhibited pre-study disease activity despite use of current therapies in a majority of subjects, which included 5-amino-salacylic acid, low dose corticosteroids, or immunomodulatory therapy.

Diverse analyses of microbiome data of patients in this trial was also a primary endpoint. Three SER-287 drug product lots, based on human donor material obtained from three separate individuals, were used in the Phase 1b study. Microbiome analyses will also be conducted to determine whether there are any observable differences in the drivers of response across the drug product lots.

An evaluation of SER-287 safety and tolerability was a primary study endpoint. Study results demonstrated no imbalance in adverse events in SER-287 treated patients, as compared to patients treated with placebo. There were no drug related serious adverse events.

Diverse analyses of microbiome data of patients in this trial, a primary endpoint, were conducted after completion of the trial. Analyses of study patients' microbiome data indicated that SER-287 induced dose-dependent engraftment of SER-287-derived bacterial species into the colonic microbiome of the patients treated with SER-287. The cohort of patients that received vancomycin pre-treatment followed by daily administration of SER-287 showed the highest level of SER-287 engraftment. We also observed the most meaningful clinical benefit in this patient cohort. Differences in the composition of the microbiome post treatment were also associated with clinical remission. Bacterial engraftment signatures were durable throughout the dosing period of the trial and were also observed at four weeks post administration of the final SER-287 dose. The SER-287 Phase 1b study microbiome data are consistent with previously reported results.

Microbiome results demonstrated engraftment of SER-287-derived bacterial species in patients pre-treated with vancomycin who received SER-287, with daily dosing providing the most rapid and robust change in patients' microbiome. Engraftment observed in these patients was maintained during the entire dosing period and was observed four weeks after the last dose of SER-287 was administered. Thus, engraftment was durable. Vancomycin pre-treatment, as compared to placebo pre-treatment, led to an immediate reduction of microbiome diversity followed by rapid and robust engraftment of SER-287-derived bacterial species. We believe these data suggest that vancomycin pre-treatment may open ecological niches for SER-287 engraftment in the human microbiome of patients with UC

In December 2017, the FDA granted Orphan Drug Designation to SER-287 for treatment of UC in pediatric patients.

Phase 1b clinical study design.

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

Patients were 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 were 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 were 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; and to compare the changes in exploratory biomarkers from mucosal biopsies and stool in each of the treatment arms from baseline through eight weeks.

This study was designed to provide a safety profile of SER-287 compared to placebo for the UC population, describe the changes in the microbiome as a result of treatment with SER-287 and provide potential predictive biomarkers for future studies. UC is characterized by a decrease in microbial diversity and richness, with a lower prevalence of spore-forming organisms within the

phylum Firmicutes. Preliminary data using FMT suggest that microbial interventions can affect clinical outcomes in UC, and this study evaluated whether the ecology of bacterial spores in SER-287 can correct the dysbiosis in UC, increase microbial diversity and safely lead to a clinical response in UC patients with mild-to-moderate disease.

Phase 1b clinical study results

Results were analyzed using the intent-to-treat (ITT) "missing equals failure" analysis and the ITT "observed case" analysis methods. The ITT "missing equals failure" analysis, included all 58 randomized subjects. For this analysis, incalculable clinical endpoints due to missing data, UC medication added due to UC flare during the treatment period and discontinuation from the trial prior to Day 48 were considered as not achieving the clinical endpoints (worst outcome). However, if the end-of-trial endoscopy at Day 48, or later, was available, and the subject didn't take any additional UC medication due to UC flare, then the observed data was used to define success or failure for the subject. A period of 48 days of microbiome therapy was considered sufficient treatment to estimate the outcome of clinical endpoints and was prespecified. The ITT "observed case" analysis included 53 of 58 subjects randomized, excluding those who were missing their end-of-treatment endoscopies and used the observed data to define success or failure for each subject in the analysis.

Clinical Efficacy

In the "missing equals failure" analysis, remission showed a statistically significant improvement in the vancomycin pre-treatment / SER-287 once-daily dosing arm as compared to the placebo/placebo daily arm: 40% (6 of 15 in SER-287) vs 0% (0 of 11 in placebo); difference from placebo (SER-287 - placebo) 40.0% (95% CI: 15.2%, 64.8%), (p-value, 0.0237). (See Figure 1).

The SER-287 weekly treatment arms also showed an improvement over placebo in both remission and endoscopic improvement but the effect was less than with the daily dosing regimen, demonstrating a dose-response to SER-287 in these efficacy endpoints. Addition of vancomycin to the SER-287 weekly dosing regimen did not clearly alter efficacy effects, although this may be due to the small size of the study.

Clinical response (data not shown), showed a numeric increase in the vancomycin/SER287 daily treatment arm compared to placebo but did not reach statistical significance.

Figure 1:SERES-101 Efficacy Data – Missing Equals Failure

Legend: Δ = change from placebo; Remission was defined as a total modified Mayo score of less than or equal to 2, and an endoscopic sub-score of 0 or 1; Endoscopic improvement was defined as a decrease in endoscopic sub score of greater than or equal to 1. Endoscopy measures were analyzed by a Central Reader.

Clinical Safety

The primary safety objective (short-term safety) was to evaluate the safety and tolerability of SER-287 in adults with active mild-to-moderate UC up to 92 days after randomization as determined by clinical and laboratory safety assessments.

The TEAEs were balanced across all the treatment arms. No drug-related serious adverse events, or SAEs, were reported. All adverse events, or AEs, were considered mild to moderate in intensity. Gastrointestinal, or GI, disorders had the greatest number of AEs compared to other system organ classes, with the most efficacious treatment arm (vancomycin/SER-287 daily) experiencing the lowest percentage of GI AEs.

SER-287 was well-tolerated in all treatment arms, showing a safety profile consistent with the placebo arm. The safety profile, when evaluating GI AEs, showed an improvement in the vancoymycin/SER-287 treatment arm compared to vancomycin/placebo and the vancomycin/SER-287 weekly treatment arms. This finding provides an independent assessment of efficacy as the GI AEs likely reflect UC disease activity.

Diverse analyses of microbiome data of patients in this trial, a primary endpoint, was completed after completion of the trial. Analyses of study patients' microbiome data, a co-primary study endpoint of the trial, demonstrate that SER-287 induced dose-dependent engraftment of SER-287-derived bacterial species into the colonic microbiome of the patients treated with SER-287. Patients administered vancomycin pre-treatment followed by daily administration of SER-287 had the highest level of SER-287 engraftment, which was statistically significant. This patient cohort corresponded with the study arm where the most significant clinical benefits were observed, including clinical remission and endoscopic improvement. Differences in the composition of the microbiome post treatment were also associated with clinical remission. Bacterial engraftment signatures were durable throughout the dosing period of the trial and were also observed at four weeks post administration of the final SER-287 dose. The SER-287 Phase 1b study microbiome data support the previously reported clinical results.

Microbiome results demonstrated engraftment of SER-287-derived bacterial species in patients pre-treated with vancomycin who received SER-287. The degree of SER-287 engraftment, as measured by the number of detectable SER-287-derived bacterial species, increased in a dose-dependent manner, with daily dosing providing the most rapid and robust change in patients' microbiome. Engraftment was maintained during the entire dosing period and was observed four weeks after the last dose of SER-287 was administered. Thus, engraftment was durable. Changes in the composition of the gastrointestinal microbiome were associated with clinical remission. Vancomycin pre-treatment, as compared to placebo pre-treatment, led to an immediate reduction of microbiome diversity followed by rapid and robust engraftment of SER-287-derived bacterial species. These data suggest that vancomycin pre-treatment opens ecological niches for SER-287 engraftment in the human microbiome of patients with UC. We plan to initiate the next clinical trial of SER-287 in the middle of 2018.

Pre-Clinical Programs

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, such as Klebsiella, Morganella and Proteus. These may be present at low levels in the healthy colon, and like C. difficile, 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 CDC. 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.

SER-401

We are also designing and developing SER-401 for use with CPIs in patients with solid tumors to enhance efficacy and improve survival. CPIs are used to block mechanisms used by cancer to evade detection and destruction by the immune system. In 2015, several groups reported that CPI efficacy in mouse models was dependent on the composition of the microbiome. That work was extended to humans in November 2017 when several groups reported

that human subjects who respond to CPI treatment have a different microbiome composition than non-responders. One of these reports was from a group led by Dr. Jennifer Wargo of MD Anderson. In November 2017, Seres announced a collaboration with MD Anderson and the Parker Institute to evaluate the potential of SER-401 to improve the outcomes of cancer patients treated with currently-available immunotherapy. Seres also received an exclusive option, with pre-defined financial terms, to license intellectual property rights from MD Anderson related to the use of bacteria in combination with CPIs. Together with our collaborators, we plan to initiate a Phase 1b study this year.

SER-301

We are designing and developing SER-301, a rationally designed Ecobiotic microbiome therapeutic candidate for the treatment of IBD. The design is being driven by insights from successful FMT for UC conducted by our academic collaborators and will leverage microbiome and metabolomic data gained from the ongoing Phase 1b study of SER-287. The SER-301 program also benefits from what we have and will learn about rationally designed Ecobiotic microbiome therapeutic development in our SER-262 program.

SER-155

We are also designing and developing SER-155, a rationally designed product candidate to prevent infections and improve gastrointestinal barrier function (including the consequences of graft versus host disease) in patients following allogeneic

hematopoietic stem cell transplants liver transplants. This preclinical program is based on published clinical evidence from our collaborators at Memorial Sloan Kettering Cancer Center showing that allo-HSCT patients with reduced microbiome diversity are far more likely to die due to infection and/or lethal GvHD (Taur et al., Blood, 2014; Jenq et al, Biology of Blood and Marrow Transplantation, 2015). The selection of the patient population will be based on pre-clinical data, and the assessment of our 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 In November 2017, we announced that we were awarded a grant from CARB-X (Combating Antibiotic-Resistant Bacteria Accelerator) to support continued preclinical research and early development work for SER-155. The CARB-X grant provides us with up to $2.5 million of research funding with potential for an additional $3.1 million upon completion of milestones.

Research and Development

A significant portion of our operating expenses consists of research and development activities related to SER-109, SER-262, SER-287, SER-401, SER-155, SER-301 and the development of new Ecobiotic microbiome therapeutic product candidates. For the years ended December 31, 2017, 2016, and 2015, our research and development expense was $89.5 million, $82.0 million, and $38.1 million, respectively. See “Management’s Discussion and Analysis of Results of Operations and Financial Condition Operating Expenses Research and Development Expenses” for more information.

Sales and Marketing

If SER-109 is approved in the United States and Canada, 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 multiply 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 UC 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 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 supply chains 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 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 50 L) enable the optimization of a wide variety of culture conditions and have been demonstrated to be scalable to larger fermentation processes and

enable technology transfer to clinical and final manufacturing sites. 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 viable microbes from soluble fermentation broth components is typically much simpler.

- Formulation. Our Ecobiotic microbiome therapeutic candidates are combinations of live bacteria and can be administered by a number of methods and by different routes. The primary goal in developing a formulation is to deliver live 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. Dosage forms for oral products may be capsules, tablets, sachets, or liquid containers.
- Analytical. We are addressing quality control requirements for our Ecobiotic microbiome therapeutic candidates using proprietary microbiological, chemical, biochemical, 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 two manufacturing facilities internal to Seres; a small-scale 7,000 ft^2 unit at our Kendall Square location in Cambridge, Massachusetts, where we conduct cGMP manufacture of Ecobiotic therapeutic candidates to support drug substance and drug product for early phase and small-scale clinical supplies, and a larger 10,000 ft^2 cGMP manufacturing facility at our headquarters, with the ability to perform both drug substance and drug product manufacturing for early and late-phase clinical development and at larger scales of operation. We may 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. We also use contract manufacturing and testing organizations to supplement our internal capacity.

Material Agreements

In January 2016, we entered into the Collaboration and License Agreement, or the License Agreement, with Nestec Ltd., or NHS, an affiliate of Nestlé Health Science US Holdings, Inc., a significant stockholder of ours, for the development and commercialization of certain product candidates in development for the treatment and management of CDI and IBD, including UC 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. We have retained full commercial rights to our entire portfolio of product candidates with respect to the United States and Canada.

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. 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.

In exchange for the license, NHS made an upfront cash payment to us of $120.0 million. NHS also agreed to pay us tiered royalties, at percentages ranging from the high single digits to high teens, of net sales of NHS Collaboration Products in the Licensed Territory. Under the License Agreement we are eligible to receive up to $285.0 million in development milestone payments, $375.0 million in regulatory payments and up to an aggregate of $1,125.0 million for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products. To date, we have received $30.0 million in development milestones under the License Agreement.

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 eight 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 our microbiome therapeutic candidates.

Our patent estate leverages both offensive and defensive strategies. As of February 10, 2018, we owned a total of fifteen 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 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 have not yet expired. Issued patents and pending patent applications as of February 10, 2018 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) two issued U.S. patents, which claim 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) three issued U.S. patents that claim certain methods of treatment of gastrointestinal diseases, including Crohn's disease and colitis, using combinations of bacterial spores and (ii) one issued U.S. patent that claims compositions and a pending continuation application and (iii) 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 six 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 pending national stage applications in the U.S. and ten ex-U.S. jurisdictions related to compositions of matter and methods of treating disorders with compositions that include, for example, ternary combinations of microbes. 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. 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, SER-401, SER-262, SER-301 and SER-155 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 announced its intention to exercise enforcement discretion and not apply 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. In March 2014, the FDA issued a draft guidance document to clarify its Enforcement Policy in the July 2013 guidance. In the March 2014 draft guidance, the FDA noted that since the issuance of its Enforcement Policy in July 2013, it has continued to review its policies in this area and it intends to continue to exercise enforcement discretion in more narrow circumstances than previously identified. Specifically, the March 2014 draft guidance indicated the FDA's intent to limit enforcement discretion in circumstances where the licensed health care professional treating the patient obtains adequate informed consent from the patient or his or her legally authorized representative for the use of FMT products; the FMT product is obtained from a donor known to either the patient or the licensed health care provider; and the stool donor and stool are qualified by screening and testing performed under the discretion of the licensed health care provider for the purposes of providing the FMT product. Following receipt of public comments on the March 2014 draft guidance proposing to modify the July 2013 Enforcement Policy, the FDA issued a new draft guidance in March 2016 announcing its intention to further modify its approach to enforcement discretion for INDs for the use of FMT products. In this draft guidance, the FDA indicated that it intends to continue to exercise enforcement discretion, provided that the licensed health care professional treating the patient obtains adequate informed consent for use of the FMT product; the FMT product is

not obtained from a stool bank; and the stool donor and stool are qualified by screening and testing performed under the direction of the licensed health care provider for purposes of providing the FMT product to treat his or her patient. The FDA further clarified in the March 2016 that, when finalized, the policy would supersede the final Enforcement Policy espoused in the July 2013 Guidance. However, to date, the FDA has not finalized the March 2016 draft guidance. The FDA provided confirmation to us that it intended 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, we have conducted and will continue to conduct all subsequent clinical studies of SER-109 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.

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. Additionally, 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, unless otherwise informed by the FDA, the FDA currently requires, as a condition for accelerated approval that all advertising and promotional materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the agency for review during the pre-approval review period, and that after 120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

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 find that our product candidates no longer satisfy the criteria for such programs for which we have already obtained the relevant designation or approval, 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 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 continues 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 or where the original applicant cannot produce sufficient quantities of product. 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 for the treatment of recurrent CDI. In December 2017, the FDA granted Orphan Drug Designation to SER-287 for treatment of UC in pediatric patients.

We may seek additional 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 marketing authorization application shall be accepted and no marketing authorization shall be granted for a similar medicinal product for the same indication. 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

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other healthcare regulatory laws restrict business practices in the biotechnology industry, which include, but are not limited to, anti-kickback, false claims, physician payment and pricing transparency and data privacy and security laws. 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 interpreted 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 federal false claims and civil monetary penalties laws, including the False Claims Act, or FCA, impose liability on persons who, among other things, knowingly present or cause to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly make, use, or cause to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly make a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. 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 authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposed new reporting requirements through the Physician Payments Sunshine Act 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 for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Manufacturers 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, and pricing information and marketing expenditures.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final 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 requirements, thus complicating compliance efforts.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

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 pharmaceutical and biological products 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 pharmaceutical and biological 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.

There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future, particularly in light of the current Presidential administration and U.S. Congress.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In For example, the Budget Control Act of 2011, enacted in August 2011, among other things, included 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 2025 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 types of providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical and biological products. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Adoption of other new legislation at the federal or state level could further limit reimbursement for pharmaceuticals, including our product candidates if approved.

Employees

As of December 31, 2017, we had 138 full-time permanent employees. 36 employees work in administration and operations and 102 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 200 Sidney Street, Cambridge, Massachusetts 02139 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.

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, accordingly, file reports, proxy statements and other information with the Securities and Exchange Commission. Such reports, proxy statements and other information can be read and copied at the public reference facilities maintained by the Securities and Exchange Commission at the Public Reference Room, 100 F Street, NE, Washington, D.C. 20549. Information regarding the operation of the Public Reference Room may be obtained by calling the Securities and Exchange Commission at 1-800-SEC-0330.

The Securities and Exchange Commission maintains a web site (http://www.sec.gov) that contains material regarding issuers that file electronically, such as ourselves, with the Securities and Exchange Commission.

We make available free of charge on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission.

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 $89.4 million for the year ended December 31, 2017, $91.6 million for the year ended December 31, 2016, and $54.8 million for the year ended December 31, 2015. As of December 31, 2017, we had an accumulated deficit of $263.6 million. To date, we have financed our operations through the initial public offering of our common stock, private placements of our preferred stock, milestone payments under the licensing agreement with Nestec, Ltd., or NHS, and loan financing. 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 have not completed development of any of our product candidates, which we call 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 may increase substantially as we:

- continue the clinical development of SER-109, our lead product candidate, in the Phase 3 clinical study;
- continue the clinical development of SER-287 for the treatment of UC in adults and children and potential other studies of IBD;
- initiate the clinical development of SER-401;
- conduct research and continue pre-clinical development of additional Ecobiotic microbiome therapeutic candidates, including SER-401, SER-155, and SER-301;
- make strategic investments in manufacturing capabilities;
- maintain and augment our intellectual property portfolio and opportunistically acquire complementary intellectual property;
- potentially establish a sales and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- perform our obligations under the collaboration agreement with NHS;
- seek to obtain regulatory approvals for our product candidates; 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 in the preliminary stages of many 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.

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.

Our expenses may increase in connection with our ongoing activities, particularly as we continue the clinical development of SER-109, including conducting the Phase 3 clinical study, continue the clinical development of SER-287, including conducting the next clinical study, complete our Phase 1b clinical study of SER-262, initiate clinical studies of SER-401, and continue to research, develop and initiate clinical trials of SER-301 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 through the first quarter of 2019. This estimate excludes net cash flows from future business development activities. In addition, the specifics of future clinical trial activities could impact capital requirements and cash projections. 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. We intend to focus in the near-term on the highest priority clinical programs, which we believe will optimally advance our pipeline: SER-287 for UC; SER-109 for recurrent CDI; and the SER-401 immuno-oncology program. Our future capital requirements will depend on many factors, including:

- the progress and results of our Phase 3 clinical study of SER-109;
- the progress and results of future clinical studies of SER-287;
- the progress and results of future clinical studies of SER-262;
- the progress and results of our studies in immuno-oncology;
- the cost of manufacturing clinical supplies for 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-301 and SER-155;
- 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 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 our clinical and pre-clinical program, building our intellectual property portfolio, developing our supply chain, planning our business, raising capital and providing general and administrative support for these operations. We have completed our Phase 1b and a Phase 2 clinical study of SER-109, our lead product candidate and have reported top-line data in our Phase 1b study of SER-287 and partial top-line data for our Phase 1b study in SER-262. We have not yet demonstrated our ability to successfully complete any Phase 3 clinical study 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 made 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

Other than SER-109, we are 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. 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 infection and treat diseases where the microbiome is implicated. We may have problems applying our technologies to these areas, and our product candidates may not be effective in preventing infection and disease. Our product candidates 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 our 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, such as SER-109, 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 prevent infection and 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, or manufactured on a commercial scale, a therapeutic based on this approach. We cannot be certain that our approach will lead to the development of approvable or marketable products or that we will be able to manufacture at commercial scale, if approved. 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. For example, our SER-109 Phase 2 clinical study's primary endpoint of reducing the relative risk of CDI recurrence at up to eight-weeks after treatment was not achieved. After analysis of the previous studies, we initiated a Phase 3 clinical study of SER-109 (ECOSPOR III) in patients with multiply recurrent CDI.

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 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.

It is difficult 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. 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 2014, the FDA had indicated that we may be required to conduct more than one Phase 3 clinical trial of SER-109 in order to gain approval. More recently, the FDA has indicated that a single Phase 3 study for SER-109 will be sufficient for approval provided that we show a persuasive clinical effect and certain chemistry, manufacturing and controls parameters.

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;
- failures or delays in reaching 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.

On July 29, 2016, we announced the interim eight-week results from our SER-109 Phase 2 clinical study for the prevention of multiply recurrent CDI. The study's primary endpoint of reducing the relative risk of CDI recurrence at up to eight-weeks after treatment was not achieved. In order to understand the difference in outcome between the Phase 1b and Phase 2 clinical studies for SER-109, we conducted an analysis of the Phase 2 clinical study. In June 2017, we initiated a Phase 3 clinical study of SER-109 (ECOSPOR III) in patients with multiply recurrent CDI. Additional clinical trials or changes in our development plans could cause us to incur significant development costs, delay or prevent the commercialization of SER-109 or otherwise adversely affect our business.

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 reduce recurrence of CDI in patients suffering from recurrent CDI. There is a limited number of patients from which to draw for clinical studies.

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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 or a delayed rate of enrollment would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials would 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 if 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 product 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 product candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of our product 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 be certain 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 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 from the FDA for SER-109 for recurrent CDI and SER-287 for pediatric ulcerative colitis, 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 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, SER-262, SER-287, and SER-301, 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, 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 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 certain aspects of 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 certain aspects of materials supply for our product candidates in 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 supply agreements by the third-party manufacturers;
- failure to supply components, intermediates, services, or product according to our specifications;
- failure to supply components, intermediates, services, or 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 inside or 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 an FDA-approved therapeutic. If our manufacturers are unable to comply with cGMP regulation or if the FDA or other regulators do 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 our clinical production facility in Massachusetts, we do not currently have arrangements in place for redundant supply of SER-109 and SER-287 product. We do not currently have a second source for required materials used for the manufacture of finished SER-109 or SER-287 product. If our current 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 manufacturing facilities at our Cambridge, Massachusetts locations 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 have not yet had any of our manufacturing facilities inspected.

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. 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.

In addition, some of our product candidates require donor material, of which we may not be able to collect sufficient quantities for commercial-scale or other manufacturing.

Risks Related to Commercialization of Our Product Candidates and

Other Legal 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 FMT and physicians may continue to rely on these treatments and our competitors and physicians may continue to seek to standardize and implement this procedure. 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
- the ability of patients to take our products.

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 employees with experience in sales and marketing, but we have limited sales or marketing infrastructure and, as a company, 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 rely 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 reducing 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 reports of 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, not-for-profits, 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 $5.0 million in product liability insurance coverage in the aggregate, with a per occurrence limit of $5.0 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 BPCIA, 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. It is possible that Congress or the FDA may take these or other measures to reduce or eliminate periods of exclusivity. The BPCIA 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 BPCIA in March 2015. However, several issues still remain unclear with respect to the FDA’s final implementation of the BPCIA, 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, 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. In addition, the FDA's regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. For example, in December 2016, the 21st Century Cures Act was signed into law, which is intended, among other things, to modernize the regulation of biologics and to spur innovation, though its ultimate implementation remains unclear. 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.

We also cannot predict the likelihood, nature, or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. For example, certain policies of the current Presidential administration may impact our business and industry. Namely, the current Presidential administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval or marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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 restrict 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 false claims and civil monetary penalties laws, including the federal False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim or from knowingly 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 our business practices, including but not limited to, research, distribution, 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, pricing information 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 we 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 laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, is 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
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future, particularly in light of the current Presidential administration and U.S. Congress. At this time, the full effect that the Affordable Care Act would have on our business remains unclear.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, the Budget Control Act of 2011, enacted in August 2011, included 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, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding 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 additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Individual states in the United States have become increasingly active in implementing regulations designed to contain pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. Legally mandated price controls on payment amounts by third-party payors or other

restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

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.

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. For some patent applications in our portfolio, we have filed national stage applications based on our Patent Cooperation Treaty, or PCT, applications, thereby limiting the jurisdictions in which we can pursue patent protection for the various inventions claimed in those applications. 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.

We have obtained licenses and options to obtain licenses from third parties and may obtain additional licenses and options in the future. 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 seven 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 or cover one or more of our products. 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 third-party preissuance submissions of prior art to the United States Patent and Trademark Office, or USPTO, or in a foreign jurisdiction in which our applications are filed, 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. For example, on April 25, 2017, we filed a notice of opposition in the European Patent Office challenging the validity of a patent issued to The University of Tokyo. See “—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.” 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 our 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, 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 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 patent 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, 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 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. For example, in view of these and subsequent court decisions, the USPTO has issued various materials to patent examiners providing guidance for determining the patent eligibility of claims reciting laws of nature, natural phenomena or 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. On March 4, 2014, the USPTO issued a memorandum reflecting the USPTO's interpretation of the cases related to patent eligibility of natural products. The March 4, 2014 memorandum was superseded by interim guidance published on December 15, 2014. Additional guidance was published in July 2015 (July 2015 Update: Subject Matter Eligibility) and May 2016 (May 2016 Subject Matter Eligibility Update). 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 third-party patent families that include issued and allowed patents, including claims that, if valid and enforceable, could be construed to cover some of our product candidates or their methods of use. On April 25, 2017, we filed a notice of opposition in the European Patent Office challenging the validity of a patent issued to The University of Tokyo and requesting that it be revoked in its entirety for the reasons set forth in our opposition. Although we believe this patent should be revoked in its entirety, the ultimate outcome of the opposition remains uncertain.

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 each of the patent families that we believe provide coverage for our product candidates, we 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 Our Operations

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. 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 may expand our operational capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We may 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 potential 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 potential 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.

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, we have incurred and will continue to incur significant legal, accounting and other expenses, particularly after we are no longer an emerging growth 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 are 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. If we are unable to maintain effective internal control over financial reporting, we may not have adequate, accurate or timely financial information, and we may be unable to meet our reporting obligations as a public company or comply with the requirements of the SEC or Section 404. This could result in a restatement of our financial statements, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Material weaknesses in our internal control over financial reporting could also reduce our ability to obtain financing or could increase the cost of any financing we obtain. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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 data and those of our current and future contractors and consultants are vulnerable to damage or compromise from computer viruses, unauthorized access, human error, 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 reputational damage 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;
- additional exposure to cybersecurity risks and vulnerabilities from any newly acquired information technology infrastructure;

- 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.

We are currently subject to securities class action litigation and may be subject to similar or other litigation in the future, which may harm our business.

On September 28, 2016, a purported stockholder filed a putative class action lawsuit in the U.S. District Court for the District of Massachusetts against us entitled Mariusz Mazurek v. Seres Therapeutics, Inc., et.al. On February 12, 2017, we received an amended complaint, and on March 30, 2017 we submitted a motion to dismiss. A hearing on the motion to dismiss was held on August 9, 2017. The lawsuit alleges violations of Sections 10(b), 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934, as amended, by making allegedly false and misleading statements and omissions about our clinical trials for our product candidate SER-109 in our public disclosures between June 25, 2015 and July 29, 2016. The lawsuit seeks, among other things, damages in connection with our allegedly inflated stock price between June 25, 2015 and July 29, 2016 as a result of those allegedly false and misleading statements, as well as interest, attorneys' fees and costs. We can make no assurances as to the time or resources that will need to be devoted to this lawsuit or its final outcome, or the impact, if any, of this lawsuit or any proceedings on our business, financial condition, results of operations and cash flows. While we are vigorously defending against all claims asserted, this litigation could result in substantial costs to us and a diversion of our management's attention and resources, which could harm our business. In addition, the uncertainty of the pending lawsuit or potential filing of additional lawsuits could lead to more volatility and a reduction in our stock price.

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.

Comprehensive tax reform bills could adversely affect our business and financial condition.

The U.S. government recently enacted comprehensive federal income tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate. Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and

financial condition could be adversely affected. This annual report on Form 10-K does not discuss any such tax legislation or the manner in which it might affect holders of our common stock. We urge our stockholders to consult with their legal and tax advisors with respect to any such legislation and the potential tax consequences of investing in our common stock.

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. Furthermore, 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, our stockholders may not be able to sell their common stock at or above the price they paid for their 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 collaborators 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 65% 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. Moreover, holders of an aggregate of approximately 18.3 million shares of our common stock as of December 31, 2017 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 promulgated under the Securities Act of 1933, as amended, or the Securities Act, 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 $1.07 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:

- not being required to include audited financial statements in our selected financial data and in any future registration statements under the Securities Act for any period prior to the earliest audited financial statements presented in our registration statement on Form S-1 for the initial public offering of our common stock;
- 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.

If securities or industry analysts issue an adverse or misleading opinion regarding our business, our common 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 stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

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

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 our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Research and Offices

Our corporate headquarters is located in Cambridge, Massachusetts, where we lease approximately 83,396 square feet of office, laboratory, and pilot manufacturing space under a lease that expires in November 2023. We also maintain a research and development facility in Cambridge, Massachusetts, where we lease approximately 7,484 square feet of office and laboratory facilities under a lease that expires in April 2020.

Clinical Manufacturing

We currently conduct part of our manufacturing operations in our leased facilities in Cambridge, Massachusetts, which both contain manufacturing facilities for clinical products. We believe our current laboratory facilities and contract relationships are sufficient to meet our current bioprocess development and manufacturing needs. We expect the new facility at our headquarters represents an important addition to our existing manufacturing network, which will broaden our capabilities in bioprocess development and manufacturing, in particular, the production of rationally designed microbiome candidates. We expect to utilize both of the manufacturing facilities to prepare for commercialization of our product candidates. Product candidates may be brought into the facilities 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 all products 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 for commercial supply.

Item 3. Legal Proceedings

Shareholder Litigation

On September 28, 2016, a purported stockholder filed a putative class action lawsuit in the U.S. District Court for the District of Massachusetts against us entitled Mariusz Mazurek v. Seres Therapeutics, Inc., et. al. On February 12, 2017, we received an amended complaint, and on March 30, 2017, we filed a motion to dismiss. A hearing on the motion to dismiss was held on August 9, 2017, and we are awaiting a decision from the court. The lawsuit alleges violations of Sections 10(b), 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934, as amended, by making allegedly false and misleading statements and omissions about our clinical trials for our product candidate SER-109 in our public disclosures between June 25, 2015 and July 29, 2016. The lawsuit seeks, among other things, damages in connection with our allegedly inflated stock price between June 25, 2015 and July 29, 2016 as a result of those allegedly false and misleading statements, as well as interest, attorneys' fees and costs. We can make no assurances as

to the time or resources that will need to be devoted to this lawsuit or its final outcome, or the impact, if any, of this lawsuit or any proceedings on our business, financial condition, results of operations and cash flows. We are vigorously defending against all claims asserted.

Opposition Proceeding

On October 19, 2016, the European Patent Office granted European Patent No. 2 575 835 B1 to The University of Tokyo. On April 25, 2017, we filed a notice of opposition to this patent in the European Patent Office, requesting that it be revoked in its entirety for the reasons set forth in our opposition. Although we believe this patent should be revoked in its entirety, the ultimate outcome of the opposition remains uncertain.

Item 4. Mine Safety Disclosures

Not applicable.

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 Senior Managing Partner and Chief Executive Officer of Flagship Pioneering, formerly known as Flagship Ventures, an early-stage venture capital firm that he co-founded. Dr. Afeyan serves on the board of directors of numerous privately and publicy held companies, including BIND Therapeutics, Inc. Eleven Biotherapeutics, Inc., and Moderna Therapeutics, Inc., and has previously served on the board of directors of several public companies, including BG Medicine, Inc., BIND Therapeutics, Inc., Eleven Biotherapeutics, Inc., and Helicos Biosciences. Dr. Afeyan received a B.S. in chemical engineering from McGill University and a Ph.D. in Biochemical Engineering from the Massachusetts Institute of Technology. He is currently a visiting lecturer of business administration at Harvard Business School and was previously a senior lecturer at the Massachusetts Institute of Technology's Sloan School of Management where he taught courses on technology-entrepreneurship, innovation and leadership.

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. Dr. Ausiello received his undergraduate degree from Harvard College and an M.D. from the University of Pennsylvania.

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, an M.S. in Mechanical Engineering and Manufacturing from EPFL in Switzerland and an MBA from INSEAD in France.

Willard Dere, M.D., has served on our board of directors since July 2017. Since November 2014, Dr. Dere has been Professor of Internal Medicine; B. Lue and Hope S. Bettilyon Presidential Endowed Chair in Internal Medicine for Diabetes Research, Executive Director of Personalized Health, and Co-Principal Investigator of the Center for Clinical and Translational Science at the University of Utah Health Sciences Center. Prior to his professorship, from 2003 until his retirement in October 2014, Dr. Dere held multiple roles at Amgen, including head of global development, and both corporate and international chief medical officer, and led development of programs in various therapeutic areas. Dr. Dere currently serves on the boards of directors of BioMarin Pharmaceutical, Ocera Therapeutics, and Radius Health. Dr. Dere received his undergraduate and medical degrees from the University of California, Davis, completed his internal medicine residency training at the University of Utah, and his postdoctoral training in endocrinology and metabolism at the University of California, San Francisco.

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 has served on the board of directors of INC Research Holdings, Inc. since 2014 and Poxel S.A. since 2015. Mr. Kender received a B.S. from Villanova University and an M.B.A. from Fairleigh Dickinson University.

Lorence H. Kim, M.D., has served as a member of our board of directors since October2014.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.

Kurt C. Graves has served as a member of 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 has served as a director of Intarcia Therapeutics, Inc. since 2012, Radius Health, Inc. since 2011, and Achillion Pharmaceuticals, Inc. since 2012. Mr. Graves received a B.S. in Biology from Hillsdale College.

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 Pioneering, formerly known as 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 ten approved infectious disease drugs for diseases including HIV, HCV and tuberculosis. He has served on the board of directors of Contrafect Corporation, a biotech company, since 2014. Dr. Pomerantz received his B.A. in Biochemistry from The Johns Hopkins University and his M.D. from The Johns Hopkins School of Medicine.

Executive Officers of the Registrant

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.

Thomas J. DesRosier has served as our Chief Legal Officer, Executive Vice President, and Secretary since May 2016. Previously, he served as Executive Vice President, Chief Legal and Administrative Officer and Secretary of ARIAD Pharmaceuticals, Inc., a biopharmaceutical company, from 2015 to 2016, as Executive Vice President, Chief Legal and Administrative Officer and Secretary of Cubist Pharmaceuticals, Inc., or Cubist, a biopharmaceutical company, from 2014 to 2015 and as Senior Vice President, Chief Legal Officer and Secretary of Cubist from 2013 to 2014. Before that, Mr. DesRosier served as Senior Vice President, General Counsel North America of Sanofi, a global biopharmaceutical company, from 2011 to 2013. From 1999 to 2011, Mr. DesRosier held several increasing leadership roles within the legal group of Genzyme Corporation, a biotechnology company, culminating in his role as Senior Vice President, Chief Legal Officer. Mr. DesRosier earned a B.A. in chemistry from the University of Vermont and a J.D. from Wake Forest University School of Law.

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.

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
2017		
First Quarter 2017	$13.32	$9.01
Second Quarter 2017	$12.34	$8.85
Third Quarter 2017	$17.42	$10.51
Fourth Quarter 2017	$15.40	$9.10

	High	Low
2016		
First Quarter 2016	$34.70	$21.12
Second Quarter 2016	$34.99	$22.88
Third Quarter 2016	$35.98	$8.05
Fourth Quarter 2016	$13.77	$8.86

On March 2, 2018, the last reported sale price for our common stock on The Nasdaq Global Select Market was $9.90 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, 2017, 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 2, 2018, there were approximately 23 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.

Recent Sales of Unregistered Securities

We did not make any sales of unregistered securities during the quarter ended December 31, 2017.

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, 2017.

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, 2017, 2016, and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The consolidated statement of operations and consolidated balance sheet data as of December 31, 2014 and 2013 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,				
	2017	2016	2015	2014	2013
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenue	$32,100	$21,766	$—	$—	$—
Operating expenses:					
Research and development	89,455	81,989	38,095	10,718	4,805
General and administrative	34,040	32,616	16,761	4,364	1,247
Total operating expenses	123,495	114,605	54,856	15,082	6,052
Loss from operations	(91,395)	(92,839)	(54,856)	(15,082)	(6,052)
Other income (expense):					
Interest income (expense), net	1,590	1,260	83	(209)	(42)
Other income	425	—	—	—	—
Revaluation of preferred stock warrant liability	—	—	(7)	(1,418)	(8)
Total other income (expense), net	2,015	1,260	76	(1,627)	(50)
Net loss	(89,380)	(91,579)	(54,780)	(16,709)	(6,102)
Accretion of convertible preferred stock to redemption value	—	—	—	(1,291)	(875)
Net loss attributable to common stockholders	$(89,380)	$(91,579)	$(54,780)	$(18,000)	$(6,977)
Net loss per share attributable to common stockholders, basic and diluted[1]	$(2.21)	$(2.30)	$(2.33)	$(2.67)	$(1.09)

(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,				
	2017	2016	2015	2014	2013
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents[1]	$36,088	$54,539	$73,933	$114,185	$1,654
Investments[1]	113,895	175,456	131,149	—	—

Working capital[2]	123,453	167,912	196,690	109,140	649
Total assets	189,522	272,646	216,900	117,345	2,125
Preferred stock warrant liability	—	—	—	1,582	164
Long-term debt, net of discount, including current portion	—	—	—	2,504	838
Convertible preferred stock[3]	—	—	—	136,077	11,583
Total stockholders' equity (deficit)	60,699	132,631	205,394	(26,721)	(11,116)

(1) In January 2016, we entered into a Collaboration and License Agreement with NHS for the development and commercialization of certain of our product candidates. In exchange for the license, NHS paid us an upfront cash payment of $120 million, which we received in February 2016.

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

(3) Convertible preferred stock was converted into our common stock upon the listing of our common stock on The NASDAQ Global Select Market 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 reduce recurrences of Clostridium difficile, or C. difficile, infection, or CDI, a debilitating infection of the colon, in patients who have received antibiotic therapy for recurrent CDI 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 oral microbiome drug. Our second product candidate, SER-287, is being developed to treat inflammatory bowel disease, or IBD, including ulcerative colitis, or UC. In addition, using our microbiome therapeutics platform, we are developing product candidates to treat diseases where the microbiome is implicated, including SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors in patients with solid tumors, SER-262, a rationally designed product candidate, to reduce recurrence of CDI in patients who have received antibiotic therapy for an initial or primary CDI, SER-301, a rationally designed IBD candidate, and SER-155, a rationally designed product candidate to prevent infections and improve gastrointestinal barrier function (including the consequences of graft versus host disease) in patients following allogeneic hematopoietic stem cell transplants or solid organ transplants. We are also using our microbiome therapeutics platform to conduct research on various indications, including: infectious diseases, metabolic diseases, and inflammatory and immune diseases, including immuno-oncology.

Since our inception in October 2010, we have devoted substantially all of our resources to developing SER-109, SER-287 and SER-262, researching our pre-clinical candidates SER-401, SER-155 and SER-301, building our intellectual property portfolio, developing our supply chain, business planning, raising capital and providing general and administrative support for these operations.

All of our product candidates other than SER-109, SER-262 and SER-287 are still in pre-clinical or research 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 $89.4 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of $263.6 million.

On July 29, 2016, we announced the interim eight-week results from our SER-109 Phase 2 clinical study, a randomized, double-blind, placebo controlled Phase 2 clinical study conducted in 89 subjects to evaluate the safety, tolerability and efficacy of SER-109 in adults with recurrent CDI. In that study, 44% of subjects (26 of 59) who received SER-109 experienced a recurrence at the eight week endpoint compared to 53% of subjects (16 of 30) who received placebo, a result that was not statically significant.

In order to understand the difference in outcome between Phase 1b/2 and Phase 2 clinical studies of SER-109, we conducted an analysis of the available clinical, microbiome and chemistry, manufacturing and control data. We identified specific factors that we believe contributed to the Phase 2 clinical study results, including issues related to both the accurate diagnosis of C. difficile recurrent infection, and potential suboptimal dosing of certain subjects in the trial. In June 2017 we initiated a Phase 3 clinical study of SER-109 in approximately 320 patients with multiply recurrent CDI. Diagnosis of CDI infection for both study entry and for endpoint analysis will be confirmed by C.

difficile cytotoxin assay, as compared to the Phase 2 clinical study, where most patients were diagnosed by PCR. Patients in the SER-109 arm will receive a total SER-109 dose, administered over three days, approximately 10-fold higher than the dose used in the Phase 2 clinical study. The new study will evaluate patients for 24 weeks and the primary endpoint will compare the C. difficile recurrence rate in subjects who receive SER-109 verses placebo at up to eight weeks after dosing.

On October 2, 2017, we announced positive topline results from our Phase 1b clinical trial of SER-287 in patients with UC. The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study enrolled patients with active mild-to-moderate UC, with Total Modified Mayo scores of 4 to 10. The study enrolled 58 patients at 20 sites across the United States. Study subjects exhibited pre-study disease activity despite use of current therapies in a majority of subjects, which included 5-amino-salacylic acid, low dose corticosteroids, or immunomodulatory therapy. An evaluation of SER-287 safety and tolerability was a primary study endpoint. Study results demonstrated no imbalance in adverse events in SER-287-treated patients as compared to patients treated with placebo. There were no drug related serious adverse events.

Analyses of study patients' microbiome data, a co-primary study endpoint of the trial, demonstrated that SER-287 induced dose-dependent engraftment of SER-287-derived bacterial species into the colonic microbiome of the patients treated with SER-287. Patients administered vancomycin pre-treatment followed by daily administration of SER-287 had the highest level of SER-287 engraftment, which was statistically significant. This patient cohort corresponded with the study arm where the most significant clinical benefits were observed, including clinical remission and endoscopic improvement. Differences in the composition of the microbiome post treatment were also associated with clinical remission. Bacterial engraftment signatures were durable throughout the dosing period of the trial and were also observed at four weeks post administration of the final SER-287 dose. The SER-287 Phase 1b study microbiome data support the previously reported clinical results.

An evaluation of SER-287 safety and tolerability was a primary study endpoint. Study results demonstrated no imbalance in adverse events in SER-287-treated patients as compared to patients treated with placebo. There were no drug related serious adverse events.

We progressed our drug discovery and development platforms with the initiation in July 2016 of a Phase 1b dose-escalating study for SER-262, the first clinical, rationally designed ecology of spore forming bacteria designed to be used following antibiotic treatment for primary CDI to prevent an initial recurrence of CDI. We believe there are several advantages to using a rationally designed approach to developing microbiome therapeutics, such as scaling up manufacturing of rationally-designed product candidates to meet global demand in a reliable and reproducible manner, with well-defined characteristics. Based on our metagenomics expertise, proprietary in silico algorithms, extensive proprietary bacterial library, and advanced manufacturing capabilities, we believe we can rationally design microbiome therapeutic candidates for specific target indications. We believe these capabilities provide us with a competitive advantage in developing microbiome therapeutics. SER-262, available in oral capsule form, is derived from a manufacturing process that does not require human donor material. SER-262 contains a consortium of 12 bacterial strains in spore form constructed from strains from our microbiome strain library via in vitro fermentation.

The Phase 1b clinical study is a 24-week, randomized, placebo-controlled, dose-escalation trial. The present study was initially designed to evaluate a single dose administration of SER-262 at ascending spore doses ranging from $1x10^4$ to $1x10^8$ Spore Colony Forming Units, or SCFU, with each dosing cohort comprised of 10 subjects treated with SER-262 and two subjects administered placebo. Following analysis of prior SER-109 clinical studies that suggest higher doses of microbiome therapeutics may be important to rapidly address dysbiosis and provide increased efficacy, in mid-2017 we added additional multiple-dose cohorts to the Phase 1b study of $1x10^6$, $1x10^7$ and $1x10^8$ SCFU per day SER-262, for a three-day period.

The primary endpoints of the study are to evaluate the safety and tolerability of SER-262 and to compare the CDI recurrence rate between the SER-262 and placebo groups at up to eight weeks post-dosing. A secondary endpoint is the analysis of the SER-262 bacterial strain engraftment in patient microbiomes. As of now, we have received unblinded clinical data on all but the final 1×10^8 multiple dose cohort, which continues to enroll subjects. No drug-related serious adverse events were observed in these first seven cohorts. No relevant differences were observed in the relative risk of recurrence rates in patients administered SER-262 as compared to placebo. However, this small, first-in-human, Phase 1b study was not powered to detect a statistically significant difference in recurrence rates compared to placebo. A small group of placebo patients were included in this study and, in that group, no recurrences were observed. In addition, there was a measurable difference in recurrence rates in patients treated with Vancomycin and SER-262, as compared to those treated with Metronidazole and SER-262 (4% versus 31%, respectively). This difference was statistically significant with a p value of 0.0049. The medical literature suggests a recurrence rate of about 25% in patients treated solely with vancomycin for primary CDI.

Microbiome analysis has been conducted on the first five, lowest dose cohorts to assess drug pharmacokinetics. We detected a majority of SER-262 strains in patients receiving SER-262; detection of strains was variable across subjects. Partial engraftment of strains was also a characteristic in our SER-109 clinical studies, and has been reported in fecal microbiota treatment of CDI. Engraftment of SER-262 strains was associated with broader changes in the

microbiome composition. Microbiome profile differences, based on the antibiotics that were used to treat each patient's CDI, were also demonstrated. Vancomycin led to more rapid and more robust engraftment of SER-262 strains as compared to Metronidazole. More detailed microbiome and metabolomic analyses remain ongoing. These SER-262 proprietary data, the first ever obtained from a rationally-designed microbiome development candidate, will be used to inform the further development of SER-262 and our other therapeutic candidates.

While we plan to focus our investment on our highest priority clinical programs in the near-term, our expenses may increase substantially in connection with our ongoing and planned activities, particularly as we:

- continue the clinical development of SER-109, our lead product candidate, in the Phase 3 clinical study;
- continue the clinical development of SER-287 for the treatment of UC and potential other studies of IBD;
- advance the pre-clinical development of SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors (CPIs) in patients with solid tumors;

- continue the clinical development of SER-262 to be used following antibiotic treatment of primary CDI to reduce recurrence after the initial episode of CDI;
- conduct research and continue pre-clinical development of additional Ecobiotic® microbiome therapeutic candidates, including SER-155 and SER-301, our rationally designed IBD product candidate;
- make strategic investments in manufacturing capabilities;
- maintain and augment our intellectual property portfolio and opportunistically acquire complementary intellectual property;
- potentially establish a sales and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- perform our obligations under the collaboration agreement with Nestec Ltd., or NHS;
- 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
- 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 UC and Crohn's disease. The License Agreement supports 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 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 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.

In exchange for the license, NHS made an upfront cash payment of $120 million to us in February 2016. NHS has also agreed to pay us 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 us 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 received a $10.0 million milestone payment in 2016 associated with the planned initiation of a Phase 1b study for SER-262 in CDI. In June 2017, we initiated a Phase 3 clinical study of SER-109 (ECOSPOR III) in patients with multiply recurrent CDI. In July 2017, we recorded revenue of $20.0 million based on the achievement of this milestone under the License Agreement. The full potential value of the upfront 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 through the first quarter of 2019. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

To date we have not generated any revenues from the sale of products. Our revenues from collaborations have been derived from the License Agreement.

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 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. All costs associated with the License Agreement are recorded in research and development expense in the consolidated statements of operations and comprehensive loss.

Our primary focus of research and development since inception has been on our microbiome therapeutics platform and the subsequent development of SER-109, SER-262, SER-287, SER-301 and SER-155. 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, CROs in connection with our pre-clinical studies and clinical trials, lab supplies and consumables, 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 for those that have begun clinical development.

	Year Ended December 31,		
	2017	2016	2015

	(in thousands)		
Microbiome therapeutics platform	$63,695	$46,611	$20,603
SER-109	16,306	25,386	13,828
SER-262	4,971	5,269	1,549
SER-287	4,483	4,723	2,115
Total research and development expenses	$89,455	$81,989	$38,095

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 SER-262, conduct our ECOSPOR III Phase 3 clinical study of SER-109, continue to discover and develop additional product candidates, including SER-401. SER-155 and SER-301, and pursue later stages of clinical development of our product candidates.

Research and development expenses of $89.5 million for the year ended December 31, 2017 were comprised of $7.4 million in external services, $23.9 million in clinical and manufacturing costs, and $58.2 million in other costs.

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.

Our general and administrative expenses may increase in the future if we increase our headcount to support the potential growth in our research and development activities and the potential commercialization of our product candidates. We also may continue 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 (Expense), Net

Interest income (expense), net consists of interest earned on our cash, cash equivalents and investments. During the year ended December 31, 2015, 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. There was no such interest expense recorded for these items in 2017 and 2016 as we held no preferred stock warrants or debt during the years ended December 31, 2017 and December 31, 2016.

Other Income

Other income consists of an award from the Massachusetts Life Sciences Center that we earned in 2017 when we met the required employment thresholds.

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 Global Select Market, ("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.

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, 2017, we had federal and state net operating loss carryforwards of $120.7 million and $121.0 million, respectively, both of which begin to expire in 2035. As of December 31, 2017, we also had federal and state research and development tax credit carryforwards of $22.6 million and $3.6 million, respectively, which begin to expire in 2031 and 2028, respectively. The federal research and development tax credits include an orphan drug credit carryforward of $14.5 million.

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. 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.

Collaboration revenue

We evaluate multiple-element arrangements based on the guidance in FASB ASC Topic 605-25, Revenue Recognition-Multiple-Element Arrangements, or ASC 605-25. Pursuant to this guidance, we identify the deliverables included in the arrangement and determine: (1) whether the individual deliverables have value to the customer on a standalone basis and represent separate units of accounting or whether they must be accounted for as a combined unit of accounting; and (2) if the arrangement includes a general right of return relative to the delivered item. This evaluation requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner, the retention of any key rights by us, and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s).

In situations where we have identified multiple units of accounting, the arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605-25 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605-25 are satisfied for that particular unit of accounting. We will recognize as revenue arrangement consideration attributed to licenses that have standalone value from the other deliverables to be provided in an arrangement upon delivery. We will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value from the other deliverables to be provided in an arrangement over the estimated performance period as the arrangement would be accounted for as a single unit of accounting.

If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement for the single unit of accounting on a time-based proportional performance method over the period we are expected to complete our performance obligations. Alternatively, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable

performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the time-based proportional performance method or effort-based proportional performance method, as applicable.

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. We recognize revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method upon successful accomplishment of each milestone, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive would be recognized as revenue over the remaining period of performance, assuming all other revenue recognition criteria are met.

Application of the above guidance requires significant judgment and requires us to make determinations based on the facts and circumstances under each arrangement.

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 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 recognize adjustments to stock compensation expense for forfeitures as they occur.

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. We adjust stock-based compensation expense for forfeitures as they occur.

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,		
	2017	2016	2015
Risk-free interest rate	2.20%	1.54%	1.80%
Expected term (in years)	6.0	6.0	6.0
Expected volatility	80.9%	84.2%	81.4%
Expected dividend yield	0 %	0 %	0 %

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

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

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Research and development	$8,115	$8,310	$5,297
General and administrative	9,247	8,547	4,397
	$17,362	$16,857	$9,694

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 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, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016:

	Year Ended December 31,		
	2017	2016	Change
	(in thousands)		
Revenue	$32,100	$21,766	$10,334
Operating expenses:			
Research and development	$89,455	$81,989	$7,466
General and administrative	34,040	32,616	1,424
Total operating expenses	123,495	114,605	8,890
Loss from operations	(91,395)	(92,839)	1,444
Other income (expense):			
Interest income (expense), net	1,590	1,260	330
Other income	425	—	425

Total other income (expense), net	2,015	1,260	755
Net loss	$(89,380)	$(91,579)	$2,199

Revenue

Total revenue was $32.1 million and $21.8 million for the years ended December 31, 2017 and 2016, respectively. Of the $32.1 million of revenue recognized for the year ended December 31, 2017, $20.0 million was received from NHS associated with the initiation of the Phase 3 study for SER-109 in patients with multiply recurrent CDI, which is a substantive milestone under the License Agreement. Of the $21.8 million of revenue recognized for the year ended December 31, 2016, $10.0 million was received from NHS associated with the initiation of the Phase 1b study for SER-262 in CDI, which was a substantive development milestone under the License Agreement. We recognize revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method, or ASC 605-28. The $20.0 million and $10.0 million payments were recognized in full as related party collaboration revenue during the years ended December 31, 2017 and 2016, respectively. The remaining revenue for both

periods principally relates to the recognition of the $120.0 million upfront payment under the License Agreement over the estimated performance period of 10 years.

Research and Development Expenses

	Year Ended December 31,		
	2017	2016	Change
	(in thousands)		
Microbiome therapeutics platform	$63,695	$46,611	$17,084
SER-109	16,306	25,386	(9,080)
SER-262	4,971	5,269	(298)
SER-287	4,483	4,723	(240)
Total research and development expenses	$89,455	$81,989	$7,466

Research and development expenses were $89.5 million for the year ended December 31, 2017, compared to $82.0 million for the year ended December 31, 2016. The increase of $7.5 million was due primarily to the following:

- an increase of $17.1 million in research expenses related to our microbiome therapeutics platform, due primarily to higher payroll and consultant costs of $6.1 million, an increase in facilities and depreciation costs of $5.3 million, an increase in sponsorship and license costs of $2.7 million, an increase in laboratory consumables and supplies of $1.6 million, an increase in IT expenses of $0.6 million, and an increase in office expenses of $0.7 million;
- a decrease of $9.1 million in expenses related to our SER-109 program, due primarily to a decrease in clinical trial costs of $1.7 million, a decrease in other consulting costs of $1.2 million, a decrease in laboratory consumables and supplies of $3.5 million, a decrease in sequencing costs of $1.3 million, a decrease in animal studies of $0.6 million, a decrease in conference costs of $0.5 million, a decrease in office expenses of $0.3 million, and a decrease in IT expenses of $0.2 million, partially offset by an increase in contract manufacturing costs of $0.3 million;
- a decrease of $0.3 million in expenses of our SER-262 program primarily driven by a decrease in contract manufacturing costs of $1.0 million, a decrease in animal studies costs of $0.2 million, and a decrease in other consulting costs of $0.2 million, partially offset by an increase in clinical trial costs of $0.9 million and an increase in sequencing costs of $0.3 million,; and
- a decrease of $0.2 million in expenses of our SER-287 program primarily driven by a decrease in contract manufacturing costs of $0.3 million a decrease in other consulting costs of $0.2 million, and a decrease in lab consumables and supplies of $0.6 million, partially offset by an increase in clinical trial costs of $0.3 million and an increase in sequencing costs of $0.6 million.

We expect that our research and development expenses may increase in the foreseeable future as we advance the clinical development of SER-109, SER-287 and SER-262, and continue to discover and develop additional product candidates, including SER-401, SER-301 and SER-155, and pursue later stages of clinical development of our product candidates.

General and Administrative Expenses

	Year Ended December 31,

	2017	2016	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$17,233	$16,623	$610
Professional fees	8,265	9,090	(825)
Facility-related and other	8,542	6,903	1,639
Total general and administrative expenses	$34,040	$32,616	$1,424

General and administrative expenses were $34.0 million for the year ended December 31, 2017, compared to $32.6 million for the year ended December 31, 2016. The increase of $1.4 million was primarily due to the following:

- an increase in personnel related costs of $0.6 million primarily due to the increase in stock-based compensation expense;

- a decrease in professional fees of $0.8 million due to a decrease in consulting costs of $0.9 million, partially offset by an increase in legal, accounting, and audit fees of $0.1 million; and
- an increase in facility-related and other costs of $1.6 million primarily due to an increase in information technology expenses of $2.5 million, partially offset by a decrease in office-related expenses of $1.0 million.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2017 was $2.0 million, compared to $1.3 million for the year ended December 31, 2016. The $0.8 million increase in other income (expense), net was primarily due to an increase of $0.3 million in interest income and the recognition of $0.3 million of non-operating income related to the Massachusetts Life Sciences Center tax incentive received in 2016.

Comparison of Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015:

	Year Ended December 31,		
	2016	2015	Change
	(in thousands)		
Revenue	$21,766	$—	$21,766
Operating expenses:			
Research and development	81,989	38,095	43,894
General and administrative	32,616	16,761	15,855
Total operating expenses	114,605	54,856	59,749
Loss from operations	(92,839)	(54,856)	(37,983)
Other income (expense):			
Interest income (expense), net	1,260	83	1,177
Revaluation of preferred stock warrant liability	—	(7)	7
Total other income (expense), net	1,260	76	1,184
Net loss	$(91,579)	$(54,780)	$(36,799)

Revenue

Total revenue was $21.8 million for the year ended December 31, 2016. Of this $21.8 million, $10.0 million was received from NHS associated with the initiation of the Phase 1b study for SER-262 in CDI which is a substantive development milestone under the License Agreement. We recognized revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method. The $10.0 million was recognized in full as related party collaboration revenue during the year ended December 31, 2016. The remaining $11.8 million relates to the recognition of the $120.0 million upfront payment from NHS over the estimated performance period of 10 years. We had no revenue for the year ended December 31, 2015.

Research and Development Expenses

	Year Ended December 31,		
	2016	2015	Change
	(in thousands)		
Microbiome therapeutics platform	$46,611	$20,603	$26,008
SER-109	25,386	13,828	$11,558
SER-262	5,269	1,549	$3,720
SER-287	4,723	2,115	2,608
Total research and development expenses	$81,989	$38,095	$43,894

Research and development expenses were $82.0 million for the year ended December 31, 2016, compared to $38.1 million for the year ended December 31, 2015. The increase of $43.9 million was due primarily to the following:

- an increase of $26.0 million in research expenses related to our microbiome therapeutics platform, due primarily to higher payroll and consultant costs of $16.0 million, which included an increase in stock-based compensation expense of $3.0

million due primarily to an increase in research and development employee headcount of 26 individuals, an increase in facilities and depreciation costs of $7.0 million due primarily to the buildout of new laboratory and manufacturing space in Cambridge, Massachusetts, an increase in license costs of $1.3 million, an increase in laboratory consumables and supplies of $1.2 million, and an increase in travel costs of $0.3 million;

- an increase of $11.6 million in expenses related to our SER-109 program, due primarily to an increase in clinical trial costs of $7.1 million in connection with our Phase 2 clinical study, an increase in other consulting costs of $0.4 million, an increase in laboratory consumables and supplies of $2.2 million, an increase in sequencing costs of $0.9 million, and an increase in conference costs of $0.5 million;
- an increase of $3.7 million in expenses of our SER-262 program primarily driven by an increase in clinical trial costs of $1.4 million, an increase in contract manufacturing costs of $0.9 million, an increase in animal studies costs of $0.1 million, an increase in other consulting costs of $0.2 million, and an increase in lab consumables and supplies of $1.0 million; these increases are due primarily to the initiation of our Phase 1b clinical study in July 2016; and
- an increase of $2.6 million in expenses of our SER-287 program primarily driven by an increase in clinical trial costs of $2.2 million, an increase in lab consumables and supplies of $0.6 million, offset in part due to a decrease in other consulting costs of $0.2 million. These increases are due primarily to the initiation of a Phase 1b clinical trial in December 2015.

General and Administrative Expenses

	Year Ended December 31,		
	2016	2015	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$16,623	$8,371	$8,252
Professional fees	9,090	5,894	3,196
Facility-related and other	6,903	2,496	4,407
Total general and administrative expenses	$32,616	$16,761	$15,855

General and administrative expenses were $32.6 million for the year ended December 31, 2016, compared to $16.8 million for the year ended December 31, 2015. The increase of $15.9 million was primarily due to the following:

- an increase in personnel related costs of $8.3 million primarily due to the hiring of additional employees from December 31, 2015 to December 31, 2016 to support corporate operations and business development activities, including an increase of $4.2 million in stock-based compensation;
- an increase in professional fees of $3.2 million due to an increase in contracted employee costs of $1.0 million, an increase in information technology project consulting costs of $0.6 million, an increase in other general consulting costs of $0.6 million, and an increase in legal, accounting, and audit fees of $0.7 million as a result of ongoing business activities; and
- an increase in facility-related and other costs of $4.4 million primarily due to an increase in office-related expenses of $2.2 million due to the build-out of the 200 Sidney facility, an increase in depreciation and rent charges of $0.9 million, an increase in information technology expenses of $0.9 million, and an increase in insurance costs of $0.5 million.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2016 was $1.3 million, compared to $0.1 million for the year ended December 31, 2015. The $1.2 million increase in other income (expense), net was primarily due to interest income from investing activities.

Liquidity and Capital Resources

Since our inception, we have generated revenue only from collaborations and have incurred recurring net losses. We anticipate that we will continue to incur losses for at least the next several years. Our research and development and general and administrative expenses may 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, additional collaborations, contract and grant revenue or other sources.

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 UC and Crohn's disease. In exchange for the license, NHS agreed to pay us an upfront cash payment of $120 million, which we received in February 2016. NHS

has also agreed to pay us tiered royalties, at percentages ranging from the high single digits to high teens, of net sales of NHS Collaboration Products in the Licensed Territory. We are eligible to receive up to $285.0 million in development milestone payments, $375.0 million in regulatory payments and up to an aggregate of $1.1 billion for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products. 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. In September 2016, we received a $10.0 million milestone payment associated with the initiation of the Phase 1b clinical study for SER-262 in CDI. In June 2017, we initiated a Phase 3 clinical study of SER-109 (ECOSPOR III) in patients with multiply recurrent CDI. In July 2017, we recorded revenue of $20.0 million based on the achievement of this milestone under the License Agreement.

For the development of NHS Collaboration Products for IBD under a global development plan, we agreed 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 agreed to pay the costs of such 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.

With respect to development of NHS Collaboration Products for CDI under a global development plan, we agreed to pay all costs of Phase 2 clinical trials for SER-109 and for 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, 2017, we had cash, cash equivalents and investments totaling $150.0 million and an accumulated deficit of $263.6 million.

Cash Flows

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

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Cash provided by (used in) operating activities	$(75,523)	$43,921	$(40,844)
Cash provided by (used in) investing activities	$56,989	(65,453)	(137,133)
Cash provided by financing activities	$83	2,138	137,725
Net decrease in cash and cash equivalents	$(18,451)	$(19,394)	$(40,252)

Operating Activities

During the year ended December 31, 2017, operating activities used $75.5 million of cash, primarily due to a net loss of $89.4 million and cash used from changes in our operating assets and liabilities of $10.6 million, partially offset by non-cash charges of $24.4 million. Net cash used by changes in our operating assets and liabilities during the year

ended December 31, 2017 consisted of a $0.9 million decrease in accounts payable and a $11.9 million decrease in deferred revenue, offset in part by a $2.2 million increase in accrued expenses and other liabilities. The decrease in our accounts payable and increase in accrued expenses were due to the timing of payments, an increase in payroll related costs, and an increase in amounts accrued for clinical trial expenses. The decrease in deferred revenue was due to the recognition of revenue related to the $120.0 million upfront payment under the License Agreement over the estimated performance period of 10 years.

During the year ended December 31, 2016, operating activities provided $43.9 million of cash, primarily due to upfront cash of $120.0 million and a milestone payment of $10.0 million received in connection with the License Agreement, and cash provided by changes in our operating assets and liabilities of $6.0 million. This increase was partially offset by a net loss of $91.6 million, less non-cash charges of $20.7 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2016 consisted of a $3.6 million increase in accounts payable and a $5.0 million increase in accrued expenses and other current liabilities, offset in part by $2.6 million increase in prepaid expenses and other current assets. 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, 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.

Investing Activities

During the year ended December 31, 2017, investing activities provided $57.0 million of cash, consisting of sales and maturities of investments of $158.3 million; these amounts were partially offset by purchases of investments of $96.5 million, purchases of property and equipment of $4.7 million, and an increase in our restricted cash balance of $0.1 million.

During the year ended December 31, 2016, we used $65.5 million of cash in investing activities, consisting of purchases of investments of $290.6 million and purchases of property and equipment of $21.5 million; these increases were offset by maturities of investments of $246.5 million and a decrease in our restricted cash balance of $0.1 million.

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.

Financing Activities

During the year ended December 31, 2017, net cash provided by financing activities was $0.1 million in connection with the exercise of options to purchase our common stock, partially offset by payments for the repurchase of common stock.

During the year ended December 31, 2016, net cash provided by financing activities was $2.1 million in connection with the exercise of options to purchase our common stock.

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.

Funding Requirements

Our expenses may increase substantially in connection with our ongoing development activities related to SER-109, SER-287, and SER-262, which are in clinical development, and our follow-on therapeutic candidates 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:

- continue the clinical development of SER-109, our lead product candidate, in the Phase 3 clinical study;
- continue the clinical development of SER-287 for the treatment of UC and potential other studies of IBD;
-

- advance the pre-clinical development of SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors in patients with solid tumors;
- continue the clinical development of SER-262 to be used following antibiotic treatment of primary CDI to reduce recurrence after the initial episode of CDI;
- conduct research and continue pre-clinical development of additional Ecobiotic® microbiome therapeutic candidates, including SER-155 and SER-301, our rationally designed IBD product candidate;
- make strategic investments in manufacturing capabilities;
- maintain and augment our intellectual property portfolio and opportunistically acquire complementary intellectual property;
- potentially establish a sales and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;

- perform our obligations under the collaboration agreement with NHS
- 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
- seek to obtain regulatory approvals for our product candidates.

We continue to expect that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements through Q1'19. This estimate excludes net cash flows from future business development activities. The specifics of future SER-109 related activities could impact capital requirements and cash projections. 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, SER-287 and SER-262 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. The near-term focus will be on the highest priority clinical programs to optimally advance our pipeline: SER-287 for UC; SER-109 for recurrent CDI; and the SER-401 immune-oncology program. Our future capital requirements will depend on many factors, including:

- the progress and results of our Phase 3 clinical study of SER-109;
- the progress and results of any future clinical studies of SER-287;
- the progress and results of any future clinical study of SER-262;
- 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-401, SER-155 and SER-301;
- the costs, timing and outcome of regulatory review of our product candidates and research activities;
- 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.

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, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our shareholders' rights as common stockholders. 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 our shareholders' ownership interest.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, in addition to the License Agreement, 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, 2017 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]	$36,370	$6,157	$12,462	$12,593	$5,158
MD Anderson/PICI collaboration[2]	1,551	762	789	—	—
Total	$37,921	$6,919	$13,251	$12,593	$5,158

[1] Amounts in the table reflect payments due for (i) our laboratory and office space in Cambridge, Massachusetts under an operating lease agreement that expires in November 2023 and (ii) our lease for office and laboratory space in Cambridge, Massachusetts with a term expiring April 2020.

[2] Amounts in the table reflect payment obligations under an agreement with MD Anderson Cancer Center and Parker Institute for Cancer Immunotherapy.

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, 2017, our cash, cash equivalents and investments consisted of cash, money market accounts, and investments in corporate bonds, commercial paper, certificates of deposit, treasury bonds, and government securities. 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

On March 7, 2018, we amended the employment agreements we have with Drs. Pomerantz, Trucksis, and Cook and Mr. Shaff to update each of their target bonuses and, with regard to Mr. Shaff, to reflect his additional role as Chief Operating Officer.

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), 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

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Securities Exchange Act, as amended.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in “Internal Control – Integrated Framework (2013)” issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on this assessment, our management concluded that, as of December 31, 2017, our internal control over financial reporting was effective.

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

On March 7, 2018, we amended the employment agreements we have with Drs. Pomerantz, Trucksis, and Cook and Mr. Shaff to update each of their target bonuses and, with regard to Mr. Shaff, to reflect his additional role as Chief Operating Officer.

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 and Directors 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 26, 2018 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 26, 2018 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 26, 2018 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 26, 2018 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 26, 2018 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.

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Restated Certificate of Incorporation, filed on July 1, 2015	8-K	001-37465	3.1	7/1/15	
3.2	Amended and Restated By-Laws	8-K	001-37465	3.2	7/1/15	
4.1	Amended and Restated Investors’ Rights Agreement, dated December 19, 2014, by and among the Registrant and each of the investors listed on Schedule A thereto	S-1	333-204484	4.1	5/27/15	
4.2	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-204484	4.2	6/16/15	
10.1#	2015 Incentive Award Plan and forms of award agreements thereunder	S-1/A	333-204484	10.2	6/16/15	
10.2#	2015 Employee Stock Purchase Plan	S-1/A	333-204484	10.3	6/16/15	
10.3#	Non-Employee Director Compensation Program	S-1/A	333-204484	10.4	6/16/15	
10.4	Lease Agreement, dated April 1, 2015, by and between the Registrant and ARE-MA Region No. 38, LLC	S-1	333-204484	10.13	5/27/15	
10.5	Lease, dated November 11, 2015, by and between the Registrant and BMR-Sidney Research Campus, LLC	10-K	001-37465	10.13	3/14/16	
10.6#	Employment Agreement, dated June 14, 2015, by and between the Registrant and Roger J. Pomerantz	S-1/A	333-204484	10.6	6/16/15	
10.7#	First Amendment to Employment Agreement, dated February 3, 2016, by and between the Registrant and Roger J. Pomerantz	8-K	001-37465	10.1	2/4/16	
10.8#	Second Amendment to Employment Agreement, dated March 7, 2018, by and between the Registrant and Roger J. Pomerantz					*
10.9#	Employment Agreement, dated June 14, 2015, by and between the Registrant and Eric D. Shaff	S-1/A	333-204484	10.7	6/16/15	
10.10#	Amendment to Employment Agreement, dated August 7, 2015 by and between the Registrant and Eric. D. Shaff	10-Q	001-37465	10.7	8/10/15	
10.11#	Amendment to Employment Agreement, dated March 7, 2018 by and between the Registrant and Eric. D. Shaff					*

10.12#	Employment Agreement, dated June 13, 2015, by and between the Registrant and David N. Cook	S-1/A	333-204484	10.8	6/16/15
10.13#	Amendment to Employment Agreement, dated June 13, 2015 by and between the Registrant and David N. Cook	10-Q	001-37465	10.9	8/10/15

Exhibit Number	Exhibit Description	Incorporated by Reference			Filing Date	Filed/ Furnished Herewith
		Form	File No.	Exhibit		
10.14#	Amendment to Employment Agreement, dated March 7, 2018 by and between the Registrant and David N. Cook					*
10.15#	Employment Agreement, dated August 10, 2015, by and between the Registrant and John G. Aunins	10-Q	001-37465	10.10	8/10/15	
10.16#	Amendment to Employment Agreement, dated February 8, 2017 by and between the Registrant and John G. Aunins	10-K	001-37465	10.13	3/16/17	
10.17#	Employment Agreement, dated June 13, 2015, by and between the Registrant and Michele Trucksis	S-1/A	333-204484	10.10	6/16/15	
10.18#	Amendment to Employment Agreement, dated August 7, 2015 by and between the Registrant and Michele Trucksis	10-Q	001-37465	10.12	8/10/15	
10.19#	Amendment to Employment Agreement, dated March 7, 2018 by and between the Registrant and Michele Trucksis					*
10.20#	Employment Agreement, dated April 26, 2016 by and between the Registrant and Thomas J. DesRosier	10-Q	001-37465	10.1	8/11/16	
10.21^	Collaboration and License Agreement, dated January 9, 2016, by and between the Registrant and Nestec Ltd.	10-Q	001-37465	10.1	5/16/16	
10.22#	2012 Stock Incentive Plan, as amended and form of option agreement thereunder	S-1	333-204484	10.1	5/27/15	
21.1	Subsidiaries of Seres Therapeutics, Inc.	S-1/A	333-204484	21.1	6/16/15	
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm					*
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer					*
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer					*
32.1	Section 1350 Certification of Chief Executive Officer					**
32.2	Section 1350 Certification of Chief Financial Officer					**
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*

*Filed herewith.
**Furnished herewith.
#Indicates management contract or compensatory plan.
^Confidential treatment has been granted with respect to redacted portions of this exhibit. Redacted portions of this exhibit have been filed separately with the SEC.

Item 16. Form 10-K Summary

None.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Seres Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Seres Therapeutics, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management's plans in regard to this matter are described in Note 1.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts

March 8, 2018

We have served as the Company's auditor since 2014.

SERES THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31,	
	2017	2016
Assets		
Current assets:		
Cash and cash equivalents	$36,088	$54,539
Investments	113,895	138,704
Prepaid expenses and other current assets	5,095	5,126
Total current assets	155,078	198,369
Property and equipment, net	32,931	36,125
Long-term investments	—	36,752
Restricted cash	1,513	1,400
Total assets	$189,522	$272,646
Liabilities and Stockholder's Equity		
Current liabilities:		
Accounts payable	$7,033	$7,587
Accrued expenses and other current liabilities	12,513	10,812
Deferred revenue - related party	12,079	12,058
Total current liabilities	31,625	30,457
Lease incentive obligation, net of current portion	8,989	10,730
Deferred rent	2,233	2,072
Deferred revenue, net of current portion - related party	84,847	96,756
Other long-term liabilities	1,129	—
Total liabilities	128,823	140,015
Commitments and contingencies (Note 11)		
Stockholders’ equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2017 and 2016; no shares issued and outstanding at December 31, 2017 and 2016	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2017 and 2016; 40,571,015 and 40,355,753 shares issued and outstanding at December 31, 2017 and 2016	40	40
Additional paid-in capital	324,376	306,931
Accumulated other comprehensive income (loss)	(146)	(149)
Accumulated deficit	(263,571)	(174,191)
Total stockholders’ equity	60,699	132,631
Total liabilities, convertible preferred stock and stockholders’ equity	$189,522	$272,646

The accompanying notes are an integral part of these consolidated financial statements.

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SERES THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Revenue:			
Collaboration revenue - related party	$32,100	$21,766	$—
Total revenue	32,100	21,766	—
Operating expenses:			
Research and development expenses	$89,455	81,989	38,095
General and administrative expenses	34,040	32,616	16,761
Total operating expenses	123,495	114,605	54,856
Loss from operations	(91,395)	(92,839)	(54,856)
Other income (expense):			
Interest income (expense), net	1,590	1,260	83
Other income	425	—	—
Revaluation of preferred stock warrant liability	—	—	(7)
Total other income (expense), net	2,015	1,260	76
Net loss	$(89,380)	(91,579)	(54,780)
Net loss per share attributable to common stockholders, basic and diluted	$(2.21)	$(2.30)	$(2.33)
Weighted average common shares outstanding, basic and diluted	40,449,410	39,846,928	23,532,400
Other comprehensive income (loss):			
Unrealized gain (loss) on investments, net of tax of $0	3	(179)	30
Total other comprehensive income (loss)	3	(179)	30
Comprehensive loss	$(89,377)	$(91,758)	$(54,750)

The accompanying notes are an integral part of these consolidated financial statements.

SERES THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Series A, A-2, B, C, D and D-1 Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated Other Comprehensive		Total Stockholders
	Shares	Amount	Shares	Par Value	Capital	Income (Loss)	Accumulated Deficit	Equity (Deficit)
Balance at December 31, 2014	22,866,987	136,077	6,890,250	7	1,104	—	(27,832)	(26,721)
Issuance of common stock upon exercise of stock options	—	—	232,970	—	93	—	—	93
Issuance of common stock upon exercise of common stock warrant	—	—	546,672	1	168	—	—	169
Issuance of common stock upon completion of initial public offering, net of offering costs	—	—	8,545,138	8	139,259	—	—	139,267
Stock-based compensation expense	—	—	—	—	9,694	—	—	9,694
Series D convertible preferred stock issuance costs	—	(24)	—	—	—	—	—	—
Reclassification of preferred stock warrant liability	—	—	—	—	1,589	—	—	1,589
Conversion of convertible preferred stock	(22,866,987)	(136,053)	22,866,987	23	136,030	—	—	136,053

upon listing								
Unrealized gain on investments	—	—	—	—	—	30	—	30
Net loss	—	—	—	—	—	—	(54,780)	(54,780)
Balance at December 31, 2015	—	—	39,082,017	39	287,937	30	(82,612)	205,394
Issuance of common stock upon exercise of stock options	—	—	1,273,736	1	2,137	—	—	2,138
Stock-based compensation expense	—	—	—	—	16,857	—	—	16,857
Unrealized loss on investments	—	—	—	—	—	(179)	—	(179)
Net loss	—	—	—	—	—	—	(91,579)	(91,579)
Balance at December 31, 2016	—	—	40,355,753	40	306,931	(149)	(174,191)	132,631
Issuance of common stock upon exercise of stock options	—	—	174,386	—	116	—	—	116
Issuance of common stock upon vesting of RSUs	—	—	40,876	—	(33)	—	—	(33)
Stock-based compensation expense	—	—	—	—	17,362	—	—	17,362
Unrealized gain on investments	—	—	—	—	—	3	—	3
Net loss	—	—	—	—	—	—	(89,380)	(89,380)
Balance at December 31, 2017	—	$—	40,571,015	$40	$324,376	$(146)	$(263,571)	$60,699

SERES THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Cash flows from operating activities:			
Net loss	$(89,380)	$(91,579)	$(54,780)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Stock-based compensation expense	17,362	16,857	9,694
Depreciation and amortization expense	7,259	4,205	728
Loss from revaluation of preferred stock warrant liability	—	—	7
Non-cash interest expense	3	—	367
Accretion of discount on investments	(216)	(386)	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	31	(2,598)	(2,470)
Deferred revenue	(11,888)	108,814	—
Accounts payable	(856)	3,581	2,682
Accrued expenses and other liabilities	2,162	5,027	2,928
Net cash provided by (used in) operating activities	(75,523)	43,921	(40,844)
Cash flows from investing activities:			
Purchases of property and equipment	(4,676)	(21,492)	(4,362)
Purchases of investments	(96,534)	(290,594)	(267,761)
Sales and maturities of investments	158,312	246,494	136,390
Changes in restricted cash	(113)	139	(1,400)
Net cash provided by (used in) investing activities	56,989	(65,453)	(137,133)
Cash flows from financing activities:			
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	—	(24)
Proceeds from exercise of stock options and common stock warrants	116	2,138	262
Proceeds from issuance of common stock upon completion of initial public offering	—	—	143,015
Payments for repurchase of common stock	(33)	—	—
Repayment of notes payable	—	—	(2,600)
Payments of initial public offering costs	—	—	(2,928)
Net cash provided by financing activities	83	2,138	137,725
Net increase (decrease) in cash and cash equivalents	(18,451)	(19,394)	(40,252)
Cash and cash equivalents at beginning of year	54,539	73,933	114,185
Cash and cash equivalents at end of year	$36,088	$54,539	$73,933
Supplemental disclosure of cash flow information:			
Cash paid for interest	$1	$109	$163

Supplemental disclosure of non-cash investing and financing activities:			
Property and equipment purchases included in accounts payable and accrued expenses	$877	$1,650	$2,953

SERES THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except share and per share data)

1. Nature of the Business and Basis of Presentation

Seres Therapeutics, Inc. (the "Company") was incorporated under the laws of the State of Delaware in October 2010 under the name Newco LS21, Inc. In October 2011, the Company changed its name to Seres Health, Inc., and in May 2015, the Company changed its name to Seres Therapeutics, Inc. The Company is a microbiome therapeutics platform company developing a novel class of biological drugs, which are designed to restore health by repairing the function of a dysbiotic microbiome. The Company's lead product candidate, SER-109, is designed to prevent further recurrences of Clostridium difficile infection ("CDI"), a debilitating infection of the colon, and, if approved by the U.S. Food and Drug Administration ("FDA"), could be a first-in-field oral microbiome drug. The Company's second product candidate, SER-287, is being developed to treat inflammatory bowel disease ("IBD") including ulcerative colitis ("UC"). The Company is also developing SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors (CPI's) in patients with solid tumors. In addition, using its microbiome therapeutics platform, the Company is developing product candidates to treat diseases where the microbiome is implicated, including SER-262, a rationally designed product candidate, to prevent an initial recurrence of primary CDI, SER-301, a rationally designed IBD product candidate, and SER-155, a rationally designed product candidate to prevent infections and improve gastrointestinal barrier function (including the consequences of graft versus host disease) in patients following allogeneic hematopoietic stem cell transplants or solid organ transplants. The Company is also using its microbiome therapeutics platform to conduct research on various indications, including: infectious diseases, metabolic diseases, and inflammatory and immune diseases, including immuno-oncology.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive pre-clinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities.

The Company's product candidates are in development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants.

The Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. The Company has experienced negative cash flows and had an accumulated deficit of $263,571 as of December 31, 2017. For the year ended December 31, 2017, the Company incurred a loss of $89,380 and used $75,523 of cash in operations. The Company expects that its operating losses and

negative cash flows will continue for the foreseeable future. The Company expects that its cash, cash equivalents and investments at December 31, 2017 of $149,983 will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from issuance of the financial statements. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company is eligible to receive contingent milestone payments under its agreement with Nestlé Health Science if certain development milestones are achieved. However, these milestones are uncertain and there is no assurance that the Company will receive any of them. Until such time, if ever, as the Company can generate substantial product revenue, the Company will finance its cash needs through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties. The Company may not be able to obtain funding on acceptable terms, or at all. If the Company is unable to raise additional funds as and when needed, it would have a negative impact on the Company's financial condition, which could constrain the Company's ability to pursue its business strategies.

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") and include the accounts of the Company and its wholly owned subsidiaries after elimination of all intercompany accounts and transactions.

SERES THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except share and per share data)

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, revenue recognition, the accrual of research and development expenses and the valuation of stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents. Cash equivalents, which consist of money market accounts, corporate bonds, and certificates of deposit purchased with original maturities of less than 90 days from the date of purchase, are stated at fair value.

Restricted Cash

The Company held cash of $1,513 as of December 31, 2017 and $1,400 as of December 31, 2016 in a separate restricted bank account as a security deposit for the lease of the Company's facilities. The Company has classified these deposits as long-term restricted cash on its balance sheet.

Investments

The Company classifies its available-for-sale investments as current assets on the consolidated balance sheet if they mature within one year from the balance sheet date.

The Company classifies all of its investments as available-for-sale securities. The Company's investments are measured and reported at fair value using quoted prices in active markets for similar securities. Unrealized gains and losses on available-for-sale securities are reported as a separate component of stockholders' equity (deficit). The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income (expense) within the consolidated statement of operations and comprehensive loss. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary", the Company reduces the investment to fair value through a charge to the consolidated statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Concentration of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. The Company has all cash, cash equivalents and investments balances at accredited financial institutions, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities of its programs, including pre-clinical and clinical testing. These programs could be adversely affected by a significant interruption in the supply of such drug substance products.

SERES THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except share and per share data)

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company’s cash equivalents and investments are carried at fair value, determined according to the fair value hierarchy described above. The Company’s investments in certificates of deposit are carried at amortized cost, which approximates fair value. Certain cash equivalents or investments that are measured at fair value using the net asset value per share (or its equivalent) practical expedient have not been classified in the fair value hierarchy. The carrying values of the Company’s accounts payable and accrued expenses approximate their fair value due to the short-term nature of these liabilities.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs (non-current) until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders’ equity (deficit) as a reduction of additional paid-in capital generated as a result of the financing.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the useful life of the asset. Laboratory equipment is depreciated over five years. Computer equipment and furniture and office equipment are depreciated over three years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is

included in loss from operations.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

SERES THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except share and per share data)

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include salaries, stock-based compensation and benefits of employees, third-party license fees and other operational costs related to the Company's research and development activities, including allocated facility-related expenses and external costs of outside vendors engaged to conduct both pre-clinical studies and clinical trials.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees and directors based on the fair value on the date of the grant and recognizes compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. Generally, the Company issues stock options, restricted stock units and restricted stock awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. For stock options or restricted stock units issued with performance-based vesting conditions, the stock compensation expense related to these awards is recognized based on the grant date fair value when achievement of the performance condition is deemed probable.

The Company measures stock-based awards granted to consultants and non-employees based on the fair value of the award on the date on 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 the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

The Company recognizes adjustments to stock compensation expense for forfeitures as they occur.

The fair value of each stock option grant is estimated on the date of grant using the Black- Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined 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 the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

SERES THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands, except share and per share data)

Revenue Recognition

The Company currently generates its revenue through collaboration and license arrangements with strategic partners for the development and commercialization of product candidates.

The Company recognizes revenue in accordance with FASB ASC Topic 605, Revenue Recognition ("ASC 605"). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists
- Delivery has occurred or services have been rendered
- The seller's price to the buyer is fixed or determinable
- Collectability is reasonably assured

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current portion. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as long-term deferred revenue.

Collaboration Revenue

In January 2016 the Company entered into a Collaboration and License Agreement (the "License Agreement") with Nestec Ltd. ("NHS"), an affiliate of Nestlé Health Science US Holdings, Inc. In connection with the License Agreement, the Company received an upfront, non-refundable payment of $120,000. Other non-refundable payments to the Company under this arrangement may include: (i) payments for research and development services, (ii) payments for the supply of clinical product, (iii) payments for the supply of commercial product, (iv) payments based on the achievement of certain development, regulatory, commercial, and sales-based milestones and (v) royalties on product sales.

The Company evaluates multiple-element arrangements based on the guidance in FASB ASC Topic 605-25, Revenue Recognition-Multiple-Element Arrangements ("ASC 605-25"). Pursuant to this guidance, the Company identifies the deliverables included in the arrangement and determines: (1) whether the individual deliverables have value to the customer on a standalone basis and represent separate units of accounting or whether they must be accounted for as a combined unit of accounting; and (2) if the arrangement includes a general right of return relative to the delivered item. This evaluation requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the Company. In assessing whether an item has standalone value, the Company considers factors such as the research, manufacturing and commercialization

capabilities of the collaboration partner, the retention of any key rights by the Company, and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s).

In situations where the Company has identified multiple units of accounting, the arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. The Company determines the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE is available.

Then, the applicable revenue recognition criteria in ASC 605-25 are applied to each of the separate units of accounting to determine the appropriate period and pattern of recognition. The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605-25 are satisfied for that particular unit of accounting. The Company will recognize as revenue, upon delivery, arrangement consideration attributed to licenses that have standalone value from the other deliverables to be provided in an arrangement. For licenses that do not have standalone value from the other deliverables to

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be provided in an arrangement over the Company's estimated performance period as the arrangement would be accounted for as a single unit of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605-25 are satisfied for that particular unit of accounting. The Company will recognize as revenue arrangement consideration attributed to licenses that have standalone value from the other deliverables to be provided in an arrangement upon delivery. The Company will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value from the other deliverables to be provided in an arrangement over the Company's estimated performance period as the arrangement would be accounted for as a single unit of accounting.

If there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement for the single unit of accounting on a straight-line basis over the period the Company is expected to complete its performance obligations. Alternatively, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. The Company recognizes revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method upon successful accomplishment of each milestone, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive would be recognized as revenue over the remaining period of performance, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

Refer to footnote 9 for further information related to the Company's collaboration and license agreement with Nestec, Ltd.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit

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that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Warrant to Purchase Convertible Preferred Stock

The Company classified a warrant to purchase shares of its Series A-2 convertible preferred stock as a liability on its consolidated balance sheets as this warrant was a free-standing financial instrument that could have required the Company 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 the warrant were recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. The Company continued to adjust the liability for changes in fair value until the warrant became a warrant to purchase common stock in connection with the IPO.

The Company used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the preferred stock warrant. The Company assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement included the fair value per share of the underlying Series A-2 convertible preferred stock, the remaining contractual term of the warrant, the risk-free interest rate, the expected dividend yield and the expected volatility of the price of the underlying preferred stock. The Company determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sales of its convertible preferred stock, results obtained from third-party valuations and additional factors that were deemed relevant. The Company historically has been a private company and lacks company-specific historical and implied volatility information of its stock. Therefore, it estimated its 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 was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrant. Expected dividend yield was based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company’s singular focus is on developing Ecobiotic microbiome therapeutics to treat dysbiosis in the colonic microbiome. Revenue to date has been generated solely through the Company's collaboration with Nestle Health Science, all of which has been earned in the United States. All tangible assets are held in the United States

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2017, 2016 and 2015, other comprehensive income (loss) consisted of changes in unrealized gains (losses) from available-for-sale investments.

Net Loss per Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed using the sum of the weighted average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential shares of common stock, including the assumed exercise of stock options and warrants and unvested restricted stock. The Company applies the two-class method to calculate its basic and diluted net loss per share attributable to common stockholders, as its convertible preferred stock, which converted to Common Stock upon completion of the listing of the Company's common stock on NASDAQ on June 26, 2015, and common stock are participating securities. The two-class method is an earnings allocation formula that treats a participating security as having rights to earnings that otherwise would have been available to common stockholders. However, the two-class method does not impact the net loss per share of common stock as the Company was in a net loss position for each of the periods presented and preferred stockholders do not participate in losses.

The Company's convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Similarly, restricted stock awards granted by the Company entitle the holder of such awards to dividends declared or paid by the board of directors, regardless of whether such

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awards are unvested, as if such shares were outstanding common shares at the time of the dividend. However, the unvested restricted stock awards are not entitled to share in the residual net assets (deficit) of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recently Issued and Adopted Accounting Pronouncements

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. In August 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date, which delayed the effective date of the new standard from January 1, 2017 to January 1, 2018. The FASB also agreed to allow entities to choose to adopt the standard as of the original effective date. In March 2016, the FASB issued ASU 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations, which clarifies the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued ASU 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies how a company identifies promised goods or services and clarifies whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). In May 2016, the FASB issued ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients related to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. In December 2016 the FASB issued ASU No. 2016-20, Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers, which amends certain narrow aspects of the guidance issued in ASU 2014-09 including guidance related to the disclosure of remaining performance obligations and prior-period performance obligations, as well as other amendments to the guidance on loan guarantee fees, contract costs, refund liabilities, advertising costs and the clarification of certain examples. ASU 2016-08, ASU 2016-10 and ASU 2016-12 have the same effective dates and transition requirements as ASU 2014-09, all of which collectively are herein referred to as "ASC 606."

The Company adopted ASC 606 using the modified retrospective transition method. The adoption of ASC 606 changed the pattern and timing of revenue recognition of amounts from the Company's collaboration agreement with NHS. Under ASC 606, the Company will recognize revenue using the cost-to-cost method which best depicts the transfer of control to the customer. Under the cost-to-cost method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified

performance obligation. Under this method, revenue will be recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. The estimate of the Company's measure of progress and estimate of transaction price will be updated at each reporting date, as a change in estimate, and will require judgement. The amount of consideration allocated to satisfied performance obligations, based on the Company's measure of progress will be recognized immediately on a cumulative catch-up basis, resulting in an adjustment to revenue in the period of change. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time. In addition, substantive development milestones, which were previously recognized in the period when the milestone was achieved, will be recognized over the remaining performance period under ASC 606. As the adoption method does not result in a recast of the prior year consolidated financial statements, ASC 606 requires the Company to provide additional disclosures during the year of adoption of the amount by which each financial statement line item is affected by adoption of the new standard and explanations of the reasons for significant changes.

During the fourth quarter of 2017, the Company substantially completed its impact assessment, and expects that the adoption of ASC 606 will require a cumulative-effect adjustment of approximately $25,000 as an increase to deferred revenue related party with a corresponding impact to accumulated deficit on January 1, 2018. The finalization of the Company's assessment may result in significant changes to estimates that may materially impact the Company's preliminary estimate of the cumulative effect.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), or ASU 2016-02, which establishes principles that lessees and lessors shall apply to report useful information to users of financial statements about the amount, timing and uncertainty of cash flows arising from a lease. In January 2018, the FASB issued ASU 2018-01, Leases (Topic 842), or ASU 2018-01, which adds two practical expedients to the new lease guidance. Topic 842 is effective for the Company for annual periods beginning after

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December 15, 2018 and interim periods therein, with early adoption permitted. The Company is currently in the process of evaluating the impact of the guidance on its consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments. This standard addresses specific cash flow issues with the objective of reducing existing diversity in practice in how certain cash receipts and cash payments are presented in the statement of cash flows. The standard is effective for the Company on January 1, 2018. The Company will adopt this standard as of the required effective date of January 1, 2018. The adoption of this standard is not expected to have any impact on its financial statements.

In November 2016, the FASB issued ASU 2016-18, Restricted Cash. The new standard requires restricted cash and restricted cash equivalents be included with cash and cash equivalents when reconciling the total beginning and ending amounts for the periods shown on the statement of cash flows. The new standard is effective for the Company on January 1, 2018. The Company will adopt the new standard as of the required effective date of January 1, 2018 and will reflect the adoption retrospectively to all periods presented. Upon adoption, the Company’s consolidated statements of cash flows will include restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on such statements.

In May 2017, the FASB issued ASU No. 2017-09, Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting. The new standard provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The new standard will be effective for the Company on January 1, 2018. The Company will adopt the new standard as of the required effective date of January 1, 2018. The adoption of the new standard will have an impact on the accounting for modification of stock-based awards, if any, after the date of adoption.

3. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company’s assets and liabilities as of December 31, 2017 and 2016 that are measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair Value Measurements as of December 31, 2017 Using:		
	Level 2	Not Subject to	Total

	Level 1	Level 2	Level 3	Leveling [1]	
Assets:					
Cash Equivalents	$—	$—	$ —	$ 25,964	$25,964
Investments:					
Commercial Paper	—	6,198	—	—	6,198
Certificates of Deposit	—	8,916	—	—	8,916
Corporate Bonds	—	58,865	—	—	58,865
Government Securities	—	22,954	—	—	22,954
Treasury Bonds	—	16,962	—	—	16,962
	$—	$113,895	$ —	$ 25,964	$139,859

[1] Certain cash equivalents and investments that are valued using the net asset value per share (or its equivalent) practical expedient have not been classified in the fair value hierarchy.

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	Fair Value Measurements as of December 31, 2016 Using:				
	Level 1	Level 2	Level 3	Not Subject to Leveling [1]	Total
Assets:					
Cash Equivalents	$—	$4,740	$ —	$ 1,567	$6,307
Repurchase Agreements	—	7,000	—	—	7,000
Investments:					
Commercial Paper	—	19,689	—	—	19,689
Certificates of Deposit	—	10,629	—	—	10,629
Corporate Bonds	—	94,609	—	—	94,609
Government Securities	—	33,466	—	—	33,466
Treasury Bonds	—	17,063	—	—	17,063
	$—	$187,196	$ —	$ 1,567	$188,763

[1] Certain cash equivalents and investments that are valued using the net asset value per share (or its equivalent) practical expedient have not been classified in the fair value hierarchy.

As of December 31, 2017, the Company's cash equivalents consisted of money market funds with original maturities of less than 90 days from the date of purchase.

As of December 31, 2016, the Company's cash equivalents consisted of money market funds, corporate bonds, certificates of deposits, and repurchase agreements with original maturities of less than 90 days from the date of purchase and were valued based on Level 2 inputs. Repurchase agreements are agreements with banks to repurchase notes that are collateralized by U.S. government securities. All repurchase agreements have overnight maturities.

The fair value of the Company's investments, which consisted of corporate bonds, commercial paper, certificates of deposit, government securities, and treasury bonds as of December 31, 2017 and 2016, were determined using Level 2 inputs. During the years ended December 31, 2017 and 2016, there were no transfers between Level 1, Level 2 and Level 3.

4. Investments

As of December 31, 2017 and 2016, the fair value of available-for-sale investments by type of security was as follows:

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Commercial Paper	$6,198	$ —	$ —	$6,198
Certificates of Deposit	8,916	—	—	8,916
Corporate Bonds	58,937	—	(72)	58,865
Government Securities	22,997	—	(43)	22,954
Treasury Bonds	16,992	—	(30)	16,962
	$114,040	$ —	$ (145)	$113,895

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	December 31, 2016			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Commercial Paper	$19,631	$ 58	$ —	$19,689
Certificates of Deposit	10,629	—	—	10,629
Corporate Bonds	94,764	—	(155)	94,609
Government Securities	33,513	—	(47)	33,466
Treasury Bonds	17,066	1	(4)	17,063
	$175,603	$ 59	$ (206)	$175,456

Investments with original maturities of less than 90 days are included in cash and cash equivalents on the consolidated balance sheets and are not included in the table above. Investments with maturities of less than 12 months are considered current and those investments with maturities greater than 12 months are considered non-current.

As of December 31, 2017, the Company’s commercial paper, certificates of deposit, corporate bonds, government securities and treasury bonds had remaining maturities of less than 12 months.

All investments with unrealized losses at December 31, 2017 have been in a loss position for less than twelve months or the loss is not material and temporary in nature. The Company does not intend to sell the investments that are in an unrealized loss position before recovery of their amortized cost basis.

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	December 31,

	2017	2016
Laboratory equipment	$ 13,181	$ 10,711
Computer equipment	2,832	1,335
Furniture and office equipment	1,033	1,010
Leasehold improvements	27,963	27,807
Construction in progress	361	442
	45,370	41,305
Less: Accumulated depreciation and amortization	(12,439)	(5,180)
	$ 32,931	$ 36,125

Depreciation and amortization expense was $7,259, $4,205 and $728 for the years ended December 31, 2017, 2016 and 2015, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2017	December 31, 2016
Development and clinical manufacturing costs	$ 3,910	$ 3,350
Payroll and payroll-related costs	4,962	3,698
Professional fees	344	448
Facility and other	3,297	3,316
	$ 12,513	$ 10,812

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7. Convertible Preferred Stock

On July 1, 2015, in connection with the closing of the IPO, the Company effected its Restated Certificate of Incorporation, which authorizes the Company to issue 10,000,000 shares of preferred stock, $0.001 par value per share.

8. Stockholders' Equity Common Stock

On July 1, 2015, the Company completed an IPO, and issued and sold 8,545,138 shares of common stock at a public offering price of $18.00 per share, resulting in net proceeds of approximately $139,267 after deducting underwriting discounts and commissions and other offering expenses totaling $3,748. The shares issued upon closing of the IPO included 1,114,583 shares of the Company's common stock, which were sold to the underwriters pursuant to the full exercise of their option to purchase additional shares of common stock. Upon the listing of the Company's common stock on NASDAQ on June 26, 2015, all outstanding shares of the Company's convertible preferred stock automatically converted into 22,866,987 shares of the Company's common stock.

As of December 31, 2014, the Company's Amended and Restated Certificate of Incorporation, as further amended, authorized the Company to issue 38,000,000 shares of common stock, $0.001 par value per share. On July 1, 2015, in connection with the closing of the IPO, the Company effected its Restated Certificate of Incorporation, which authorizes the Company to issue 200,000,000 shares of common stock, $0.001 par value per share.

2012 Stock Incentive Plan

The Company's 2012 Stock Incentive Plan, as amended, (the "2012 Plan") provides for the Company to sell or issue common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, members of the board of directors and consultants of the Company. The 2012 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years. The Company generally grants stock-based awards with service conditions only ("service-based" awards).

Stock options granted under the 2012 Plan generally vest over four years and expire after ten years, although options have been granted with vesting terms less than four years. As of December 31, 2017, there were no shares available

for future grant under the 2012 Plan.

2015 Incentive Award Plan

On June 16, 2015, the Company's stockholders approved the 2015 Incentive Award Plan (the "2015 Plan"), which became effective on June 25, 2015. The 2015 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares initially reserved for issuance under the 2015 Plan is the sum of (i) 2,200,000 shares of common stock and (ii) the number of shares subject to awards outstanding under the 2012 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company on or after the effective date of the 2015 Plan. In addition, the number of shares of common stock that may be issued under the 2015 Plan is subject to increase on the first day of each calendar year, beginning in 2016 and ending in 2025, equal to the lesser of (i) 4% of the number of shares of the Company's common stock outstanding on the last day of the preceding applicable calendar year and (ii) an amount determined by the Company's board of directors. As of December 31, 2017, there were 1,450,792 shares available for future grant under the 2015 Plan.

2015 Employee Stock Purchase Plan

On June 16, 2015, the Company's stockholders approved the 2015 Employee Stock Purchase Plan (the "ESPP"), which became effective on June 25, 2015. A total of 365,000 shares of common stock were reserved for issuance under the ESPP. In addition, the number of shares of common stock that may be issued under the ESPP will automatically increase on the first day of each calendar year, beginning in 2016 and ending in 2025, by an amount equal to the least of (i) 400,000 shares, (ii) 1% of the number of shares of the Company's common stock outstanding on the last day of the applicable preceding calendar year and (iii) an amount determined by

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the Company's board of directors. Offering periods under the ESPP will commence when determined by the plan administrator. As of December 31, 2017, there were no shares issued under the ESPP.

Stock Option Valuation

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

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate	2.20%	1.54%	1.80%
Expected term (in years)	6.0	6.0	6.0
Expected volatility	80.9%	84.2%	81.4%
Expected dividend yield	0 %	0 %	0 %

Stock Options

The following table summarizes the Company's stock option activity for the twelve months ended December 31, 2017:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2016	5,069,133	$ 14.36	8.26	$ 16,736
Granted	1,749,000	10.21		
Exercised	(174,386)	0.67		
Forfeited	(518,055)	21.07		

Outstanding as of December 31, 2017	6,125,692	$ 13.00	7.70	$ 15,808
Options vested and expected to vest as of December 31, 2017	6,125,692	$ 13.00	7.70	$ 15,808
Options exercisable as of December 31, 2017	3,235,166	$ 11.37	7.00	$ 14,074

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2017, 2016 and 2015 was $7.07, $18.45, and $14.56 per share, respectively. The total intrinsic value of stock options exercised during the years ended December 31, 2017, 2016, and 2015 was $1,912, $34,871, and $4,125.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company’s common stock for those stock options that had exercise prices lower than the fair value of the Company’s common stock.

The Company granted performance-based stock options to certain employees. These stock options were exercisable only upon achievement of specified performance targets. During the year ended December 31, 2016, the Company determined that the achievement of specified performance targets occurred. Upon achievement of the performance targets, 60,000 options became immediately vested. The Company recorded stock based compensation expense of $235 during the year ended December 31, 2016 related to these awards. The grant date fair value of these awards was $3.92 per share.

As of December 31, 2017and 2016, there were outstanding unvested service-based stock options held by non-employees for the purchase of 45,000 and 63,375 shares, respectively, of common stock.

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Restricted Stock Units

The Company has granted restricted stock units with time-based vesting conditions. The table below summarizes the Company's restricted stock activity for the twelve months ended December 31, 2017:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested restricted stock units as of December 31, 2016	115,500	$ 9.78
Granted	332,500	$ 10.08
Forfeited	(47,100)	$ 9.93
Vested	(44,122)	$ 10.02
Unvested restricted stock units as of December 31, 2017	356,778	$ 10.01

The aggregate intrinsic value of restricted stock units that vested during the years ended December 31, 2017, 2016 and 2015 was $445, $0, and $1,508, respectively.

Stock-based Compensation

The Company recorded stock-based compensation expense related to stock options and restricted stock units in the following expense categories of its consolidated statements of operations and comprehensive loss:

	Year Ended December 31,		
	2017	2016	2015
Research and development expenses	$8,115	$8,310	$5,297
General and administrative expenses	9,247	8,547	4,397
	$17,362	$16,857	$9,694

As of December 31, 2017, the Company had an aggregate of $28,102 of unrecognized stock- based compensation cost, which is expected to be recognized over a weighted average period of 2.14 years.

9. Collaboration Revenue

Nestec Ltd.

In January 2016, the Company entered into the Collaboration and License Agreement ("License Agreement") with Nestec Ltd. ("NHS"), an affiliate of Nestlé Health Science US Holdings, Inc., a significant stockholder of the Company, for the development and commercialization of certain product candidates in development for the treatment and management of CDI and IBD, including UC and Crohn's disease. The License Agreement will support the development of the Company's portfolio of products for CDI and IBD in markets outside of the United States and Canada (the "Licensed Territory"). The Company has retained full commercial rights to its entire portfolio of product candidates with respect to the United States and Canada.

Under the License Agreement, the Company granted to NHS an exclusive, royalty-bearing license to develop and commercialize, in the Licensed Territory, certain products based on its microbiome technology that are being developed for the treatment of CDI and IBD, including SER-109, SER-262, SER-287 and SER-301 (collectively, the "NHS Collaboration Products"). The License Agreement sets forth the Company's 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.

In exchange for the license, NHS agreed to pay the Company an upfront cash payment of $120,000, which the Company received in February 2016. NHS 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. The Company is eligible to receive up to $285,000 in development milestone payments, $375,000 in regulatory payments and up to an aggregate of $1,125,000 for the achievement of certain commercial milestones related to the sales of NHS Collaboration Products.

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At the inception of the License Agreement, the Company identified the following deliverables: (i) a license to develop and commercialize the NHS Collaboration Products in the Licensed Territory, (ii) obligation to perform research and development services, (iii) participation on a joint steering committee, and (iv) manufacturing services to provide clinical supply to complete future clinical trials. The Company also identified a contingent deliverable, the obligation to perform manufacturing services to provide commercial supply if commercialization occurs, which is contingent upon regulatory approval. This contingent deliverable has been excluded from the initial allocation and will be treated as a separate unit of accounting when and if delivered.

The Company concluded that none of the four deliverables identified at the inception of the License Agreement has standalone value from the other undelivered elements. Accordingly, all deliverables represent a single unit of accounting.

All consideration received relating to the four identified deliverables that comprise the single unit of accounting will be recognized over the period of performance. The period of performance will be through the completion of development services for the NHS Collaboration Products which has been estimated to be ten years. The Company will periodically review and, if necessary, revise the estimated development period.

The Company will recognize revenue utilizing a time-based proportional performance model where revenue related to each payment is recognized over the ten-year performance period. As of December 31, 2017, the only consideration that is fixed and determinable is the non-refundable upfront payment of $120,000 and $793 for the reimbursement of development services since the inception of the arrangement. For additional consideration that could be received for research and development services and/or manufacturing services for clinical supply, the Company will recognize a cumulative catch-up for the amount of time that has elapsed and spread the unrecognized portion over the remaining performance period.

Development and regulatory milestones that involve substantial effort on the Company’s part and the achievement of which are not considered probable at the inception of the License Agreement are considered substantive milestones, and will be recognized in their entirety in the period in which the milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

During the year ended December 31, 2016, the Company received $10,000 from NHS in connection with the initiation of the Phase 1b study for SER-262 in CDI. The Company recognizes revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method. The $10,000 was recognized in full as related party collaboration revenue during the year ended December 31, 2016.

During the year ended December 31, 2017, the Company received $20,000 from NHS in connection with the initiation of the Phase 3 study for SER-109. The Company recognizes revenue associated with substantive milestones in accordance with FASB ASC Topic 605-28, Revenue Recognition-Milestone Method. The $20,000 was recognized in

full as related party collaboration revenue during the year ended December 31, 2017.

Royalties will be recorded as revenue in the period they are earned assuming all other revenue recognition criteria are met.

During the years ended December 31, 2017 and 2016, the Company recognized $32,100 and $21,766, respectively, of related party revenue associated with the License Agreement. As of December 31, 2017, there was $96,926 of deferred revenue related to the License Agreement, which is classified as current or non-current in the consolidated balance sheets based on the Company's estimate of revenue that will be recognized within the next twelve months. All costs associated with the License Agreement are recorded in research and development expense in the consolidated statements of operations and comprehensive loss.

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10. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31,		
	2017	2016	2015
Numerator:			
Net loss attributable to common stockholders	$(89,380)	$(91,579)	$(54,780)
Denominator:			
Weighted average common shares outstanding, basic and diluted	40,449,410	39,846,928	23,532,400
Net loss per share attributable to common stockholders, basic and diluted	$(2.21)	$(2.30)	$(2.33)

The Company's potential dilutive securities, which include stock options and unvested restricted common stock, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential common shares, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,		
	2017	2016	2015
Stock options to purchase common stock	6,125,692	5,069,133	5,026,246
Unvested restricted stock units	356,778	115,500	—
	6,482,470	5,184,633	5,026,246

11. Commitments and Contingencies

Leases

The Company previously leased office and laboratory space with a lease term expiring in January 2018 and no extension periods. In May 2016, upon mutual agreement with the landlord, the Company accelerated the termination of the operating lease to June 30, 2016. Upon termination of the lease, the Company recorded a benefit to rent expense of $136 to write off amounts previously recorded as deferred rent. The outstanding security deposit of $119, which was secured by a cash collateralized letter of credit, was released in September 2016.

On April 1, 2015, the Company entered into a lease for additional office and laboratory space with a term expiring in April 2020.

On November 11, 2015, the Company entered into a non-cancelable property lease with BMR-Sidney Research Campus LLC (“BMR”) for 83,396 square feet of office, laboratory and pilot manufacturing space at 200 Sidney Street, Cambridge, Massachusetts. The lease term commenced in March 2016 and ends in November 2023. The Company has the option to extend the lease twice, each for a five-year period. The Company moved its corporate headquarters to this location in April 2016. BMR has contributed a total of $12,509 toward the cost of tenant improvements. BMR’s contributions toward the cost of tenant improvements is recorded as a lease incentive obligation on the Company’s consolidated balance sheet. The lease incentive obligation is amortized to the Company’s consolidated statement of operations as reductions to rent expense over the lease term. As of December 31, 2017, the Company recorded a lease incentive obligation of $10,312. During the year ended December 31, 2017, the Company amortized $1,768 of this lease incentive obligation as a reduction to rent expense.

During the years ended December 31, 2017, 2016 and 2015, the Company recognized $4,458, $3,826, and $1,246, respectively, of rental expense related to office and laboratory space.

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Future minimum lease payments for these operating leases as of December 31, 2017 are as follows:

Year Ending December 31,	
2018	$6,157
2019	6,342
2020	6,120
2021	6,221
2022	6,372
2023 and thereafter	5,158
Total	$36,370

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2017 or 2016.

Legal Proceedings

On September 28, 2016, a purported stockholder of the Company filed a putative class action lawsuit in the U.S. District Court for the District of Massachusetts against the Company entitled Mariusz Mazurek v. Seres Therapeutics, Inc., et.al. On February 12, 2017, the Company received an amended complaint and on March 30, 2017, the Company filed a motion to dismiss. A hearing on the motion to dismiss was held on August 9, 2017 and we are awaiting a decision from the court. The lawsuit alleges violations of Sections 10(b), 20(a) and Rule 10b-5 of the Securities

Exchange Act of 1934, as amended, by making allegedly false and misleading statements and omissions about the Company's clinical trials for its product candidate SER-109 in the Company's public disclosures between June 25, 2015 and July 29, 2016. The lawsuit seeks, among other things, damages in connection with the Company's allegedly inflated stock price between June 25, 2015 and July 29, 2016 as a result of those allegedly false and misleading statements, as well as interest, attorneys' fees and costs. The Company can make no assurances as to the time or resources that will need to be devoted to this lawsuit or its final outcome, or the impact, if any, of this lawsuit or any proceedings on its business, financial condition, results of operations and cash flows. While the Company is vigorously defending against all claims asserted, this litigation could result in substantial costs to the Company and a diversion of the Company's management's attention and resources, which could harm its business. In addition, the uncertainty of the pending lawsuit or potential filing of additional lawsuits could lead to more volatility and a reduction in the Company's stock price. Given the early stage of the litigation, at this time the Company is unable to reasonably estimate possible losses or form a judgment that an unfavorable outcome is either probable or remote. It is not currently possible to assess whether or not the outcome of these proceedings may have a material adverse effect on the Company.

12. Income Taxes

During the years ended December 31, 2017, 2016 and 2015, the Company recorded no income tax benefits for the net operating losses incurred in each year or interim period, due to its uncertainty of realizing a benefit from those items.

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A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	(34.0)%	(34.0)%	(34.0)%
Research and development tax credits	(7.7)	(8.8)	(5.7)
State taxes, net of federal benefit	(4.8)	(5.8)	(5.3)
Stock-based compensation	1.2	(6.3)	4.1
Revaluation of preferred stock warrant liability	33.1	—	—
Other	(0.3)	0.1	0.3
Change in deferred tax asset valuation allowance	12.5	54.8	40.6
Effective income tax rate	— %	— %	— %

Net deferred tax assets as of December 31, 2017 and 2016 consisted of the following:

	December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$32,997	$18,481
Research and development tax credit carryforwards	25,405	14,991
Capitalized organization costs	306	483
Stock-based compensation expense	7,714	5,624
Charitable Contributions	8	6
Deferred Revenue	26,480	42,742
Accrued expenses	4,613	5,560
Capitalized research and development expenses	73	115
Total deferred tax assets	$97,596	88,002
Deferred tax liabilities:		
Depreciation and amortization	(3,470)	(5,008)
Total deferred tax liabilities	(3,470)	(5,008)
Valuation allowance	$(94,126)	(82,994)
Net deferred tax assets	$—	$—

On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into United States law. The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from 35% to 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). The tax rate change resulted in (i) a reduction in the gross amount of the Company's deferred tax assets recorded as of December 31, 2017, without an impact on the net amount of its deferred tax assets, which are recorded with a full valuation allowance, and (ii) no income tax expense or benefit being recognized as of the enactment date of the TCJA.

The staff of the Securities and Exchange Commission issued Staff Accounting Bulletin No. 118 to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the TCJA. In connection with the initial analysis of the impact of the TCJA, the Company remeasured its deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21% for federal tax purposes. The remeasurement of the Company's deferred tax assets and liabilities was offset by a change in the valuation allowance.

The Company is still in the process of analyzing the impact to the Company of the TCJA and its analysis is not yet complete. Where the Company has been able to make reasonable estimates of the effects related to the TCJA, the Company has recorded

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provisional amounts. The ultimate impact to the Company's consolidated financial statements of the TCJA may differ from the provisional amounts.

The provisional amount recorded related to the remeasurement of our deferred tax balance was a $29,546 expense that was offset by a valuation allowance.

As of December 31, 2017, the Company had net operating loss carryforwards for federal and state income tax purposes of $120,707 and $121,016, respectively, which both begin to expire in 2035. As of December 31, 2017, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $22,557 and $ 3,606, respectively, which begin to expire in 2031 and 2028, respectively. The federal research and development tax credits include an orphan drug credit carryforward of $14,475. Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. Since our formation, we have raised capital through the issuance of capital stock on several occasions. These financings, combined with the purchasing shareholders' subsequent disposition of those shares, may have resulted in a change of control as defined by Section 382 or could result in a change of control in the future upon subsequent disposition. We conducted an analysis under Section 382 to determine if historical changes in ownership through August 31, 2015 would limit or otherwise restrict our ability to utilize these NOL and R&D credit carryforwards. As a result of this analysis, we do not believe there are any significant limitations on our ability to utilize these carryforwards. However, future changes in ownership after August 31, 2015 could affect the limitation in future years. Any limitation may result in expiration of a portion of the NOL or R&D credit carryforwards before utilization.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2017 and 2016. Management reevaluates the positive and negative evidence at each reporting period.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2017, 2016 and 2015 related primarily to the increases in net operating loss carryforwards, research and development tax credit carryforwards, stock-based compensation and decrease of deferred rate due to tax reform were as follows:

	Year Ended December 31,		
	2017	2016	2015
Valuation allowance at beginning of year	$(82,994)	$(32,777)	$(10,522)
Decreases recorded as benefit to income tax provision	29,546	—	—
Increases recorded to income tax provision	(40,678)	(50,217)	(22,255)
Valuation allowance as of end of year	$(94,126)	$(82,994)	$(32,777)

As of December 31, 2017, 2016, and 2015, the Company had no unrecognized tax benefits. Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense. The Company does not expect any significant change in its uncertain tax positions in the next 12 months.

During the year ended December 31, 2016, the Company was awarded a tax incentive for job creation from the Massachusetts Life Sciences Center. The program was established in 2008 in order to incentivize life sciences companies to create new sustained jobs in Massachusetts. Jobs must be maintained for at least five years, during which time the grant proceeds can be recovered by the Massachusetts Department of Revenue ("DOR") if the Company does not meet and maintain its job creation commitments. The award was received in 2016 and recorded in other current liabilities as of December 31, 2016 as the Company did not meet the job creation commitments. During the year ended December 31, 2017, the Company met the job creation commitments and recorded $0.3 million as other income in the consolidated statement of operations for the portion of the award earned through the year ended December 31,

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2017. The balance of the incentive award has been recorded in our consolidated balance sheet as a liability until such time that the award is fully earned.

13. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2017 and 2016. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

2017	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue - related party [1]	$3,015	$3,014	$23,015	$3,056	$32,100
Total operating expenses	28,905	31,430	30,329	32,831	123,495
Loss from operations	(25,890)	(28,416)	(7,314)	(29,775)	(91,395)
Net loss	(25,474)	(28,018)	(6,935)	(28,953)	(89,380)
Net loss per share applicable to common stockholders - basic and diluted	$(0.63)	$(0.69)	$(0.17)	$(0.72)	$(2.21)

2016	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue - related party [1]	$2,710	$3,004	$13,015	$3,037	$21,766
Total operating expenses	22,626	31,144	32,110	28,725	114,605
Loss from operations	(19,916)	(28,140)	(19,095)	(25,688)	(92,839)
Net loss	(19,704)	(27,913)	(18,688)	(25,274)	(91,579)
Net loss per share applicable to common stockholders - basic and diluted	$(0.50)	$(0.70)	$(0.46)	$(0.63)	$(2.30)

(1) In January 2016, the Company entered into a Collaboration and License Agreement with NHS for the development and commercialization of certain of its product candidates. In exchange for the license, NHS paid the Company an upfront cash payment of $120,000, which the Company received in February 2016 and is being recognized as revenue over the ten year performance period. During the quarter ended September 30, 2016, the Company received $10,000 from NHS related to achievement of a milestone within this agreement, which was recognized in full as related party collaboration revenue during 2016. During the quarter ended September 30, 2017, the Company received $20,000 from NHS related to achievement of a milestone within this agreement, which was recognized in full as related party collaboration revenue during 2017.

14. Related Party Transactions

In October 2010, the Company entered into a services agreement with Flagship Ventures Management, Inc., an affiliate of one of its stockholders (and now known as Flagship Pioneering), Flagship Venture Funds, to provide general and administrative services to the Company, including the employer portions of employee health and dental benefit plans for Seres Therapeutics employees and consulting services. The Company made payments under the agreement of $17 and $502 during the years ended December 31, 2016 and 2015, respectively. There were no payments made during the year ended December 31, 2017. There were no amounts due to Flagship Pioneering related to the services agreement as of December 31, 2017 and 2016.

As described in Note 9, in January 2016 the Company entered into a License Agreement with NHS for the development and commercialization of certain product candidates in development for the treatment and management of CDI and IBD, including UC and Crohn’s disease. NHS is a related party since NHS is an affiliate of Nestlé Health Science, one of the Company’s significant stockholders. During the year ended December 31, 2017, the Company recognized $32,100 of related party revenue associated with the License Agreement. As of December 31, 2017, there was $96,926 of deferred revenue related to the License Agreement, which is classified as current or non-current in the consolidated balance sheets. The Company has made no payments to NHS during the year ended December 31, 2017. There is $510 due from NHS as of December 31, 2017 for the reimbursement of development costs, which is classified as other current assets in the Company’s consolidated balance sheet.

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15. 401(k) Savings Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Effective January 1, 2016, the Company has elected to match 50% of the first 6% of an employee's deferral. Company contributions are expensed in the year for which they are declared. During the year ended December 31, 2017, the Company recorded expense of $484 for 401(k) match contributions.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SERES THERAPEUTICS, INC.

Date: March 8, 2018 By: /s/ Roger J. Pomerantz
Roger J. Pomerantz
President, Chief Executive Officer and Chairman of the Board

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Roger J. Pomerantz Roger J. Pomerantz, M.D.	President, Chief Executive Officer and Chairman of the Board (principal executive officer)	March 8, 2018
/s/ Eric D. Shaff Eric D. Shaff	Chief Operating and Financial Officer and Executive Vice President (principal financial and accounting officer)	March 8, 2018
/s/ Noubar B. Afeyan Noubar B. Afeyan, Ph.D.	Director	March 8, 2018
/s/ Dennis Ausiello Dennis Ausiello, M.D.	Director	March 8, 2018
/s/ Willard Dere Willard Dere	Director	March 8, 2018
/s/ Grégory Behar Grégory Behar	Director	March 8, 2018
/s/ Kurt C. Graves Kurt C. Graves	Director	March 8, 2018

/s/ Richard N. Kender Richard N. Kender	Director	March 8, 2018
/s/ Lorence H. Kim Lorence H. Kim, M.D.	Director	March 8, 2018