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, 2019

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	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	MCRB	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 every Interactive Data File required to be submitted 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 such files). **Yes** ☒ **No** ☐

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," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	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 28, 2019, was $132,300,726.

As of February 25, 2020, there were 71,071,068 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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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” or the negative 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;
- our ability to successfully manage our growth; and
- our ability to continue as a going concern.

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.

TRADEMARKS, SERVICE MARKS AND TRADENAMES

We have proprietary rights to trademarks used in this Annual Report on Form 10-K, including Ecobiotic, which are important to our business and many of which are registered under applicable intellectual property laws. Solely for convenience, the trademarks, service marks, logos and trade names referred to in this Annual Report on Form 10-K are without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights to these trademarks, service marks and trade names. This Annual Report on Form 10-K contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies’ trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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 ecosystem 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 approximately 30 – 50 trillion microorganisms that live in our intestines, mouth, skin and elsewhere in or on 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 antibiotics or following gastrointestinal infection. These changes in composition may result in the loss of key commensal microbes and/or the gain of pathogenic microbes, resulting in a state of dysbiosis, and associated loss or gain of metabolic and/or immune function. 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 conditions, including: infectious diseases, metabolic diseases, and inflammatory and immune diseases and cancer.

We are developing a new approach to treating disease by modulation of the dysbiotic colonic microbiome by using our Ecobiotic microbiome therapeutics to improve patient outcomes. 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. We believe that the restoration of a dysbiotic colonic microbiome using Ecobiotic microbiome therapeutics represents a paradigm shift in the approach to treating underlying 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, i.e. reverse translation that leverages data on the human microbiome that we gather from clinical studies. From these clinical data, we identify the microbiological and functional differences between a healthy and a diseased microbiome, which we then use to design potential Ecobiotic microbiome therapeutics. After further in-lab preclinical 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 that target the microbiological and functional deficiencies identified in the setting of human disease. 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 pharmacokinetic and pharmacodynamic analytics, and 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 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 focusing our resources on obtaining clinical results from our highest-priority, clinical programs in ulcerative colitis, or UC, a form of inflammatory bowel disease, or IBD, with SER-287, *Clostridium difficile* infection, or CDI, with SER-109, and our Phase 1b study with SER-401 in patients with metastatic melanoma, as well as our preclinical SER-301 program in UC.

The clinical development of SER-287 to treat UC, is supported by successful preclinical and clinical studies. Preclinical colitis animal models and *in vitro* screens provide evidence that SER-287 administration has the potential to reduce pathology and modulate inflammatory and immunological functional pathways. Published clinical reports also suggest that modulation of the microbiome through repetitive fecal microbiota transplantation, or FMT may lead to meaningful clinical response in UC patients.

We completed our Phase 1b clinical study for SER-287, in subjects with active mild to moderate UC who were failing their current therapies. The results of 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 were positive. The study enrolled 58 subjects who exhibited pre-study disease activity despite on going treatment with standard-of-care therapeutics. SER-287 safety and tolerability was a primary study endpoint. The study showed no imbalance in adverse events in SER-287-treated patients as compared to patients treated with placebo and no drug-related serious adverse events were observed.

Analyses of microbiome data, a co-primary endpoint of the trial, showed that SER-287 induced regimen-dependent engraftment of SER-287 derived bacterial species into the colonic microbiome of 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 pharmacologic impact of the SER-287 engraftment was supported by metabolomic and transcriptomic data. Analysis of metabolites and gene expression signatures associated with inflammation and immune modulation, showed correlations with remission in SER-287 treated subjects.

Based on these encouraging data from the Phase 1b trial, in December 2018, we initiated our Phase 2b trial, ECO-RESET, evaluating SER-287 in patients with active mild-to-moderate UC. Based on feedback obtained from the FDA on the SER-287 Phase 2b study design, we believe the study could serve as one of two required pivotal trials supporting potential future registration of SER-287. The Phase 2b study is a three-arm placebo-controlled trial of approximately 200 patients with active mild-to-moderate UC. Two groups of patients will receive different doses of SER-287, both following pretreatment with a short course of oral vancomycin. A third study arm will receive placebo. The study's primary endpoint will evaluate clinical remission measured after 10 weeks of SER-287 administration. Endoscopic improvement will be measured as a secondary efficacy measure. We expect to report top-line data in the second half of 2020.

Our Phase 3 clinical candidate, SER-109, is designed to rapidly and durably correct dysbiosis in the colonic microbiome in the setting of recurrent CDI. CDI is most often caused by the use of broad-spectrum antibiotics which create a dysbiosis of the microbiome, thus increasing susceptibility to infection by *Clostridium difficile*, or *C. difficile*, a spore forming bacterium. *C. difficile* expresses toxins leading to debilitating diarrhea in affected individuals, and which can also cause 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 in incidence of disease. 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 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 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 beneficial bacteria indiscriminately, 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, it is likely that dysbiosis of the microbiome 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 as high as 60% for those experiencing two or more recurrences.

SER-109 is a donor-derived, purified bacterial spore-based microbiome therapeutic candidate consisting of over 50 bacterial species purified from healthy donor stool. Our SER-109 manufacturing process includes inactivation and clearance steps designed to eliminate potential pathogens. SER-109 is designed to prevent further recurrences of CDI in patients with a history of multiple infections by restructuring the dysbiotic microbiome to a state that resists *C. difficile* colonization and growth.

We have been enrolling a double-blind, placebo-controlled SER-109 Phase 3 study, ECOSPOR III, in 188 subjects with multiply recurrent CDI. All patients entering ECOSPOR III must have tested positive for *C. difficile* toxin, as recommended by the Infectious Diseases Society of America guidelines (McDonald Clin Infect Dis 2018). This inclusion criterion was implemented in an effort to ensure enrollment of only patients with active CDI and to ensure accurate diagnosis of the study endpoint. The on-going 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. The size and powering calculations of the study are informed by prior SER-109 study results, published CDI trial data utilizing toxin testing, and preliminary blinded and open label CDI recurrence rate data from the ongoing ECOSPOR III study. Toxin testing is required for patients in ECOSPOR III at both study entry and at the time of suspected recurrence in an effort to ensure optimal diagnostic accuracy of active infection, as recommended by the Infectious Diseases Society of America. We believe the use of toxin testing for all subjects in the study is essential to ensure valid, interpretable study results.

Based on prior discussions with the FDA, we believe this study, if successful, has the potential to be a single pivotal study supporting product registration. However, this would depend on the strength of the data and it is also possible that additional safety data may be required. We expect to report top-line data in mid-2020.

We are also advancing our next generation, rationally-designed, fermented microbiome drug discovery capabilities, focusing on advancing SER-301, a therapeutic candidate for UC. We have finalized the composition for SER-301. The bacterial strains included in SER-301 were informed by our human clinical study results designed using our reverse translation capabilities as well as preclinical mechanistic studies. We have established various capabilities to enable the development of rationally designed microbiome therapeutics including metagenomic and metabolomic profiling, use of curated reference computational databases and proprietary in silico algorithms for drug design, an extensive proprietary bacterial library, advanced manufacturing processes, and capabilities to conduct pharmacokinetics and pharmacodynamics analyses in clinical studies. We have initiated clinical development activities for SER-301. We plan to conduct the initial clinical study in Australia and New Zealand and, if authorized by the local regulatory agencies to initiate the study, we expect to begin enrolling subjects later in 2020.

We are also developing SER-401 for use with checkpoint inhibitors, or CPIs, in patients with solid tumors to enhance efficacy and improve survival. SER-401 is a microbiome therapeutic candidate sourced from healthy individuals who have been identified to have a microbiome signature that is similar to that observed in cancer patient responders to CPIs. CPIs block the mechanisms by which cancers evade detection and destruction by the immune system. Observational studies of humans by a group led by our collaborator, Dr. Jennifer Wargo of MD Anderson Cancer Center, or MD Anderson, suggest that microbiome composition impacts response to CPIs. This has been supported by mouse model studies conducted by us and at MD Anderson that show that colonization with human responder microbes affected tumor response to CPI treatment, versus mice colonized with CPI non-responder microbes. These effects are thought to be a result of a specific microbiome “signature” enriched in certain members of the Firmicutes phylum of bacteria. We are working in collaboration with MD Anderson and the Parker Institute for Cancer Immunotherapy, or the Parker Institute, to evaluate the potential of SER-401. Based upon this signature, and to modulate the immunological tone of subjects to improve response in patients with metastatic melanoma to CPI treatment. MD Anderson granted Seres 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. In collaboration with the Parker Institute and MD Anderson, we initiated a Phase 1b study of SER-401 in patients with metastatic melanoma. Patients will be treated with either CPI alone, or in combination with SER-401, and observed for biomarkers of response to CPI and tumor regression. We expect preliminary results in the second half of 2020.

We have finalized the composition for SER-155, a rationally designed, fermented microbiome therapeutic candidate to correct dysbiosis in patients undergoing allogeneic hematopoietic stem cell transplant, or allo-HSCT, or solid organ transplants. This preclinical program is based in part on published clinical evidence from our collaborators at Memorial Sloan Kettering Cancer Center showing that allo-HSCT patients with dysbiosis are significantly more likely to die due to infection and/or lethal graft versus host disease, or GvHD. In November 2017, we were awarded a highly competitive grant from Combating Antibiotic-Resistant Bacteria Accelerator, or CARB-X, to support continued preclinical research and early development work for SER-155. In 2019, Seres was awarded additional funding from CARB-X to support continued preclinical development and early clinical development of SER-155, including support through investigational new drug application, or IND, and Phase 1b evaluation. The CARB-X grant provides us with up to $4.8 million of funding for research, manufacture, and IND, with potential for an additional $7.0 million for phase 1b development, upon completion of milestones.

We have completed early stages of researching Ecobiotic microbiome therapeutics for the treatment of metabolic diseases, such as non-insulin dependent diabetes, non-alcoholic steatohepatitis, or NASH, and metabolic syndrome. Research in these indications has focused on identifying microbiome signatures associated with various disease states and early discovery efforts to identify Ecobiotic consortia that could impact specific functional defects in the microbiome.

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. 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 Eric Shaff, our President and Chief Executive Officer, our experienced management team possesses core capabilities in microbiome therapeutics, drug development, commercialization, chemistry, manufacturing and controls, or CMC, public company management and finance. Our management team has extensive experience in microbial ecology, microbiology and live biological products, 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. We also intend to continue to strengthen our next generation of rationally designed, fermented microbiome therapeutic approach with SER-301 for UC being our lead candidate. The critical components of our strategy include:

Advancing our Programs

- ***Continuing clinical development of SER-287 for the treatment of UC.*** The clinical development of SER-287 to treat UC is supported by both clinical and preclinical studies in multiple animal models of colitis that provide evidence that SER-287 administration may result in reduced inflammation. Published clinical reports 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 who were failing current therapies. In October 2017, we announced positive top-line 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. Based on the encouraging data from the Phase 1b trial, in December 2018, we initiated our Phase 2b trial, ECO-RESET, evaluating SER-287 in patients with active mild-to-moderate UC. Based on feedback obtained from the FDA on the SER-287 Phase 2b study design, the study could serve as one of two required pivotal trials supporting potential future registration of SER-287. The Phase 2b study is a three-arm placebo-controlled trial of approximately 200 patients with active mild-to-moderate UC. Two groups of patients will receive different doses of SER-287, both following pretreatment with a short course of oral vancomycin. A third study arm will receive placebo. The study's primary endpoint will evaluate clinical remission measured after 10 weeks of SER-287 administration. Endoscopic improvement will be measured as a secondary efficacy measure. SER-287 has been awarded Orphan Drug Designation designation for pediatric UC.
- ***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 our earlier Phase 1b/2 clinical study and following discussions with the FDA, our phase 3 SER-109 clinical study is intended to enroll 188 patients with multiply recurrent CDI. Study participants are being randomized 1:1 between SER-109 and placebo and receiving a total dose that is approximately 10-fold higher than in the Phase 2 study, administered over three consecutive days. All patients entering ECOSPOR III must have tested positive for *C. difficile* toxin. This inclusion criterion was implemented in an effort to ensure enrollment of only patients with active CDI and to ensure accurate diagnosis of the study endpoint. We believe the use of toxin testing is essential to ensure valid, interpretable study results.
- ***Developing SER-401 for use with CPIs in patients with solid tumors.*** We are 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 have initiated a Phase 1b multicenter study in metastatic melanoma patients as part of our collaboration with MD Anderson and the Parker Institute.
- ***Developing SER-301 for the treatment of IBD.*** We are developing SER-301, a rationally designed, fermented, Ecobiotic microbiome therapeutic candidate for the treatment of IBD leveraging pharmacokinetic and pharmacodynamic data from our SER-287 clinical trial, our knowledge of modulation of dysbiosis seen in patients with UC, as well as insights from our SER-262 clinical study.
- ***Developing SER-155 to correct dysbiosis in patients undergoing allo-HSCT.*** We have finalized the composition for SER-155, a rationally designed, fermented microbiome therapeutic candidate to correct dysbiosis in patients undergoing allogeneic hematopoietic stem cell transplant (or allo-HSCT) or solid organ transplants.

Advancing Our Capabilities

- ***Leveraging our leading reverse translation 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 and inflammatory disease and disease associated with modulation of host immunity.*** 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.
- ***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.

Our Microbiome Therapeutics Platform

We have developed the leading microbiome therapeutics platform which we believe enables us to apply our capabilities to efficiently identify, manufacture and develop novel microbiome therapeutics for serious human diseases. We use reverse translation, the practice of driving discovery based on human data sets to improve the translatability of a preclinical program. Specifically, we start with data sets from both healthy subjects and patients to delineate at high-resolution the composition of the microbiome and physiological state of subjects and identify specific signatures in the microbiome that associate with disease or the onset of disease; these in-human insights are leveraged in preclinical drug design and development.

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 or disease state, revealing the ecological and functional differences between various states of disease and during the transition from health to disease or vice versa. We then develop our Ecobiotic microbiome therapeutic candidates to target these differences. Our clinical data from the SER-109, SER-262 and SER-287 programs, and microbiome data generated with external collaborators, serve to instruct us on how the introduction of certain keystone microbes have the potential to restructure a dysbiotic colonic microbiome and shift it to a non-disease state.

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 bacterial species and individual strains. We have also developed tools integrating gene profiling and 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. Further, we have established de novo analytics for pharmacokinetic and pharmacodynamic assessments of microbiome therapeutics.

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 HMP's "most wanted" and many novel species not described in other databases or the scientific literature. Using proprietary assays and full-genome sequences, 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 human immune cells. We also seek to understand how these microbes improve the health of barrier cells in the gut and how this may impact 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 vivo animal models. Our animal models include conventional mice, germ-free mice, and "humanized" mice that possess only bacteria derived from humans, which we developed to minimize confounding variables presented by murine microbes. Data from our *in vitro* and *in vivo* screens are analyzed and used to optimize compositional designs; introducing new bacterial strains and optimizing existing strains until we identify a lead composition suitable 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 unique manufacturing capacities position us to exploit the insights of our proprietary human data and the novel biology of species and strains that have not previously been used for therapeutics. 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 non-spore bacteria. Our manufacturing facility in Cambridge, Massachusetts was designed to be 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 sequence-based testing schemes, including high-throughput quantitative analytics to assess the identity, potency and purity of the final product. These methods have been qualified to meet regulatory standards for live biotherapeutic products.

Taken together, we believe our platform, spanning drug discovery, preclinical 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. 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 have designed SER-301, a rationally-designed, fermented Ecobiotic microbiome therapeutic candidate, for the treatment of UC. 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 are conducting a Phase 3 SER-109 clinical study in approximately 188 patients with multiply recurrent CDI. We are designing SER-401 for combination therapy with immune CPIs in cancer. We have also conducted early stage research on potential Ecobiotic microbiome therapeutic candidates for the treatment of metabolic disorders, such as early-stage, non-insulin dependent diabetes, NASH, 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.

Ulcerative Colitis, SER-287 and SER-301

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, 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)

UC 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 UC also experience increased risk of CDI 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 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 may target 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.

Management of UC includes medications that decrease general inflammation (e.g., 5-aminosalicylate derivatives, or 5-ASA, 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-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 (e.g. 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 reduce the triggers of immune activation. We believe 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; Paramsothy et al., 2017; Costello SP et al JAMA 2019). 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 a donor-derived, microbiome therapeutic candidate 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. This 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-ASA, low dose corticosteroids, or immunomodulatory therapy. Three SER-287 drug product lots, based on human donor material obtained from three separate individuals, were used in the Phase 1b study.

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 top-line results from our Phase 1b clinical trial of SER-287 in patients with UC. Study results showed no imbalance in adverse events in SER-287 treated patients, as compared to patients treated with placebo. No drug related serious adverse events were observed.

Analyses of study patients' microbiome data, a primary endpoint, 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 pharmacologic impact of the SER-287 engraftment was supported by metabolomic and transcriptomic data. Analysis of metabolites and gene expression signatures associated with inflammation and immune modulation, were observed to be correlated with remission in SER-287 treated subjects.

Microbiome results showed 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.

Further Details of 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 had mild-to-moderate UC as defined by a Total Modified Mayo score between 4 and 10, inclusive, with a modified Mayo endoscopic subscore ≥ 1, who were failing current therapies.

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 evidence of safety 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 repetitive enema FMT suggest that microbial interventions can affect clinical outcomes in UC, and this study evaluated whether the ecology of bacterial spores in SER-287 could 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 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 did not take 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 Results

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); change from placebo of 40.0% (95% confidence interval: 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, showing 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 results, although we believe 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.

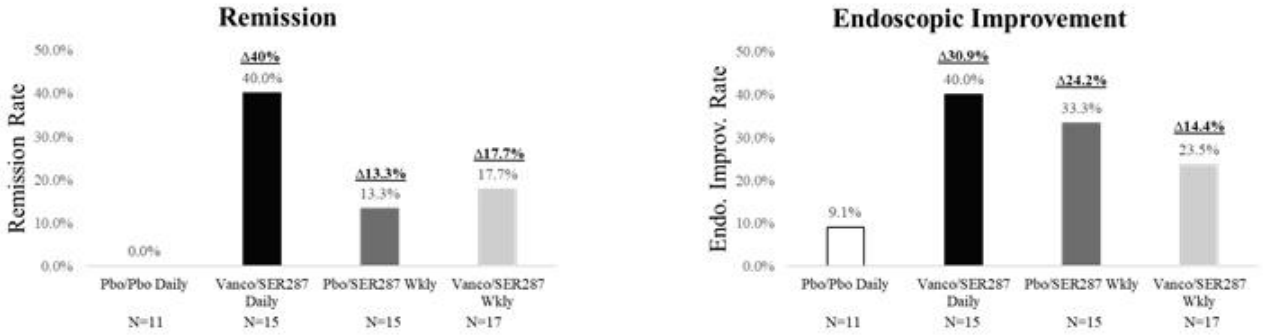


Figure 1: SER-287 Phase 1b Clinical Study Efficacy Data – Missing Equals Failure

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 Results

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 treatment-emergent adverse events, or 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 observed to be 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 vancomycin/SER-287 treatment arm compared to vancomycin/placebo and the vancomycin/SER-287 weekly treatment arms.

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, indicate 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 showed 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 GI microbiome were associated with clinical remission and further associated with changes in stool metabolite and intestinal biopsy gene expression signatures associated with inflammation and immune modulation. 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.

Phase 2b Clinical Study Design

Based on feedback from the FDA, we believe that the results from the SER-287 Phase 2b ECO-RESET study in conjunction with data from a second pivotal study designed to also evaluate maintenance, could enable submission of a SER-287 Biologics License Application.

The Phase 2b study, initiated in December 2018, is a three-arm placebo-controlled trial of approximately 200 patients with active mild-to-moderate UC. Two groups of patients will receive different doses of SER-287, both following pretreatment with a short course of oral vancomycin. A third study arm will receive placebo. The study's primary endpoint will evaluate clinical remission measured after 10 weeks of SER-287 administration. Endoscopic improvement will be measured as a secondary efficacy measure.

SER-301

SER-301 has been being rationally designed by utilizing our reverse translational platforms to incorporate learnings from our SER-287 clinical study, as well as our SER-262 clinical study. We have identified specific bacterial species that engraft and are associated with clinical remission, and further we have identified metabolic products made by these bacteria that have correlated with clinical efficacy. We also have gene expression data from patient gut mucosal biopsies showing which genes and pathways are favorably altered by SER-287 treatment. All of these data have been leveraged in the design of SER-301. We have initiated clinical development activities for SER-301. We plan to conduct the initial clinical study in Australia and New Zealand and, if authorized by the local regulatory agencies to initiate the study, we expect to begin enrolling subjects later in 2020.

CDI Overview and SER-109

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, or colitis, toxic megacolon and death. *C. difficile* bacteria express toxins that disrupt the structural architecture of cells causing leakage of fluids through the GI epithelium. The cells disrupted by these toxins eventually undergo apoptosis and die, disrupting the epithelial barrier and exposing the immune system to inflammatory stimuli, 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 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 8 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).

Current and developing treatment alternatives and their limitations

Patients with CDI utilize antibiotics, unapproved FMT and over-the-counter probiotics, and antibodies. Several therapeutic vaccines and drugs 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 GI 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 an unapproved 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 hundreds of unknown strains of bacteria, fungi, viruses and potentially parasites from donor to subject, and is difficult to perform on a mass scale. In November 2019 the FDA held a public hearing to obtain input on the use of FMT to treat *Clostridium difficile* infection not responsive to standard therapies. Presentations were made by the academic community and development companies regarding the current and future use of FMT. Our presentation at the meeting focused on the accurate assurance of the diagnosis of CDI – specifically the necessity to use toxin testing. In January, 2020, we submitted comments to the docket for the meeting that recommended: 1) increased scrutiny and regulation of unapproved, commercially available FMT that does not comply with IND requirements; 2) implementation of guidance for establishing safety of source materials for all microbiome products; and 3) safety and efficacy of all microbiome products to reduce recurrent CDI must be based on adequate and well controlled clinical trials including accurate assurance of diagnosis of the disease state – specifically toxin testing.

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 United States, 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 a donor-derived, purified bacterial spore-based microbiome therapeutic candidate consisting of over 50 bacterial species purified from healthy donor stool. Our SER-109 manufacturing process includes inactivation and clearance steps designed to eliminate potential pathogens. SER-109 is designed to prevent further recurrences of CDI in patients with recurrent CDI by restructuring the dysbiotic microbiome to a state that resists *C. difficile* growth and colonization. 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 antibiotic treatment. 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 GI 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 x 10^7 and 2 x 10^{10} spores. 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 observed to be well tolerated in this study. The most common AEs were diarrhea, nausea, and abdominal pain. The majority of 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 10^8 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 AEs in both the SER-109 and placebo arms were in the GI 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 SAEs 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 patients with multiply recurrent CDI was initiated. Study participants are randomized 1:1 between SER-109 and placebo and receive a total dose that is approximately 10-fold higher than in the Phase 2 study, administered over three consecutive days. Diagnosis of CDI for both study entry and for endpoint analysis is 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 stated that this 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 identified key factors that potentially explain the Phase 2 clinical study results, including issues related to both the accurate diagnosis of *C. difficile* recurrent infection, and potential suboptimal dosing of 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;
- The safety profile of SER-109, which may include 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 recurrent CDI; and
- 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 GI 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 patients with multiply recurrent CDI. Study participants are being randomized 1:1 between SER-109 and placebo. Diagnosis of CDI for both study entry and for endpoint analysis utilizes 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 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 study evaluates patients for 24 weeks and the primary endpoint is to 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 unformed bowel movements/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 is being 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 GI 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 a 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.

Other Programs

SER-401

We are also developing SER-401, for use with CPIs in patients with solid tumors to enhance efficacy and improve survival. SER-401 is a microbiome therapeutic candidate sourced from healthy individuals who have been identified to have a microbiome signature that is similar to that observed in cancer patient responders to CPIs. CPIs block the mechanisms by which cancers evade detection and destruction by the immune system. Observational studies of humans by a group led by our collaborator Dr. Jennifer Wargo of MD Anderson suggest that microbiome composition impacts response to CPIs. This has been supported by mouse model studies conducted by us and at MD Anderson that show that colonization with human responder microbes affected tumor response to CPI treatment, versus mice colonized with CPI non-responder microbes. These effects are thought to be a result of a specific microbiome ‘signature’ that is enriched with certain members of the Firmicutes phylum of bacteria. We are working in collaboration with MD Anderson and the Parker Institute to evaluate the potential of SER-401, based upon this signature, to modulate the immunological tone of subjects to improve response in patients with metastatic melanoma to CPI treatment. 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. In collaboration with the Parker Institute and MD Anderson, we have initiated a study of SER-401 in patients with metastatic melanoma. Patients will be treated with either CPI alone, or in combination with SER-401, and observed for tumor regression and immunological markers of response to CPI.

SER-155

We have finalized the composition for SER-155, a rationally designed, fermented microbiome therapeutic candidate to correct dysbiosis in patients undergoing allogeneic hematopoietic stem cell transplant (or allo-HSCT) or solid organ transplants. This preclinical program is based in part on published clinical evidence from our collaborators at Memorial Sloan Kettering Cancer Center showing that allo-HSCT patients with dysbiosis are significantly more likely to die due to infection and/or lethal graft versus host disease, or GvHD. In November 2017, we were awarded a highly competitive grant from CARB-X to support continued preclinical research and early development work for SER-155. In 2019, Seres was awarded additional funding from CARB-X to support continued preclinical development and early clinical development of SER-155, including support through IND filing and Phase 1b evaluation. The CARB-X grant provides us with up to $4.8 million of funding for research, manufacture, and IND application, with potential for an additional $7.0 million for phase 1b development, upon completion of milestones.

Sales and Marketing

If SER-109 is approved in the United States and Canada, we believe it can be commercialized with a focused specialty sales force 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 preparation for ECOSPOR III study results scenarios and potential regulatory submissions, we have initiated commercial readiness activities that include: *C. difficile* market assessments, publication and presentation planning, stakeholder and advocacy relationship mapping, and initiation of payer and reimbursement strategic planning.

In January 2016, we entered into an agreement with Nestec Ltd., or 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 are designed to 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 a 10,000 square foot cGMP manufacturing facility at our headquarters 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 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 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 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.

In November 2018, we executed a letter agreement with NHS, or the Letter Agreement, modifying certain terms of the License Agreement. Under the Letter Agreement, NHS agreed to accelerate the payment of the $20.0 million Phase 3 commencement milestone to be payable upon the commencement of the Phase 2b study for SER-287. Further, based on the results of the Phase 2b study, the Letter Agreement modifies certain terms and conditions related to the extent and timing of expense reimbursement associated with the ongoing SER-287 clinical trials. The Phase 2b study was initiated and the $40.0 million of milestone payments were received in December 2018.

To date, we have received $70.0 million in development milestones under the License Agreement.

In March 2019, we entered into a Research Collaboration and Option Agreement, or the Research Agreement, with MedImmune, LLC, a wholly owned subsidiary of AstraZeneca Inc., or AstraZeneca. Pursuant to the Research Agreement, we and AstraZeneca agreed to conduct certain research and development activities with the goal of advancing the mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy, including potential synergy with AstraZeneca compounds in accordance with a mutually agreed research plan. AstraZeneca has agreed to bear all costs of conducting its activities under the Research Agreement and to reimburse us for certain of our costs incurred under the Research Agreement. Additionally, AstraZeneca has agreed pay to us a total of $20.0 million in three equal installments, the first of which we received in April 2019, the second of which we received in December 2019 and third of which becomes due in January 2021. We granted AstraZeneca the exclusive option to negotiate certain exclusive license rights. If AstraZeneca exercises an option, we have agreed to enter into good faith negotiations with them for terms and conditions of such license agreement for a specified time period.

In October 2019, we entered into a loan and security agreement with Hercules, pursuant to which a term loan in an aggregate principal amount of up to $50.0 million, or the Term Loan Facility, is available to us in three tranches. We received the first tranche of $25.0 million upon signing the agreement on October 29, 2019. Upon satisfaction of certain milestones, the second tranche will be available and will allow us to borrow an additional amount up to $12.5 million through March 15, 2021. The third tranche, which allows us to borrow an additional $12.5 million, will be available upon Hercules' approval on or prior to June 30, 2021.

In November 2019, we entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, to sell shares of the Company's common stock, par value $0.001 per share, with aggregate gross sales proceeds of up to $25,000,000, from time to time, through an "at the market" equity offering program under which Cowen will act as sales agent.

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 issued U.S. patents and patent applications in various stages of prosecution, including ex-U.S. international counterparts. We believe that issued claims will provide protection for our microbiome therapeutic candidates.

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, and 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, preclinical 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 the 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 preclinical, 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 preclinical 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.

Preclinical and clinical trials

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical 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 preclinical 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 preclinical 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 other than the rare disease or condition for which the product candidate has orphan designation. 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 preclinical 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. Preclinical 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 preclinical 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 marketed pursuant to approved 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 ACA, 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 False Claims Act, or FCA, imposes 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 ACA, among other things, imposed new reporting requirements through the Physician Payments Sunshine Act on certain manufacturers of drugs covered by a federal healthcare program for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals beginning in 2022 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 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.

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, reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement, 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 ACA 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 ACA:

- 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 70% 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 ACA, as well as efforts to repeal or replace certain aspects of the ACA. For example, the Tax Cuts and Jobs Act was enacted, which, among other things, removes the penalties for not complying with the ACA's individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the district court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the ACA will impact the ACA or our business.

Other legislative changes have been proposed and adopted in the United States since the ACA 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 2029 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 and enacted legislation 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.

Data Privacy and Security

We may also be subject to U.S. federal and state and foreign health information privacy, security and data breach notification laws, which may govern the collection, use, disclosure and protection of health-related and other personal information. In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule.

In addition, certain state govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context.

Employees

On February 7, 2019, we announced corporate changes to focus our resources. We are now concentrated on completing the SER-287 Phase 2b study in mild-to-moderate UC, obtaining results from the ongoing SER-109 Phase 3 study for recurrent CDI and advancing the SER-401 Phase 1b study, in collaboration with the Parker Institute and MD Anderson, to evaluate augmenting CPI response in patients with metastatic melanoma. We will also continue to pursue clinical development of SER-301, a rationally-designed microbiome therapeutic candidate for UC, leveraging learnings obtained from our prior clinical study results. In connection with the prioritization of these therapeutic candidates, we made changes to our management team and reduced headcount by approximately 30 employees.

As of December 31, 2019, we had 108 full-time permanent employees. Fifteen employees work in administration and operations and 93 work in research and development. A portion of our personnel costs are reimbursable under our Research Agreement with AstraZeneca and our grant from CARB-X.

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. 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. As a result of our recurring losses from operations and negative cash flows from operations, there is substantial doubt about our ability to continue as a going concern.

Since inception, we have incurred significant operating losses. Our net loss was $70.3 million for the year ended December 31, 2019, $98.9 million for the year ended December 31, 2018, and $89.4 million for the year ended December 31, 2017. As of December 31, 2019, we had an accumulated deficit of $459.6 million. To date, we have financed our operations through the public offerings of our common stock, private placements of our preferred stock, payments under our collaboration agreements, 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 preclinical 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-287 in our Phase 2b clinical trial for the treatment of UC;
- continue the clinical development of SER-109 in our Phase 3 clinical study for the prevention of recurrent CDI;
- continue the clinical development of SER-401 in our Phase 1b clinical trial for use with checkpoint inhibitors in patients with metastatic melanoma;

- conduct research and initiate clinical development of SER-301 for the treatment of UC;
- 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 our agreements with our collaborators;
- 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 preclinical 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.

As discussed in Note 1 of the consolidated financial statements included in this Annual Report under Accounting Standards Update, or ASU, 2014-15, *Presentation of Financial Statements-Going Concern* (Subtopic 205-40), or, ASC 205-40, we have the responsibility to evaluate whether conditions and/or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. Under ASC 205-40, this evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Since we currently anticipate that our existing financial resources will enable us to meet forecasted operating plans into the second quarter of 2021, we have determined that our cash runway along with our accumulated deficit, history of losses, and future expected losses meet the ASC 205-40 standard for raising substantial doubt about our ability to continue as a going concern. We may not be successful in our mitigation efforts, which primarily consist of raising additional capital through some combination of equity or debt financings, and/or potential new collaborations and reducing cash expenditures. Our plans concerning these matters are discussed in “Management’s Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources” of this Annual Report on Form 10-K. Lack of necessary funds may require us, among other things, to delay, scale back, or eliminate some or all of our planned clinical trials. Our future is dependent on our ability to execute our plans successfully or otherwise address these matters. If we fail to do so for any reason, we would not be able to continue as a going concern and could potentially be forced to seek relief through a filing under the U.S. Bankruptcy Code.

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-287, including conducting the Phase 2b clinical study, continue the clinical development of SER-109, including conducting the Phase 3 clinical study, continue clinical studies of SER-401, and continue to research, develop and initiate clinical trials of SER-301 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 cash, cash equivalents and investments as of December 31, 2019 will be sufficient to fund our operating expenses, debt service obligations and capital expenditure requirements into the second quarter of 2021, subject to compliance with the conditions and covenants of our Loan and Security Agreement with Hercules Capital, Inc. This estimate excludes net cash flows from future business development activities. In addition, the specifics of existing and 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. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical studies;
- 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;
- 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 and may decrease our stock price. 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 preclinical 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 and have reported top-line data in our Phase 1b studies of SER-287 and 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 and SER-287, 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 preclinical studies and clinical trials with positive results;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers for, or establishing 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 preclinical 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 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 therapeutics, 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.

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 candidates.

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 preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failed clinical trial can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim or preliminary results of a clinical trial, that we may from time to time announce, 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 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. For example, based on feedback from the FDA, the smaller study design of our Phase 3 clinical trial for SER-109 could require additional confirmatory evidence of efficacy, such as a second Phase 3 clinical trial.

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.

In June 2017, we initiated a Phase 3 clinical study of SER-109 (ECOSPOR III) in patients with multiple recurrent CDI. In May 2019 we implemented modifications to the Phase 3 study design, reducing the size of the study to 188 patients. 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 preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. We are developing 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.

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, including the use of unapproved fecal microbiota transplant, or FMT, for CDI;
- 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. We continue to enroll the SER-109 Phase 3 study for patients with recurrent CDI despite the widespread use of unapproved, FMT to treat CDI. As interference from this uncontrolled procedure has impacted the enrollment rate of our placebo-controlled clinical trial, we modified the study design with the goal of expediting clinical results. Enrollment delays in our clinical trials 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.

The size of our ongoing Phase 3 trial of SER- 109 may make it make it necessary to conduct an additional clinical trial of SER-109 to generate sufficient safety and efficacy data to allow us to gain approval of SER-109.

The FDA has previously indicated that an ECOSPOR III trial could be sufficient to allow us to file a BLA for SER-109 if the trial demonstrated a sufficient level of statistical significance. The trial size of 188 patients may not demonstrate the heightened level of statistical significance required by the FDA. The FDA has also indicated that it may require additional confirmatory evidence of efficacy for approval, which may include conducting a second Phase 3 study prior to seeking approval of SER-109. Moreover, we may also be required to treat additional patients with SER-109 in order to generate a sufficient safety database to allow us to seek approval of SER-109. The need to conduct additional clinical trials of SER 109 and any delay in gaining regulatory approval of SER-109 would increase our development costs and could cause the value of our company to decline and limit our ability to obtain additional financing.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, top-line or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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 preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval 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 preclinical 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 preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. 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, or they may require additional confirmatory or safety evidence beyond our existing 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 or gather more 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. SER-287 received Fast Track designation from the FDA for the induction and maintenance of clinical remission in adults with mild-to-moderate UC. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during preclinical 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 another particular product candidate is eligible for this designation, we cannot be certain that the FDA would decide to grant it. Even with 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 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.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to our Dependence on Third Parties and Manufacturing

The Collaboration and License Agreement, or the License Agreement, with Nestec Ltd., or NHS, is important to our business. If we or NHS fail to adequately perform under the License Agreement, or if we or NHS terminate the License Agreement, the development and commercialization of our CDI and IBD product candidates, including SER-109, 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-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 preclinical 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 preclinical 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 manufacturers we rely on to produce our product candidates have 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 product. We do not currently have a second source for required materials used for the manufacture of finished 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 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, preclinical 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 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 continues 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, the FDA continues to implement 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 or promotions. 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.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We 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. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Our relationships with customers, physicians and third-party payors are and 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 current and future arrangements with third-party payors, physicians and customers 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 Act, imposes, 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals beginning 2022 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. By way of example, the California Consumer Privacy Act, or CCPA, effective January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. In Europe, the General Data Protection Regulation, or GDPR, which went into effect in May 2018, introduces strict requirements for processing the personal data of European Union data subjects. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater.

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, reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement, 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 ACA, 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 ACA 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;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 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;
- 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.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. For example, the Tax Cuts and Jobs Act of 2017 was enacted, which, among other things, repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the ACA will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted since the ACA 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 2029 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 laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain.

We expect that the ACA, 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.

We currently have, and may have in the future, certain funding arrangements, such as our grant from CARB-X to support certain work for SER-155. Such funding arrangements impose various obligations on us, including reporting obligations, and may subject certain of our intellectual property, such as intellectual property made using the applicable funding, to the rights of the U.S. government under the Bayh-Dole Act. In addition, under our CARB-X grant, we may be required in the future to grant a private sector charitable organization a license to certain of our intellectual property related to the subject matter of the CARB-X grant if, after a certain period of time, we are not developing and have not licensed a third party to develop the applicable technology for certain indications in a given country, and the organization wishes to do so. Any failure to comply with our obligations under a funding arrangement may have an adverse effect on our rights under the applicable agreement or our rights in the applicable intellectual property. Compliance with our obligations or the exercise by the government or other funder of its rights, may limit certain opportunities or otherwise have an adverse effect on our business.

Our patent portfolio currently includes 21 active patent application families (which includes an option to license IP from MD Anderson and exclusive licenses to Memorial Sloan Kettering Cancer Center IP). Of these, 13 applications have been nationalized and 1 is pending at the provisional stage. While we have obtained 13 issued U.S. patents to date, 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, 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 Supreme Court, other federal courts, 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); *Alice Corp. v. CLS Bank International*, 573 U.S. 13-298 (2014); and *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 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 in the United States, 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. The oral proceedings were held at the European Patent Office on February 18, 2019 and the Opposition Division required The University of Tokyo to narrow the scope of the claims of the patent. We expect The University of Tokyo to appeal.

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 new corporate strategy and restructuring may not be successful.

On February 7, 2019, following a strategic business review, we announced our new strategy to focus our resources on advancing our highest-priority, clinical-stage microbiome therapeutic candidates. As a result, we are concentrating on completing the SER-287 Phase 2b study in mild-to-moderate UC patients, obtaining results from the ongoing SER-109 Phase 3 study for recurrent CDI, advancing the SER-401 Phase 1b study, in collaboration with PICI and MD Anderson, to evaluate augmenting checkpoint inhibitor response in patients with metastatic melanoma and advancing SER-301 into clinical development. The success of this strategic shift will depend on our ability to successfully advance our therapeutic candidates, complete our ongoing studies, retain senior management or other highly qualified personnel, prioritize competing projects and efforts and obtain sufficient resources, including additional capital. Accordingly, there are no assurances our change in strategic focus will be successful, which may have an adverse effect on our results of operations and financial condition.

Also, on February 7, 2019, we announced the restructuring of our executive team and a reduction in our workforce by approximately 30 percent. The positions eliminated were primarily related to research, manufacturing, and general and administrative services. Following the reduction in workforce we believe we are appropriately resourced to continue executing on our current strategy. However, our workforce may not be sufficient to fully execute our strategic shift, and we may not be able to effectively retain the management or personnel needed to fully implement our strategy. Our restructuring and reduction in workforce activities may also result in unexpected risks or costs, such as employee claims and contractual disputes, and the risk that the actual financial and other impacts of the reductions could vary materially from the outcomes anticipated, which may have a material adverse effect on our results of operations or financial condition.

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

We are highly dependent on Eric Shaff, our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements 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 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 or a smaller reporting 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 Securities and Exchange Commission 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 conduct clinical studies in Canada and intend to begin conducting clinical studies in Australia and New Zealand. We may conduct clinical studies in other countries as well. We currently plan to rely on collaborators, including NHS, to commercialize certain approved products outside of North America. 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, 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 a formal, comprehensive cyber-security program, 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, loss of data privacy, 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, there have been successful but immaterial cyber-attacks, and if such an event were to occur again in a more material manner 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 have in the past been subject to securities class action litigation and may be subject to similar or other litigation in the future, which may harm our business.

Securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. 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. alleging 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. Although this lawsuit has been dismissed by the court, should we face similar or other litigation again, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business. In addition, the uncertainty of a 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.

Changes in U.S. tax law may materially adversely affect our financial condition, results of operations and cash flows.

The Tax Cuts and Jobs Act of 2017, or TCJA, has significantly changed the U.S. federal income taxation of U.S. corporations. The TCJA remains unclear in many respects and has been, and may continue to be, the subject of amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service, which have lessened or increased certain adverse impacts of the TCJA and may do so in the future. We continue to work with our tax advisors to determine the full impact that the TCJA will have on us. We urge our investors to consult with their legal and tax advisors with respect to the TCJA.

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

As of December 31, 2019, we had net operating loss carryforwards, or NOLs, of $266.5 million for federal income tax purposes and $265.7 million for state income tax purposes, which may be available to offset our future taxable income, if any. Our federal and state NOLs begin to expire in various amounts in 2035, provided that federal NOLs generated after December 31, 2017 will not be subject to expiration. As of December 31, 2019, we also had federal and state research and development and other tax credit carryforwards of approximately $31.8 million and $6 million, respectively, available to reduce future tax liabilities. Our tax credit carryforwards begin to expire in various amounts in 2031 and 2028, respectively. The federal research and development tax credit carryforwards include an orphan drug credit carryforward of $18.8 million. These NOLs and tax credit carryforwards could expire unused, to the extent subject to expiration, and be unavailable to offset future taxable income or income tax liabilities. In addition, in general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to use its pre-change NOLs and tax credit carryforwards to offset future taxable income and income taxes. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership of one or more stockholders or groups of stockholders owning at least 5% of a corporation's stock exceeds 50 percentage points over a three year period. We believe we have experienced an ownership change in the past and may experience ownership changes in the future as a result of future transactions in our stock, some of which may be outside our control. If we undergo an ownership change, our ability to use our NOLs and tax credit carryforwards could be further limited. For these reasons, we may not be able to use a material portion of our NOLs or tax credit carryforwards, even if we attain profitability. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future tax benefits of such assets. Under the TCJA, although the treatment of NOLs arising on or before December 31, 2017 has generally not changed, NOLs arising on or after January 1, 2018 will generally only be able to offset 80% of taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

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

In October 2019, we entered into a loan and security agreement with Hercules pursuant to which a term loan facility in aggregate principal amount up to $50.0 million, or the Term Loan Facility, is available to us in three tranches. We received the first tranche of $25.0 million upon signing the agreement on October 29, 2019. Upon satisfaction of certain milestones, the second tranche will be available and will allow us to borrow an additional amount up to $12.5 million through March 15, 2021. The third tranche, which allows us to borrow an additional $12.5 million, will be available upon Hercules' approval on or prior to June 30, 2021. The Term Loan Facility is secured by a lien on substantially all of our assets, other than intellectual property. We also agreed not to pledge or secure our intellectual property to others.

The Term Loan Facility includes affirmative and negative covenants and events of default applicable to us. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports and maintain insurance coverage. The negative covenants include, among others, restrictions on our transferring collateral, making changes to the nature of our business, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, engaging in transactions with affiliates. The Term Loan Facility also includes a liquidity covenant that commences either October 31, 2020, or December 31, 2020 based upon our satisfaction of certain performance milestones. Events of default include, among other things and subject to customary exceptions: (i) insolvency, liquidation, bankruptcy or similar events; (ii) failure to pay any debts due under the loan and security agreement with Hercules or other loan documents on a timely basis; (iii) failure to observe certain covenants under the loan and security agreement with Hercules; (v) occurrence of a material adverse effect; (vi) material misrepresentation by us; (vii) occurrence of any default under any other agreement involving material indebtedness; and (viii) certain material money judgments. If we default under the loan and security agreement, Hercules may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lenders' right to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. Any declaration by Hercules of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

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 77% 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, 2019 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 a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting 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 December 31, 2020. 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 and from having to disclose the ratio of compensation of our chief executive officer to the median compensation of our employees.

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

We are also a "smaller reporting company" as defined under the rules promulgated under the Exchange Act. We will remain a smaller reporting company until the fiscal year following the determination that both (i) the value of our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter and (ii) our annual revenues are more than $100 million during the most recently completed fiscal year and the value of our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, or supplemental financial information.

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.

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. In addition, our loan and security agreement with Hercules Capital currently prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be 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.

Clinical Manufacturing

We currently conduct part of our manufacturing operations in our leased facilities in Cambridge, Massachusetts, which 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. 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

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. The oral proceedings were held at the European Patent Office on February 18, 2019 and the Opposition Division required The University of Tokyo to narrow the scope of the claims of the patent. The University of Tokyo has appealed certain aspects of the Opposition Division's decision, as have we and other opponents.

Item 4. Mine Safety Disclosures

Not applicable.

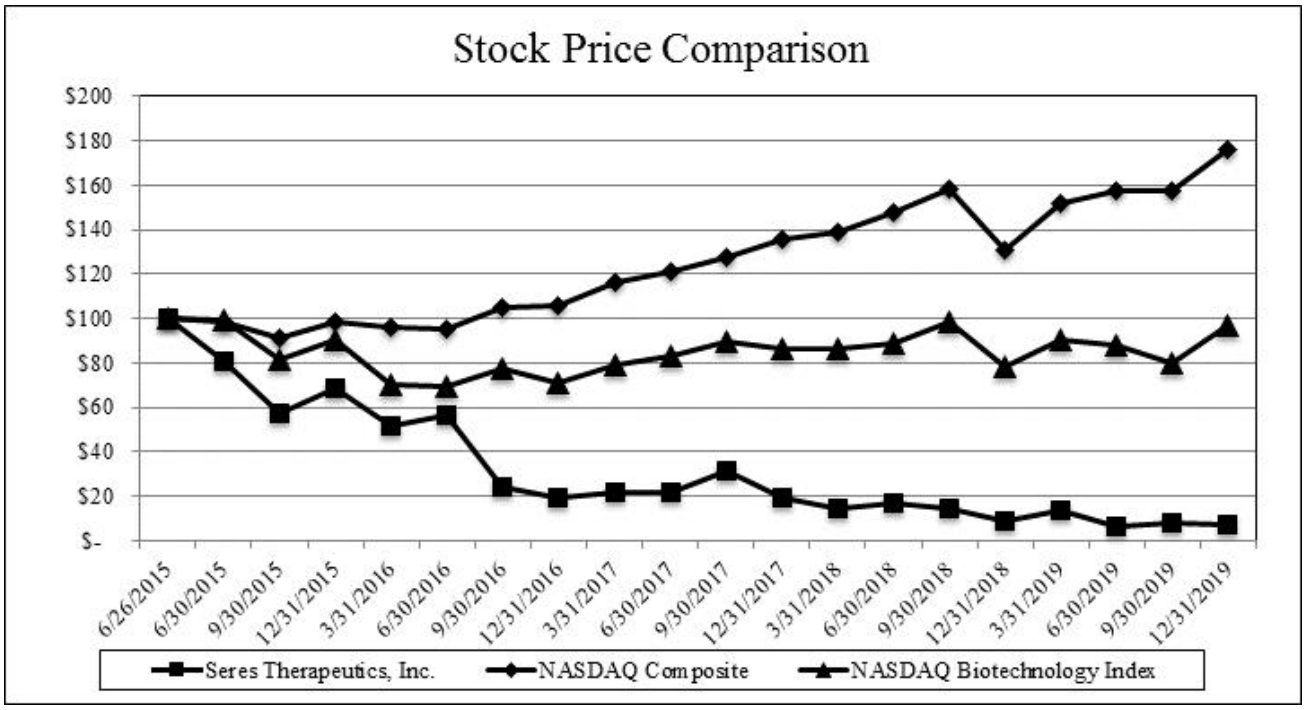
PART II

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

Our common stock is traded on The Nasdaq Global Select Market under the symbol "MCRB."

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, 2019, 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 February 28, 2020, there were approximately 20 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. In addition, our loan and security agreement with Hercules Capital currently prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. See "Management's Discussion and Analysis of Financial Condition and Results of Operations – Liquidity and Capital Resources."

Recent Sales of Unregistered Securities

We did not make any sales of unregistered securities during the quarter ended December 31, 2019.

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, 2019.

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, 2019, 2018, and 2017 and the consolidated balance sheet data as of December 31, 2019 and 2018 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, 2016 and 2015 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,				
	2019	2018	2017	2016	2015
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Collaboration revenue - related party[1]	$ 27,188	$ 26,917	$ 32,100	$ 21,766	$ —
Grant revenue	1,102	1,350	—	—	—
Collaboration revenue	6,215	—	—	—	—
Total revenue	34,505	28,267	32,100	21,766	—
Operating expenses:					
Research and development	80,141	95,955	89,455	81,989	38,095
General and administrative	24,748	32,596	34,040	32,616	16,761
Restructuring expenses	1,492	—	—	—	—
Total operating expenses	106,381	128,551	123,495	114,605	54,856
Loss from operations	(71,876)	(100,284)	(91,395)	(92,839)	(54,856)
Other income (expense):					
Interest income	1,033	1,172	1,590	2,229	638
Interest expense	(502)	—	—	(969)	(555)
Other income	1,066	170	425	—	—
Revaluation of preferred stock warrant liability	—	—	—	—	(7)
Total other income (expense), net	1,597	1,342	2,015	1,260	76
Net loss	$ (70,279)	$ (98,942)	$ (89,380)	$ (91,579)	$ (54,780)
Net loss per share attributable to common stockholders, basic and diluted[2]	$ (1.24)	$ (2.43)	$ (2.21)	$ (2.30)	$ (2.33)

(1) We adopted ASC 606 on January 1, 2018, using the modified retrospective method for all contracts not completed as of the date of adoption. Our reported results after the adoption date reflect the application of ASC 606 guidance while our reported results prior to the adoption date were prepared under the guidance outlined in ASC 605. See Note 12 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K for further details.

(2) See Note 13 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,				
	2019	2018	2017	2016	2015
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 65,126	$ 85,820	$ 36,088	$ 54,539	$ 73,933
Investments	29,690	—	113,895	175,456	131,149
Working capital[1]	54,196	50,624	123,453	167,912	196,690
Total assets[2]	132,440	120,472	189,522	272,646	216,900
Total stockholders' equity (deficit)	(48,324)	(48,045)	60,699	132,631	205,394

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

(2) We adopted ASC 842 on January 1, 2019 using the modified retrospective approach with no restatement of prior periods or cumulative adjustment to accumulated deficit. Our reported results after the adoption date reflect the application of ASC 842 guidance while our reported results prior to the adoption date were prepared under the guidance outlined in ASC 840. See Note 7 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. SER-287 is being developed to treat ulcerative colitis, or UC. SER-109 is designed to reduce recurrences of *Clostridium 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. In addition, using our microbiome therapeutics platform, we are developing product candidates to treat diseases where the microbiome is implicated, including SER-301, a rationally designed, fermented UC candidate, and SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors in patients with metastatic melanoma. Supporting our R&D efforts are our deep capabilities related to microbiome therapeutic drug discovery, manufacturing, quality, and clinical development. We believe that these capabilities provide us with important competitive advantages related to the advancement of this novel treatment modality.

Since our inception in October 2010, we have devoted substantially all of our resources to developing our programs, 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-287, SER-109, SER-401 and SER-301 are still in preclinical development or early stage discovery. 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 $70.3 million for the twelve months ended December 31, 2019. As of December 31, 2019, we had an accumulated deficit of $459.6 million and cash, cash equivalents and investments totaling $94.8 million. Based on our current plans and forecasted expenses, we believe that our existing cash, cash equivalents and investments as of December 31, 2019, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second quarter of 2021. In accordance with the requirements of Accounting Standards Update, or ASU, No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, or ASC 205-40, we have determined that there is substantial doubt about our ability to continue as a going concern. 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. As further discussed in "—Liquidity and Capital Resources."

In February 2019, we implemented corporate changes to focus our resources on advancing our clinical-stage therapeutic candidates. As a result, we are concentrating on completing our SER-287 Phase 2b study in mild-to-moderate UC patients, obtaining results from our ongoing SER-109 Phase 3 study for the treatment of recurrent CDI, advancing our SER-401 Phase 1b study, in collaboration with the Parker Institute for Cancer Immunotherapy, or PICI and MD Anderson Cancer Center, or MD Anderson, to evaluate augmenting checkpoint inhibitor response in patients with metastatic melanoma, and advancing SER-301 into clinical development. In connection with the prioritization of these therapeutic candidates, we made changes to our management team and reduced headcount by approximately 30 percent.

In March 2019, we entered into a Research Collaboration and Option Agreement, or the Research Agreement, with MedImmune, LLC, a wholly owned subsidiary of AstraZeneca Inc., or AstraZeneca. Pursuant to the Research Agreement, we and AstraZeneca agreed to conduct certain research and development activities with the goal of advancing the mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy, including potential synergy with AstraZeneca compounds in accordance with a mutually agreed research plan. AstraZeneca has agreed to bear all costs of conducting its activities under the Research Agreement and to reimburse us for certain of our costs incurred under the Research Agreement. Additionally, AstraZeneca has agreed to pay to us a total of $20.0 million in three equal installments, the first of which we received in April 2019, the second of which we received in December 2019 and third of which becomes due in January 2021. We granted AstraZeneca the exclusive option to negotiate certain exclusive license rights. If AstraZeneca exercises an option, we have agreed to enter into good faith negotiations with them for terms and conditions of such license agreement for a specified time period.

In June 2019, we completed an underwritten public offering, in which we sold 26,666,667 shares of our common stock at a price to the public of $2.25 per share. We received aggregate net proceeds from the offering of approximately $56.0 million, after deducting underwriting discounts and commissions and offering expenses payable by us. In addition, we granted the underwriters a 30-day option to purchase up to an additional 2,666,666 shares of common stock at the public offering price, less underwriting discounts and commissions. In June 2019, we sold an additional 2,151,911 shares of our common stock at a price to the public of $2.25 per share. We received net proceeds of approximately $4.6 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

In October 2019, we entered into a loan and security agreement with Hercules pursuant to which the Term Loan Facility in an aggregate principal amount of up to $50.0 million, is available to us in three tranches. We received the first tranche of $25.0 million ($24.6 million, net of $0.4 million of closing costs), upon signing the agreement on October 29, 2019. Upon satisfaction of certain milestones, the second tranche will be available and will allow us to borrow an additional tranche of $12.5 million through March 15, 2021. The third tranche, which allows us to borrow an additional $12.5 million, will be available upon Hercules' approval on or prior to June 31, 2021.

In November 2019, we entered into a Sales Agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, to sell our common stock with aggregate gross sales proceeds of up to $25.0 million from time to time, through an "at the market" equity offering program, or ATM under which Cowen acts as sales agent. See "—Liquidity and Capital Resources."

SER-287

SER-287 is an oral, donor-derived microbiome therapeutic candidate designed to normalize the gastrointestinal microbiome of individuals with UC. In December 2018, we commenced a three-arm placebo-controlled Phase 2b clinical trial to evaluate SER-287 in approximately 201 patients with mild-to-moderate UC. Two groups of patients will receive different doses of SER-287, both following pretreatment with a short course of oral vancomycin. A third study arm will receive placebo. The study's primary endpoint will evaluate clinical remission measured after 10 weeks of SER-287 administration. Patients then enter a 2-week exploratory maintenance follow-up period. Endoscopic improvement will be measured as a secondary efficacy measure. Based on feedback from the FDA, if the data from this trial is positive, we expect that the Phase 2b clinical trial could be one of two pivotal trials to enable a Biologics License Application, or BLA, to be submitted for SER-287 for the treatment of UC. We expect to report top-line data in the second half of 2020.

There are approximately 700,000 UC patients in the United States and fewer than one-third of patients on current therapies achieve remission. Approved treatments are often inadequate to control disease activity and are often associated with significant side effects, including immunosuppression. We believe that SER-287 may address underlying drivers of inflammation in UC and, based on the favorable tolerability profile observed in our clinical trials of SER-287, has the potential to be developed as both a foundational monotherapy, as well as a combination therapy with other UC drugs. SER-287 has been granted Fast Track Designation by the FDA for the induction and maintenance of clinical remission in adult subjects with active mild-to-moderate UC.

SER-109

SER-109 is a donor-derived, purified bacterial spore-based microbiome therapeutic candidate consisting of over 50 bacterial species purified from healthy donor stool. Our SER-109 manufacturing process includes inactivation and clearance steps designed to eliminate potential pathogens. SER-109 is designed to prevent further recurrences of CDI in patients with a history of multiple infections by restructuring the dysbiotic microbiome to a state that resists *C. difficile* colonization and growth.

We have been enrolling a double-blind, placebo-controlled SER-109 Phase 3 study, ECOSPOR III, in 188 subjects with multiply recurrent CDI. All patients entering ECOSPOR III must have tested positive for *C. difficile* toxin, as currently recommended by the Infectious Diseases Society of America guidelines (McDonald Clin Infect Dis 2018). This inclusion criterion was implemented in an effort to ensure enrollment of only patients with active infection rather than simple colonization. The on-going 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. The size and powering calculations of the study are informed by prior SER-109 study results, published CDI trial data utilizing toxin testing, and preliminary blinded and open label CDI recurrence rate data from the ongoing ECOSPOR III study. Toxin testing is required for patients in ECOSPOR III at both study entry and at the time of suspected recurrence in an effort to ensure optimal diagnostic accuracy of active infection, as recommended by the Infectious Diseases Society of America. We believe the use of toxin testing for all subjects in the study is essential to ensure valid, interpretable study results. Notably, no published placebo-controlled FMT trial in recurrent CDI has required toxin testing, which raises concerns about appropriate subject selection and estimates of FMT efficacy.

Based on prior discussions with the FDA, we believe this study, if successful, has the potential to be a single pivotal study supporting product registration. However, this would depend on the strength of the data and it is also possible that additional safety data may be required. We expect to report top-line data in mid-2020.

SER-401

SER-401 is an oral microbiome therapeutic candidate comprising a bacterial signature similar to that observed in checkpoint inhibitor immunotherapy responders. In March 2019, the first patient was dosed in the Phase 1b clinical study with MD Anderson and PICI, to evaluate SER-401's potential to augment the response of anti-PD-1 checkpoint inhibitor therapy. The study is designed to enroll 30 patients with metastatic melanoma who are being treated with nivolumab, an anti-PD-1 therapy. Patients are randomized at a 2-to-1 ratio to either SER-401 or placebo. The study's primary endpoints are to evaluate safety and tolerability. Its secondary endpoints are to evaluate the correlation of microbiome biomarkers of response to various clinical and immunological outcome measures. We expect preliminary results in the second half of 2020.

SER-301

We are also advancing our next generation, rationally-designed, fermented microbiome drug discovery capabilities, focusing on advancing SER-301, a therapeutic candidate for UC. We have finalized the composition for SER-301. The bacterial strains included in SER-301 were informed by our human clinical study results designed using our reverse translation capabilities as well as preclinical mechanistic studies. We have initiated clinical development activities for SER-301. We plan to conduct the initial clinical study in Australia and New Zealand and, if authorized to initiate the study, we expect to begin enrolling subjects later in 2020. In connection with the initiation of the SER-301 phase 1 study, we will be entitled to receive a $10.0 million milestone payment under our collaboration with Nestec Ltd.

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-287 in our Phase 2b clinical trial for the treatment of UC;
- continue the clinical development of SER-109 in our Phase 3 clinical study for the prevention of recurrent CDI;
- continue the clinical development of SER-401 in our Phase 1b clinical trial for use with checkpoint inhibitors in patients with metastatic melanoma;
- conduct research and initiate clinical development of SER-301 for the treatment of UC;
- 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 our agreements with our collaborators;
- 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.

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. If we are unable to raise sufficient capital to fund our current operating plans when needed, we may need to reduce our expenditures, potentially requiring us, among other things, to delay, scale back, or eliminate some or all of our planned clinical trials and other research and development programs. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

To date we have not generated any revenues from the sale of products. Our revenues have been derived primarily from our agreements with our collaborators.

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, preclinical activities and clinical trials on our behalf as well as contract manufacturing organizations that manufacture drug products for use in our preclinical 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 preclinical 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. Costs incurred under our agreements with our collaborators, are included in the costs listed above. 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 our programs. 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 preclinical 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,		
	2019	2018	2017
	(in thousands)		
Microbiome therapeutics platform	$ 52,340	$ 62,804	$ 63,695
SER-109	10,281	18,482	16,306
SER-262	122	3,090	4,971
SER-287	17,398	11,579	4,483
Total research and development expenses	$ 80,141	$ 95,955	$ 89,455

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

General and Administrative Expenses

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

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 the requirements of the Securities and Exchange Commission, director and officer insurance costs and investor and public relations costs.

Other Income (Expense), Net

Interest Income (Expense), Net

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

Interest expense consists of interest incurred under our loan and security agreement with Hercules.

Other Income

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

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, 2019, we had federal and state net operating loss carryforwards of $266.5 million and $265.7 million, respectively, both of which begin to expire in 2035. As of December 31, 2019, we also had federal and state research and development tax credit carryforwards of $31.8 million and $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 $18.8 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.

Revenue Recognition

We recognize revenue in accordance with the guidance under ASC 606, *Revenue from Contracts with Customers*. ASC 606 applies to all contracts with customers, except those contracts that are within the scope of other guidance, such as leases, insurance, and financial instruments. We enter into agreements that are within the scope of ASC 606, under which we license certain of our product candidates and perform research and development services in connection with such arrangements. The terms of these arrangements typically include payment of one or more of the following: nonrefundable up-front fees, reimbursement of research and development costs, development, clinical, regulatory and commercial sales milestone payments, and royalties on net sales of licensed products. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. When determining the timing and extent of revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligation(s) in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligation(s) in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services transferred to our customer.

At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within the contract to determine whether each promised good or service is a performance obligation. The promised goods or services in our arrangements typically consist of a license to our intellectual property and/or research and development services. We may provide options to additional items in such arrangements, which are accounted for as separate contracts when our customer elects to exercise such options, unless the option provides a material right to our customer. Performance obligations are promises in a contract to transfer a distinct good or service to our customer that (i) our customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised goods or services until such combined group of promises meets the requirements of a performance obligation.

We determine transaction price based on the amount of consideration we expect to receive for transferring the promised goods or services in the contract. Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, we estimate the probability and extent of consideration we expect to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. We then consider any constraints on the variable consideration and include in the transaction price variable consideration to the extent it is deemed probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

We then allocate the transaction price to each performance obligation based on the relative standalone selling price and recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to our customer and the performance obligation is satisfied. For performance obligations which consist of licenses and other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

We record amounts as accounts receivable when the right to consideration is deemed unconditional. When consideration is received, or such consideration is unconditionally due, from our customer prior to transferring goods or services to our customer under the terms of a contract, a contract liability is recorded for deferred revenue.

We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by our customer and the transfer of the promised goods or services to our customer will be one year or less. Incremental costs of obtaining a contract are expensed as and when incurred if the expected period over which we would have amortized the asset is one year or less, or the amount is immaterial.

Collaboration revenue

Arrangements with collaborators may include licenses to intellectual property, research and development services, manufacturing services for clinical and commercial supply, and participation on joint steering committees. We evaluate the promised goods or services to determine which promises, or group of promises, represent performance obligations. In contemplation of whether a promised good or service meets the criteria required of a performance obligation, we consider the stage of development of the underlying intellectual property, the capabilities and expertise of our customer relative to the underlying intellectual property, and whether the promised goods or services are integral to or dependent on other promises in the contract. When accounting for an arrangement that contains multiple performance obligations, we must develop judgmental assumptions, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success to determine the stand-alone selling price for each performance obligation identified in the contract.

When we conclude that a contract should be accounted for as a combined performance obligation and recognized over time, we must then determine the period over which revenue should be recognized and the method by which to measure revenue. We generally recognize revenue using a cost-based input method.

Licenses of intellectual property

If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue allocated to the license when the license is transferred to our customer and our customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue associated with the bundled performance obligation. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of progress and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes developmental and regulatory milestone payments, we evaluate whether the achievement of each milestone specifically relates to our efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. If the achievement of a milestone is considered a direct result of our efforts to satisfy a performance obligation or transfer a distinct good or service and the receipt of the payment is based upon the achievement of the milestone, the associated milestone value is allocated to that distinct good or service, otherwise it will be allocated to all performance obligations of the arrangement based on the initial allocation.

We evaluate each milestone to determine when and how much of the milestone to include in the transaction price. We first estimate the amount of the milestone payment that we could receive using either the expected value or the most likely amount approach. We primarily use the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, we consider whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty). We update the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any revenue related to sales-based royalties or milestone payments based on the level of sales.

Manufacturing supply services

For arrangements that include a promise of supply of clinical or commercial product, we determine if the supply is a promise in the contract or a future obligation at our customer’s option. If determined to be a promise at inception of the contract, we evaluate the promise to determine whether it is a separate performance obligation or a component of a bundled performance obligation. If determined to be an option, we determine if the option provides a material right to our customer and if so, account for the option as a separate performance obligation. If determined to be an option but not a material right, we account for the option as a separate contract when our customer elects to exercise the option.

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 preclinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of preclinical and clinical supplies.

We base our expenses related to preclinical 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.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 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, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018:

	Year Ended December 31,		
	2019	2018	Change
	(in thousands)		
Revenue:			
Collaboration revenue - related party	$ 27,188	$ 26,917	$ 271
Grant revenue	1,102	1,350	(248)
Collaboration revenue	6,215	—	6,215
Total revenue	34,505	28,267	6,238
Operating expenses:			
Research and development	$ 80,141	$ 95,955	$ (15,814)
General and administrative	24,748	32,596	(7,848)
Restructuring expenses	1,492	—	1,492
Total operating expenses	106,381	128,551	(22,170)
Loss from operations	(71,876)	(100,284)	28,408
Other income (expense):			
Interest income	1,033	1,172	(139)
Interest expense	(502)	—	(502)
Other income	1,066	170	896
Total other income (expense), net	1,597	1,342	255
Net loss	$ (70,279)	$ (98,942)	$ 28,663

Revenue

Total revenue was $34.5 million and $28.3 million for the years ended December 31, 2019 and 2018, respectively. The revenue for both periods principally relates to the recognition of amounts received under the License Agreement. The increase is mainly due to recognition of amounts received under the Research Agreement entered into in March 2019.

Research and Development Expenses

	Year Ended December 31,		
	2019	2018	Change
	(in thousands)		
Microbiome therapeutics platform	$ 52,340	$ 62,804	$ (10,464)
SER-109	10,281	18,482	(8,201)
SER-262	122	3,090	(2,968)
SER-287	17,398	11,579	5,819
Total research and development expenses	$ 80,141	$ 95,955	$ (15,814)

Research and development expenses were $80.1 million for the year ended December 31, 2019, compared to $95.9 million for the year ended December 31, 2018. The decrease of $15.8 million was due primarily to the following:

- a decrease of $10.5 million in research expenses related to our microbiome therapeutics platform, due primarily to a decrease of $10.7 million in employee and consultant expenses, and a decrease of $0.3 million of professional fees, and is partially offset by an increase of $0.6 million of facility and supply costs;
- a decrease of $8.2 million in expenses related to our SER-109 program, due primarily to a decrease of $3.2 million in contract manufacturing costs, a $3.1 million decrease in clinical trial consulting expenses, a $1.0 million decrease in facility and supply costs, and a decrease of $0.9 million in sequencing costs;

- a decrease of $3.0 million in expenses of our SER-262 program primarily driven by a decrease in clinical trial costs of $2.4 million, and decrease in sequencing costs $0.5 million; and
- an increase of $5.8 million in expenses of our SER-287 program primarily driven by an increase in clinical trials costs of $4.8 million, an increase in contract manufacturing of $3.4 million, this is partially offset by a $1.2 million decrease in facility and supply costs, and a $0.8 million decrease sequencing and a $0.4 million decrease in employee and consultant expenses.

We expect that our research and development expenses may increase in the foreseeable future as we advance the clinical development of SER-109 and SER-287, 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,		
	2019	2018	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$ 9,586	$ 15,765	$ (6,179)
Professional fees	9,279	7,609	1,670
Facility-related and other	5,883	9,222	(3,339)
Total general and administrative expenses	$ 24,748	$ 32,596	$ (7,848)

General and administrative expenses were $24.7 million for the year ended December 31, 2019, compared to $32.6 million for the year ended December 31, 2018. The decrease of $7.8 million was primarily due to the following:

- a decrease in personnel related costs of $6.2 million primarily due to the decrease in stock-based compensation expense of $4.6 million and a decrease in salary costs of $1.8 million;
- an increase in professional fees of $1.7 million primarily due to an increase in consulting fees of $0.7 million, an increase in accounting related fees of $0.7 million, and an increase in legal fees of $0.3 million; and
- a decrease in facility-related and other costs of $3.3 million primarily due to a decrease in information technology expenses.

Restructuring

During the year ended December 31, 2019 we recorded charges of $1.5 million related to severance and other termination benefits, of which $1.3 million was paid during the year ended December 31, 2019. No restructuring charges were recorded during the year ended December 31, 2018.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2019 was $1.6 million, compared to $1.3 million for the year ended December 31, 2018. The $0.3 million increase in other income (expense), net was primarily due to sublease income of $0.9 million. This increase was partially offset by interest expense of $0.5 million incurred under the Term Loan Facility.

Comparison of Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31,		
	2018	2017	Change
	(in thousands)		
Revenue			
Collaboration revenue - related party	$ 26,917	$ 32,100	$ (5,183)
Grant revenue	1,350	—	1,350
Total revenue	28,267	32,100	(3,833)
Operating expenses:			
Research and development	95,955	89,455	6,500
General and administrative	32,596	34,040	(1,444)
Total operating expenses	128,551	123,495	5,056
Loss from operations	(100,284)	(91,395)	(8,889)
Other income (expense):			
Interest income	1,172	1,590	(418)
Other income	170	425	(255)
Total other income (expense), net	1,342	2,015	(673)
Net loss	$ (98,942)	$ (89,380)	$ (9,562)

Revenue

Total revenue was $28.3 million and $32.1 million for the year ended December 31, 2018 and 2017, respectively. The revenue for both periods principally relates to the recognition of amounts received under the License Agreement. The decrease is mainly due to the adoption of ASC 606, described in detail in Note 12. Additionally, we recognized a $20.0 million substantive milestone under the License Agreement during the twelve months ended December 31, 2017.

Research and Development Expenses

	Year Ended December 31,		
	2018	2017	Change
	(in thousands)		
Microbiome therapeutics platform	$ 62,804	$ 63,695	$ (891)
SER-109	18,482	16,306	$ 2,176
SER-262	3,090	4,971	$ (1,881)
SER-287	11,579	4,483	7,096
Total research and development expenses	$ 95,955	$ 89,455	$ 6,500

Research and development expenses were $96.0 million for the year ended December 31, 2018, compared to $89.5 million for the year ended December 31, 2017. The increase of $6.5 million was due primarily to the following:

- a decrease of $0.9 million in research expenses related to our microbiome therapeutics platform, due primarily to a decrease in research consulting expenses of $2.0 million and IT expenses of $0.4 million and is partially offset by an increase in salary and consulting costs of $1.4 million and facilities and supplies costs of $0.1 million;
- an increase of $2.2 million in expenses related to our SER-109 program, due primarily to an increase in contract manufacturing costs of $2.7 million, an increase in clinical trial consulting expenses of $0.6 million and an increase of $0.2 million in sequencing costs. This is partially offset by a decrease of $1.3 million in other consulting costs;
- a decrease of $1.9 million in expenses of our SER-262 program primarily driven by a decrease in clinical trial costs of $1.2 million, and decrease in lab supplies and consumables of $0.7 million; and
- an increase of $7.1 million in expenses of our SER-287 program primarily driven by an increase in clinical trials costs of $4.3 million, an increase in other consulting costs of $1.4 million and increase in lab supplies and consumables of $1.4 million.

General and Administrative Expenses

	Year Ended December 31, 2018	2017	Change
	(in thousands)		
Personnel related (including stock-based compensation)	$ 15,765	$ 17,233	$ (1,468)
Professional fees	7,609	8,265	(656)
Facility-related and other	9,222	8,542	680
Total general and administrative expenses	$ 32,596	$ 34,040	$ (1,444)

General and administrative expenses were $32.6 million for the year ended December 31, 2018, compared to $34.0 million for the year ended December 31, 2017. The decrease of $1.4 million was primarily due to the following:

- a decrease in personnel related costs of $1.5 million primarily due to the decrease in stock-based compensation expense;
- a decrease in professional fees of $0.7 million due primarily to a decrease in legal fees of $0.8 million and a decrease in consulting fees of $0.3 million, partially offset by an increase in recruiting fees of $0.4 million; and
- an increase in facility-related and other costs of $0.7 million primarily due to an increase in information technology expenses of $1.4 million, partially offset by a decrease in office-related expenses of $0.7 million.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2018 was $1.3 million, compared to $2.0 million for the year ended December 31, 2017. The $0.7 million decrease in other income (expense), net was primarily due to a decrease in interest income from lower cash and investment balances in 2018 versus 2017.

Liquidity and Capital Resources

In June 2019, we completed an underwritten public offering, in which we sold 26,666,667 shares of our common stock at a price to the public of $2.25 per share. We received aggregate net proceeds from the offering of approximately $56.0 million, after deducting underwriting discounts and commissions and offering expenses payable by us. In addition, we granted the underwriters a 30-day option to purchase up to an additional 2,666,666 shares of common stock at the public offering price, less underwriting discounts and commissions. In June 2019, we sold an additional 2,151,911 shares of our common stock at a price to the public of $2.25 per share. We received net proceeds of approximately $4.6 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

In October 2019, we entered into a loan and security agreement with Hercules, pursuant to which the Term Loan Facility in an aggregate principal amount up to $50.0 million is available to us in three tranches. We received the first tranche of $25.0 million upon signing the agreement on October 29, 2019. Upon satisfaction of certain milestones, the second tranche will be available and will allow us to borrow an additional amount up to $12.5 million through March 15, 2021. The third tranche, which allows us to borrow an additional $12.5 million, will be available upon Hercules' approval on or prior to June 30, 2021.

In November 2019, we entered into the Sales Agreement with Cowen to sell shares of our common stock with aggregate gross sales proceeds of up to $25.0 million, from time to time, through an ATM under which Cowen acts as sales agent. From November 27, 2019, the date we entered into the Sales Agreement, to December 31, 2019, we sold 128,400 shares of common stock under the ATM, raising aggregate net proceeds of approximately $0.5 million and paying Cowen an aggregate commission of approximately 3%.

Since our inception, we have generated revenue primarily 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.

As of December 31, 2019, we had cash, cash equivalents and investments totaling $94.8 million and an accumulated deficit of $459.6 million. Based on our current plans and forecasted expenses, we believe that our existing cash, cash equivalents and investments as of December 31, 2019, will enable us to fund our operating expenses, debt service obligation and capital expenditure requirements into the second quarter of 2021. 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. These factors raise substantial doubt about our ability to continue as a going concern.

Collaboration Agreements

Agreement with NHS

In January 2016, we entered into the License Agreement, 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 $120.0 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 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, in markets outside of the United States and Canada, or the Licensed Territory. We have retained full commercial rights to the NHS Collaboration Products with respect to the United States and Canada, where we plan to build our own commercial organization. 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. In November 2018, we executed a letter agreement with NHS, or the Letter Agreement, modifying certain terms of the License Agreement. Under the Letter Agreement, NHS agreed to pay us the $20.0 million Phase 3 milestone payment upon commencement of the Phase 2b study for SER-287. In December 2018, we received $40.0 million in milestone payments in connection with the commencement of the Phase 2b study for SER-287.

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. The License Agreement also provides scenarios under which NHS' reimbursement to us for certain Phase 3 development costs would be reduced or delayed depending on the outcomes of the SER-287 Phase 2b study. 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.

Agreement with AstraZeneca

In March 2019, we entered into the Research Agreement with AstraZeneca. Pursuant to the Research Agreement, we and AstraZeneca agreed to conduct certain pre-clinical and development activities and may conduct certain clinical research with the goal of advancing the mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy, including potential synergy with AstraZeneca compounds in accordance with a mutually agreed research plan. Pursuant to the Research Agreement, we agreed not to conduct research or development of any microbiome products specifically designed by us during the term of the Research Agreement for the treatment of cancer with or on behalf of any third-party without the prior approval of the joint steering committee for the Research Agreement until at least three years after the effective date of the Research Agreement.

AstraZeneca has agreed to bear all costs of conducting its activities under the research plan and to reimburse us for certain of our costs incurred under the research plan. Additionally, AstraZeneca has agreed to pay to us a total of $20.0 million in three equal installments, the first of which we received in April 2019, the second of which we received in December 2019 and third of which becomes due in January 2021. Such payments are payable even if the Research Agreement is terminated in accordance with its terms, unless the Research Agreement is terminated by AstraZeneca for our uncured material breach.

We also granted AstraZeneca an exclusive option to negotiate exclusive license rights to certain of our technologies and assets. If AstraZeneca exercises this option, we have agreed to enter into good faith negotiations with them for terms and conditions of such license agreement for a specified time period.

Loan and Security Agreement with Hercules

In October 2019, we entered into a loan and security agreement with Hercules, pursuant to which the Term Loan Facility in an aggregate principal amount up to $50.0 million is available to us in three tranches. We received the first tranche of $25.0 million upon signing the agreement on October 29, 2019. Upon satisfaction of certain milestones, the second tranche will be available and will allow us to borrow an additional amount up to $12.5 million through March 15, 2021. The third tranche, which allows us to borrow an additional $12.5 million, will be available upon Hercules' approval on or prior to June 30, 2021.

Advances under the Term Loan Facility will bear interest at a rate equal to the greater of either (i) the Prime Rate (as reported in The Wall Street Journal) plus 4.40%, and (ii) 9.65%. We will make interest only payments through December 1, 2021, or extended to June 1, 2022 upon satisfaction of certain milestones, and will then repay the principal balance and interest of the advances in equal monthly installments after the interest only period and continuing through November 1, 2023. We paid Hercules a commitment fee of $0.4 million at the closing. We may prepay advances under the loan and security agreement with Hercules, in whole or in part, at any time subject to a prepayment charge equal to: (a) 3.0% of amounts so prepaid, if such prepayment occurs during the first year; (b) 2.0% of the amount so prepaid, if such prepayment occurs during the second year, and (c) 1.0% of the amount so prepaid, if such prepayment occurs after the second year. Upon prepayment or repayment of all or any of the term loans, we will pay (in addition to the prepayment premium) an end of term charge of 4.85% of the aggregate funded amount under the Term Loan Facility.

The Term Loan Facility is secured by substantially all of our assets, other than our intellectual property. We have agreed to not pledge or secure our intellectual property to others.

The Term Loan Facility includes affirmative and negative covenants applicable to us. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports and maintain insurance coverage. The negative covenants include, among others, restrictions on our transferring collateral, making changes to the nature of our business, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, engaging in transactions with affiliates, creating liens and selling assets, in each case subject to certain exceptions, including, among others, the ability for us to issue up to $150.0 million in convertible notes and entering into exclusive outbound licenses for our intellectual property. The Term Loan Facility also includes a liquidity covenant that commences either October 31, 2020, or December 31, 2020 based upon our satisfying certain performance milestones. If our market capitalization exceeds $350.0 million, we do not have to comply with the liquidity covenant if such covenant is required.

The Term Loan Facility also includes events of default, the occurrence and continuance of which provide Hercules with the right to demand immediate repayment of all principal and unpaid interest, and to exercise remedies against us and the collateral. These events of default include, among other things and subject to customary exceptions: (i) insolvency, liquidation, bankruptcy or similar events; (ii) failure to pay any debts due under the loan and security agreement with Hercules or other loan documents on a timely basis; (iii) failure to observe certain covenants under the loan and security agreement with Hercules; (v) occurrence of a material adverse effect; (vi) material misrepresentation by us; (vii) occurrence of any default under any other agreement involving material indebtedness; and (viii) certain material money judgments.

Cash Flows

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

	Year Ended December 31,		
	2019	2018	2017
	(in thousands)		
Cash used in operating activities	$ (76,520)	$ (62,854)	$ (75,523)
Cash (used in) provided by investing activities	$ (30,518)	$ 112,318	$ 55,702
Cash provided by financing activities	$ 86,231	$ 268	$ 83
Net (decrease) increase in cash and cash equivalents and restricted cash	$ (20,807)	$ 49,732	$ (19,738)

Operating Activities

During the year ended December 31, 2019, operating activities used $76.5 million of cash, primarily due to a net loss of $70.3 million and by cash used in changes in our operating assets and liabilities of $24.6 million and partially offset by non-cash changes of $18.4 million. Net cash used in changes in our operating assets and liabilities during the year ended December 31, 2019 consisted of a $17.5 million decrease in deferred revenue, a $4.2 million decrease in operating lease liabilities, a $2.9 million decrease in accrued expenses and other liabilities, a $1.8 million increase in accounts receivable and offset in part by a $3.3 million decrease in prepaid expenses and other current assets. The decrease in deferred revenue is due to recognition of revenue during the year and partially offset by the receipt of $15.0 million of payments from AstraZeneca under the Research Agreement. The decrease in operating lease liabilities was due to the cash payment of lease obligations.

During the year ended December 31, 2018, operating activities used $62.9 million of cash, primarily due to a net loss of $98.9 million and partially offset by cash provided by changes in our operating assets and liabilities of $11.8 million and non-cash charges of $24.3 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2018 consisted of a $13.5 million increase in deferred revenue, a $0.8 million increase in accrued expenses and other liabilities, offset in part by a $2.1 million decrease in prepaid expenses and other current assets. The increase in deferred revenue is due to the receipt of the $40 million milestone payments under the License Agreement offset by recognition of collaboration revenue during the year. The increase in accrued expenses was due to the timing of payments.

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.

Investing Activities

During the year ended December 31, 2019, investing activities used $30.5 million of cash, consisting of purchases of investments of $46.4 million, and purchases of property and equipment of $1.0 million; these amounts were partially offset by sales and maturities of investments of $16.9 million.

During the year ended December 31, 2018, investing activities provided $112.3 million of cash, consisting of sales and maturities of investments of $136.1 million; these amounts were partially offset by purchases of investments of $21.8 million, and purchases of property and equipment of $1.9 million.

During the year ended December 31, 2017, investing activities provided $55.7 million of cash in investing activities, consisting of sales and maturities of investments of $158.3 million; these amounts were partially offset by purchases of investments of $97.9 million and purchases of property and equipment of $4.7 million.

Financing Activities

During the year ended December 31, 2019, net cash provided by financing activities was $86.2 million in connection with $60.5 million of proceeds from the public offering of common stock, net of costs, $25.0 million of proceeds from the issuance of debt, $0.5 million from the issuance of common stock under at the market sales agreement, $0.3 million received from the issuance of common stock under our employee stock purchase plan, $0.2 million from the issuance of restricted common stock, and $0.1 million from the issuance of common stock and exercise of stock options. These were partially offset by payments for debt issuance costs of $0.4 million.

During the year ended December 31, 2018, net cash provided by financing activities was $0.3 million in connection with $0.3 million received from the issuance of common stock under our employee stock purchase plan and $0.2 million from the issuance of common stock and exercise of stock options. These were partially offset by payments for employee tax obligations relating to vesting of restricted stock units of $0.2 million.

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.

Funding Requirements

Our expenses may increase substantially in connection with our ongoing and planned activities related to our pipeline products, 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-287 in our Phase 2b clinical trial for the treatment of UC;
- continue the clinical development of SER-109 in our Phase 3 clinical study for the prevention of recurrent CDI;
- continue the clinical development of SER-401 in our Phase 1b clinical trial for use with checkpoint inhibitors in patients with metastatic melanoma;
- conduct research and initiate clinical development of SER-301 for the treatment of UC;
- 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 our agreements with our collaborators;
- 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.

Because of the numerous risks and uncertainties associated with the development of our programs, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical studies and pre-clinical development;
- the cost of manufacturing clinical supplies of our product candidates;
- 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 preclinical 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. 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. Our loan and security agreement with Hercules currently includes, and any 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. Additional debt or preferred equity financing may also 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 our existing collaboration agreements, 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.

As discussed in Note 1 of the consolidated financial statements included in this Annual Report we have the responsibility to evaluate whether conditions or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. This evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued or potential contingent milestone payments under the License Agreement that we have not earned. As such, we have determined that our cash runway along with our accumulated deficit, history of losses, and future expected losses raise substantial doubt about our ability to continue as a going concern within one year of the issuance date of the consolidated financial statements included in this Annual Report on Form 10-K. While we have plans in place to mitigate this risk, which primarily consist of raising additional capital through a combination of equity or debt financings, and, depending on the availability and level of additional financings, potentially new collaborations and reducing cash expenditures, there is no guarantee that we will be successful in these mitigation efforts. Lack of necessary funds may require us, among other things, to delay, scale back, or eliminate some or all of our planned clinical trials.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2019 and the effect such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period				
	Total	Less Than 1 Year	2 - 3 Years	4 - 5 Years	More Than 5 Years
	(in thousands)				
Operating lease commitments[1]	$ 24,310	$ 6,302	$ 12,851	$ 5,157	$ —
Long-term debt obligation, including interest and end of term charge[2]	33,536	2,453	17,190	13,893	—
Total	$ 57,846	$ 8,755	$ 30,041	$ 19,050	$ —

(1) Amounts in the table reflect payments due for our laboratory and office space in Cambridge, Massachusetts under an operating lease agreement that expires in November 2023.

(2) Amounts in the table reflect payments due for our term loan under an arrangement with Hercules for $25,000. The amounts in the table above reflect interest-only payments through December 1, 2021 with payments on principal beginning thereafter. For purposes of the table above, interest payments were calculated using an annual interest rate of 9.65%, which was the interest rate in effect as of December 31, 2019. Additionally, the table above includes a payment due upon maturity of the loan of $1,213. See Note 9 of the consolidated financial statements for further discussion of the Hercules term loan.

We enter into contracts in the normal course of business with CROs for clinical trials, preclinical 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, 2019, our cash and cash equivalents consisted of cash and money market accounts. Our interest income is sensitive to 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.

As of December 31, 2019, we had outstanding borrowings under the Term Loan Facility. We accrue interest at a rate equal to the greater of either (i) the Prime Rate (as reported in The Wall Street Journal) plus 4.40%, and (ii) 9.65%. An immediate 10% change in the Prime Rate would not have a material impact on our debt-related obligations, financial position or results of operations

Item 8. Financial Statements and Supplementary Data

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

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

None.

Item 9A. Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

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

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Securities Exchange Act of 1934, as amended), 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 has 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 of 1934, 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, 2019, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies.”

Changes in Internal Control over Financial Reporting

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

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors of the Registrant

Name	Age	Position
Noubar B. Afeyan, Ph.D. (3)	57	Director
Dennis A. Ausiello, M.D.	74	Director
Grégory Behar (3)	50	Director
Stephen Berenson	59	Chairman of the Board of Directors
Willard H. Dere, M.D. (1)	66	Director
Kurt C. Graves (2)	52	Director
Richard N. Kender (1)(2)	64	Director
Lorence H. Kim, M.D. (2)(3)	45	Director
Eric D. Shaff	44	President, Chief Executive Officer and Director
Meryl S. Zausner (1)	63	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

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, which conceives, creates, resources and develops first-in-category life sciences companies. Dr. Afeyan serves on the boards of directors of numerous privately and publicly held companies, including Moderna, Inc., Rubius Therapeutics, Inc., Kaleido Biosciences, Inc. and Evelo Biosciences, Inc. He has previously served on the boards of directors of several public companies including, BG Medicine, Inc., BIND Therapeutics, Inc., and Sensen Bio (formerly Eleven Biotherapeutics, Inc.). 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, or MIT. He is currently a visiting lecturer of business administration at Harvard Business School and was previously a senior lecturer at the MIT's Sloan School of Management where he taught courses on technology-entrepreneurship, innovation and leadership. We believe Dr. Afeyan is qualified to serve on our board of directors because of his extensive investment experience and his knowledge of the biotechnology industry.

Dennis A. Ausiello, M.D., has served as a member of our board of directors since April 2015. Dr. Ausiello serves as the Director of the Center for Assessment Technology and Continuous Health (CATCH), which he co-founded, 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 served on the board of directors of Alnylam Pharmaceuticals since April 2012 and previously served on the board of directors of Pfizer Inc. Dr. Ausiello also serves on the boards of directors of numerous privately held companies. Dr. Ausiello received a B.A. in Biochemistry from Harvard College and an M.D. from the University of Pennsylvania. We believe that Dr. Ausiello is qualified to serve on our board of directors because of his extensive experience as a physician and as a director of pharmaceutical companies.

Grégory Behar has served as a member of our board of directors since December 2014. Mr. Behar has served as Chief Executive Officer of Nestlé Health Science S.A., a health sciences company, since October 2014. From July 2011 to July 2014, Mr. Behar was President and Chief Executive Officer of Boehringer Ingelheim Pharmaceuticals Inc. (USA), a pharmaceutical company. From 2010 to July 2011, Mr. Behar was Corporate Vice President Region NECAR (North European Union, Canada and Australasia) for Boehringer-Ingelheim GmbH, a pharmaceutical company. Mr. Behar has served on the boards of directors of Aimmune Therapeutics, Inc. since November 2016 and Axcella Health, Inc. since February 2016. Mr. Behar also serves on the boards of directors of numerous privately held companies. Mr. Behar received his B.S. in Mechanical Engineering 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. We believe that Mr. Behar is qualified to serve on our board of directors because of his extensive business experience in the health sciences and pharmaceutical industries.

Stephen Berenson has served as Chairman of our board of directors since December 2019. Mr. Berenson has served as a member of our board of directors since August 2019. Mr. Berenson is a Managing Partner at Flagship Pioneering, an early stage venture capital firm, since June 2017. Prior to Flagship, Mr. Berenson spent 33 years in various roles as an investment banker at J.P. Morgan, an investment bank, most recently serving in the role of Vice Chairman of Investment Banking from 2005 to April 2017, where he focused on providing high-touch strategic advice and complex transaction execution to leading companies across all industries globally. He was co-founder of J.P. Morgan's Global Strategic Advisory Council and co-founder of the firm's Board Initiative. Mr. Berenson also serves on the boards of directors of Moderna, Inc. and CiBO Technologies, Inc. Mr. Berenson received an S.B. in Mathematics from MIT. We believe that Mr. Berenson is qualified to serve on our board of directors because of his extensive experience working with rapidly-growing companies across various industries.

Willard H. Dere, M.D., has served as a member our board of directors since July 2017. 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 since November 2014 and Associate Vice President for Research since September 2019. Prior to his professorship, from 2003 until his retirement in October 2014, Dr. Dere held multiple roles at Amgen, Inc., including Head of Global Development, and both corporate and international Chief Medical Officer, and led development of programs in various therapeutic areas. Dr. Dere serves on the board of directors of several companies including BioMarin Pharmaceutical, Inc. since 2016, Radius Health since 2014, and Mersana Therapeutics, Inc. since 2018. From October 2016 to December 2018, he served on the board of directors of Ocera Therapeutics. Dr. Dere received his B.A. in History and Zoology and M.D. 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. We believe Dr. Dere is qualified to serve on our board of directors due to his extensive academic experience and his knowledge of the biotechnology industry.

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, Inc., or Intarcia, a biotechnology company, since April 2012 and Executive Chairman from August 2010 to April 2012. Mr. Graves previously served as Executive Chairman of Biolex Therapeutics, from November 2010 to March 2012, and as Executive Chairman of Intarcia 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., or Vertex, from July 2007 to October 2009. Prior to joining Vertex, Mr. Graves held various leadership positions at Novartis Pharmaceuticals Corporation, or Novartis Corp., from 1999 to June 2007, including the Chief Marketing Officer for the pharmaceuticals division of Novartis Corp. from September 2003 to June 2007. He also has served on the boards directors of Intarcia Therapeutics, Inc. since 2010, Radius Health, Inc. since 2011, and Achillion Pharmaceuticals, Inc. since 2012. Mr. Graves received a B.S. in Biology from Hillsdale College. We believe Mr. Graves is qualified to serve as a member of our board of directors because of his extensive experience in the life sciences industry, membership on various boards of directors and his leadership and management experience.

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 & Co., Inc., or Merck, a pharmaceutical company, most recently serving as Senior Vice President of Business Development and Corporate Licensing. Mr. Kender has served on the boards of directors of Poxel S.A. since 2015, Bicycle Therapeutics PLC since 2019, and ReViral Ltd since 2019. He previously served on the boards of directors of INC Research Holdings, Inc. between 2014 and 2017 and Abide Therapeutics, Inc. between 2015 and 2019. Mr. Kender received a B.S. in Accounting from Villanova University and an M.B.A. from Fairleigh Dickinson University. We believe Mr. Kender is qualified to serve on our board of directors because of his finance experience and knowledge of the biotechnology industry.

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

Eric D. Shaff has served as our Chief Executive Officer and a member of our board of directors since January 2019. Previously, he served as our Chief Operating and Financial Officer and Executive Vice President from January 2018 until January 2019 and as our Chief Financial Officer from November 2014 until January 2019. Mr. Shaff has also served on the board of directors of Sigilon Therapeutics, Inc. since November 2017. From January 2012 to November 2014, Mr. Shaff was Vice President of Corporate Finance for Momenta Pharmaceuticals, or Momenta, 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, 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 M.B.A. from Cornell University. We believe Mr. Shaff is qualified to serve on our board of directors because of his extensive business and finance experience and his knowledge of the biotechnology industry.

Meryl Zausner has served as a member of our board of directors since August 2018. From April 2012 to November 2014, Ms. Zausner served as Chief Financial and Administrative Officer and a member of the Pharmaceutical Executive Committee and Global Finance Leadership Team of Novartis Pharmaceuticals Inc., or Novartis, in the United States. At Novartis, she helped launch the Oncology Business Unit, as well as the company's shared services organization. Prior to serving as Chief Financial and Administrative Officer, Ms. Zausner was a member of the Novartis Global Oncology leadership team, where she contributed to the development and commercialization of therapies, including Gleevec® (imatinib). Ms. Zausner has also served on the boards of directors of Neon Therapeutics, Inc. since 2017 and the Multiple Myeloma Research Foundation since 2009. Ms. Zausner received a B.S. in Accounting and Economics from the University at Albany, SUNY. We believe Ms. Zausner is qualified to serve on our board of directors because of her finance and leadership experience and knowledge of the pharmaceutical industry.

Executive Officers of the Registrant

Name	Age	Position
Eric D. Shaff	44	President, Chief Executive Officer and Director
John G. Aunins, Ph.D.	59	Executive Vice President of Bioprocess & Manufacturing and Chief Technology Officer
Marcus Chapman	49	Vice President, Finance and Principal Financial and Accounting Officer
Thomas J. DesRosier	65	Executive Vice President and Chief Legal Officer
Matthew Henn, Ph.D.	45	Executive Vice President and Chief Scientific Officer

Information concerning Eric D. Shaff, our President and Chief Executive Officer, may be found above in the section entitled "Directors 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 MIT.

Marcus Chapman has served as our Vice President, Finance since January 2018 and as Principal Financial and Accounting Officer since April 2019. Since joining our company in March 2015, he has held positions of increasing seniority, most recently as our Senior Director of Finance from March 2015 to January 2018. Prior to joining our company in March 2015, Mr. Chapman served in roles of increasing seniority from August 2007 to March 2015, culminating as Senior Director of Finance and Interim Head of Finance for Takeda Oncology, or Takeda, the oncology business unit of Takeda Pharmaceuticals Co. Ltd. In these roles, Mr. Chapman oversaw finance functions supporting U.S. sales, U.S. and global marketing, operations, global medical affairs and manufacturing. Prior to Takeda, Mr. Chapman held senior roles at Clarion Healthcare Consulting and Strategic Decisions Group. He began his career at LaSalle Partners in their Investment Banking and Investment Management groups. Mr. Chapman received his B.A. in Economics from Wheaton College and his MBA from The Tuck School of Business at Dartmouth College.

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, Executive Vice President, Chief Legal and Administrative Officer and Secretary of Cubist Pharmaceuticals, Inc., or Cubist, a biopharmaceutical company, from 2014 to 2015 and 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 S.A., a global biopharmaceutical company, from 2011 to 2013. From 1999 to 2011, Mr. DesRosier held leadership roles of increasing seniority within the legal group of Genzyme Corporation, a biotechnology company, culminating in his role as Senior Vice President, Chief Legal Officer. Mr. DesRosier serves as a member of the board of directors of Avanir Pharmaceuticals, a wholly-owned subsidiary of Otsuka Pharmaceutical Company, Ltd. Mr. DesRosier earned a B.A. in Chemistry from the University of Vermont and a J.D. from Wake Forest University School of Law.

Matthew Henn, Ph.D., has served as our Executive Vice President and Chief Scientific Officer since February 2019. Since joining our Company at its launch in June 2012, he has held positions of increasing seniority, most recently as Executive Vice President, Head of Discovery and Microbiome R&D from January 2018 to February 2019, and previously as Senior Vice President, Head of Discovery and Bioinformatics from June 2012 to January 2018. Prior to joining our Company, he was the Director of Viral Genomics and Assistant Director of the Genome Sequencing Center for Infectious Diseases at the Broad Institute of MIT and Harvard. He currently serves on the scientific advisory boards of the Forsyth Institute and Growcentia, Inc., an agricultural microbiome company. Dr. Henn earned his B.S. in Ecology and Evolutionary Sciences from the University of New Hampshire and his Ph.D. in Ecosystem Sciences from the University of California at Berkeley, where he was a NASA Earth Systems Sciences Fellow, and trained as a NSF Postdoctoral Fellow in Microbiology at Duke University.

Code of Ethics

Our board of directors has adopted a Code of Business Conduct and Ethics applicable to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, 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 in the preceding sentence.

Audit Committee and Audit Committee Financial Expert

We have a separately-designated standing audit committee, or the Audit Committee. The members of the Audit Committee are Richard N. Kender, Willard H. Dere, M.D. and Meryl S. Zausner. Mr. Kender serves as the Chairperson of the committee. The members of our Audit Committee meet the requirements for financial literacy under the applicable rules of the SEC and Nasdaq. Our board of directors has determined that each of Mr. Kender and Ms. Zausner is an "audit committee financial expert" as defined by Item 407(d)(5)(ii) of Regulation S-K.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, certain officers and stockholders who beneficially own more than 10% of any class of our equity securities registered pursuant to Section 12 of the Exchange Act, or the Reporting Persons, to file initial statements of beneficial ownership of securities and statements of changes in beneficial ownership of securities with respect to our equity securities with the SEC. Based on our review of the copies of such forms filed with the SEC and upon any written representations of the Reporting Persons received by us, we believe that there has been compliance with all Section 16(a) filing requirements applicable to such Reporting Persons with respect to the year ended December 31, 2019, except that following form was filed late: one Form 3 (reporting one transaction) for Matthew R. Henn.

Item 11. Executive Compensation

This section discusses the material components of the executive compensation program offered to our named executive officers, or NEOs, identified below. For 2019, our NEOs were:

- Eric D. Shaff, our current President and Chief Executive Officer;
- Thomas J. DesRosier, our Chief Legal Officer, Executive Vice President and Secretary;
- Matthew R. Henn, Ph.D., our Executive Vice President and Chief Scientific Officer; and
- Roger J. Pomerantz, M.D., our former President and Chief Executive Officer.

Dr. Pomerantz resigned his employment and offices with us in January 2019 and was succeeded by Mr. Shaff, our current President and Chief Executive Officer.

Compensation Philosophy

We intend that the total compensation of our NEOs reflect a "pay for performance" compensation philosophy. We generally target total compensation relative to the 50th percentile of our peer group, but the Compensation Committee retains discretion to adjust compensation reflecting individual factors or performance. Our executive compensation program consists of three primary components: base salary, annual performance-based cash incentive awards and periodic equity-based incentives, which, in 2019, consisted of grants of stock options. We also prohibit our employees and directors from engaging in hedging transactions with regard to the Company's securities.

Compensation Setting Process

The Compensation Committee makes compensation decisions regarding all of our NEOs. Our President and Chief Executive Officer makes recommendations to the Compensation Committee to assist it in determining compensation levels for our other executive officers and reviews the performance of our other executive officers. While the Compensation Committee utilizes this information and values management's observations with regard to compensation, the ultimate decisions regarding executive compensation are made by the Compensation Committee.

Our Compensation Committee has the authority under its charter to engage the services of a consulting firm or other outside advisor to assist it in designing our compensation programs and in making executive compensation decisions. Our Compensation Committee has engaged Radford, a compensation consulting firm, as its compensation consultant to assess and make recommendations with respect to the amount and types of compensation to provide our executives and directors. When making executive compensation decisions in 2019, our Compensation Committee considered advice and data provided by Radford, and also met with Radford to discuss compensation of our executive officers, including Mr. Shaff. Radford reported directly to the Compensation Committee; however, Mr. Shaff, our President and Chief Executive Officer, consulted with Radford with respect to its assessments of the compensation of executive officers other than himself. Radford provided the Compensation Committee with peer group and market information that the Compensation Committee used when determining whether our executive compensation is competitive, commensurate with the executive officers' responsibilities and consistent with market trends in executive compensation practices for comparable companies. Radford also provides additional services to us that are unrelated to executive and director compensation. The fees for these additional services were less than $120,000 during 2019. The Compensation Committee has considered the adviser independence factors required under SEC rules and Nasdaq listing standards as they relate to Radford and does not believe Radford's work in 2019 raised a conflict of interest.

The Compensation Committee recognizes the very competitive market for executive talent in our industry, and the importance of attracting and retaining strong talent as our business continues to evolve. Our positioning on compensation is intended to keep the Company competitive while strongly incentivizing performance and appropriately controlling executive compensation cost.

In connection with the Compensation Committee's review of our executive compensation programs in 2019, Radford provided market data and analysis relative to the following peer group of pre-commercial, publicly traded companies with a similar market capitalization selected by the Compensation Committee in consultation with Radford. Compared to the prior year, the Compensation Committee removed five companies due to changes in peer company profiles related to market capitalization and development stage and added six new peer companies that better aligned with the Company's stage of development and market capitalization:

Ardelyx, Inc.	Concert Pharmaceuticals, Inc.	Corbus Pharmaceuticals, Inc.
Cytokinetics, Inc.	Evelo Biosciences, Inc.	ImmunoGen, Inc.
Inovio Pharmaceuticals, Inc.	Intra-Cellular Therapeutics, Inc.	Jounce Therapeutics, Inc.
Kaleido BioSciences, Inc.	Karyopham Therapeutics, Inc.	MacroGenics, Inc.
Novavax, Inc.	Revance Therapeutics, Inc.	Scholar Rock, Inc.

The Compensation Committee believes the constituent companies in the peer group are similar to us based on development stage, revenue, industry, executive role considerations and market capitalization and are representative of our competitors for talent and capital. Radford provides the Compensation Committee with a competitive assessment of our compensation program for executive officers against the peer group with respect to pay philosophies, pay mix, cash and equity-linked compensation. The Compensation Committee utilizes the peer group in making compensation decisions to help ensure our compensation program for executive officers adheres to our compensation philosophy of maintaining executive pay that rewards performance while remaining competitive, commensurate with the executive officers' responsibilities and consistent with market trends in executive compensation practices for comparable companies.

2019 Summary Compensation Table

Name and Principal Position	Year	Salary	Options Awards (3)	Non-Equity Incentive Plan Compensation (4)	All Other Compensation	Total
Eric D. Shaff(1)	2019	$ 540,000	$ 1,231,148	$ 253,000	$ 8,400 (5)	$ 2,032,548
President and Chief Executive Officer	2018	435,000	845,520	158,300	8,250	1,447,070
Thomas J. DesRosier	2019	428,300	379,641	161,000	8,400 (5)	977,341
Chief Legal Officer, Executive Vice President, and Secretary	2018	413,800	1,268,280	149,000	8,250	1,839,330
Matthew R. Henn, Ph.D.	2019	385,000	329,052	137,000	8,400 (5)	859,452
Executive Vice President and Chief Scientific Officer						
Roger J. Pomerantz, M.D.(2)	2019	79,708 (6)	33,152	—	581,173 (7)	694,033
Former President and Chief Executive Officer	2018	595,000	1,958,788	278,200	186,072	3,018,060

(1) In January 2019, Mr. Shaff succeeded Dr. Pomerantz as our President and Chief Executive Officer.

(2) Dr. Pomerantz resigned his employment with us in January 2019, and was succeeded by Mr. Shaff, our current President and Chief Executive Officer. Dr. Pomerantz served on our board of directors until December 12, 2019.

(3) Represents the aggregate grant date fair value of the option awards computed in accordance with FASB ASC Topic 718. For a description of the assumptions used in valuing these awards, see Notes [2 and 8] to our audited consolidated financial statements included in this Annual Report on Form 10-K for the fiscal year ended December 31, 2019.

(4) Represents amounts paid under our annual cash bonus program. For additional information regarding these amounts, refer to "—Narrative Disclosure to Summary Compensation Table—Annual Cash Bonuses."

(5) Consists of company matching contributions under our 401(k) plan.

(6) Consists of $24,792 in annual base salary earned prior to Dr. Pomerantz's resignation of employment with us, $53,014 in fees earned for his service on our board of directors prior to Dr. Pomerantz's resignation from our board of directors on December 12, 2019 and $1,902 in advisor fees earned for his service as an advisor to our board of directors during 2019.

(7) Includes company matching contributions under our 401(k) plan of $372, $10,593 in reimbursements of travel and lodging expenses associated with working in the Cambridge, Massachusetts area in 2019, and $570,208 in payments paid to Dr. Pomerantz in connection with his resignation as our President and Chief Executive Officer. Refer to the description of these payments under the heading "Employment and Separation Agreements—Roger J. Pomerantz, M.D." for additional information.

Narrative Disclosure to Summary Compensation Table

The primary elements of compensation for our NEOs are base salary, annual cash bonuses and long-term, equity-based compensation awards. Our NEOs also participate in employee benefit plans and programs that we offer to our other full-time employees on the same basis and have from time to time received relocation or other expense reimbursements from us.

Base Salary

Our NEOs receive base salary to compensate them for the satisfactory performance of duties to our company. The base salary payable to each NEO is intended to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities.

Our Compensation Committee periodically reviews NEO base salaries in consultation with management and Radford to determine whether any adjustments are necessary or appropriate. The following table shows the annual base salaries of our NEOs for 2018, 2019 and 2020. Except as otherwise noted, all annual base salary increases were effective January 1 of the given year.

Name	2018 Annual Base Salary	2019 Annual Base Salary	2020 Annual Base Salary
Eric D. Shaff(1)	$ 435,000	$ 540,000	$ 590,000
Thomas J. DesRosier	413,800	428,300	450,000
Matthew R. Henn, Ph.D.	350,000	385,000	397,000
Roger J. Pomerantz, M.D.(2)	595,000	595,000	—

(1) Mr. Shaff's 2019 Annual Base Salary reflects an increase related to his promotion to Chief Executive Officer on January 14, 2019.
(2) Dr. Pomerantz ceased serving as an employee on January 14, 2019.

Annual Cash Bonuses

Our NEOs have the opportunity to earn annual performance bonuses based on the achievement of short-term performance goals. The NEOs' 2019 target annual cash bonuses, expressed as a percentage of base salary, were: 55% for Mr. Shaff, 40% for Mr. DesRosier, and 40% for Dr. Henn. Dr. Pomerantz ceased serving as an employee on January 14, 2019 and was not eligible to receive an annual performance bonus in respect of 2019 performance.

Our Compensation Committee generally determines annual bonuses for our NEOs by multiplying (a) base salary, by (b) target cash bonus percentage, by (c) the level of achievement of corporate and/or individual performance objectives. In addition, the Compensation Committee retains discretion to adjust annual bonuses as it determines to be appropriate to reflect company performance, individual performance or other factors that the committee believes to be appropriate. For Mr. DesRosier and Dr. Henn, the achievement of 2019 corporate objectives was weighted 80% and the achievement of individual objectives was weighted at 20%. Mr. Shaff's 2019 bonus was weighted 100% on corporate objectives.

For 2019, our corporate bonus objectives were based on operational and developmental milestones related to our clinical and preclinical development programs and business and corporate development initiatives. For each of our NEOs who was eligible to receive an annual bonus for 2019, the 2019 individual performance considerations focused on their respective areas of responsibility within our company. In January 2020, in consultation with management and based on guidance from Radford, the Compensation Committee determined to award Messrs. Shaff and DesRosier, and Dr. Henn 2019 performance bonuses of approximately 85% of the corporate objective portion of their target bonus levels. The actual amounts paid to our NEOs under our 2019 annual cash bonus program are set forth in the Summary Compensation Table above.

Equity-Based Compensation

We have historically offered stock options and, in 2017, restricted stock units to our employees, including our NEOs, as the long-term incentive component of our compensation program. We typically grant options to employees when they commence employment with us and may thereafter grant additional options in the discretion of our board of directors or Compensation Committee. Our stock options allow employees to purchase shares of our common stock at a price equal to the fair market value of our common stock on the grant date and may be intended to qualify as "incentive stock options" under the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code. Each restricted stock unit represents the right to receive one share of our common stock or its cash value equivalent upon vesting. In 2019, the long-term incentive component of the compensation of our NEOs consisted solely of stock options.

Our stock options typically vest as to 25% of the shares subject to the option on the first anniversary of the grant date (or service commencement date for initial grants) and in 12 quarterly installments during the three-year period thereafter, subject to the holder's continued service with us. From time to time, our board of directors or Compensation Committee may also construct alternate vesting schedules as it determines are appropriate to motivate particular employees. Stock options and restricted stock units granted to our employees may be subject to accelerated vesting in certain circumstances, as described in the section titled "Employment Agreements."

We awarded stock options to our NEOs during 2019 in the following amounts and with the vesting schedules indicated below.

Name	Time-Based Options Granted		Milestone Based Options Granted (2)
Eric D. Shaff	275,000	(1)	286,000
Thomas J. DesRosier	84,800	(1)	84,800
Matthew R. Henn, Ph.D.	73,500	(1)	73,500
Roger J. Pomerantz, M.D.	15,000	(3)	—

(1) Option vests as to 25% of the total shares subject to the option on the first anniversary of the vesting commencement date, and as to 6.25% of the shares subject to the option upon each consecutive three months of service during the three-year period thereafter, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting as described in the section titled "Employment Agreements."

(2) Option vests in full upon the day our board of directors determines that the primary endpoint in the SER-287 Phase 2b study has been attained, subject to the holder's continued employment with us through the applicable vesting date.

(3) Option vests in full on June 13, 2020, in accordance with our Non-Employee Director Compensation Program.

Retirement, Health, Welfare and Additional Benefits

Our NEOs are eligible to participate in our employee benefit plans and programs, including medical and dental benefits, life insurance, short term disability and long term disability to the same extent as our other full-time employees, subject to the terms and eligibility requirements of those plans. We also sponsor a 401(k) defined contribution plan in which our NEOs may participate, subject to limits imposed by the Internal Revenue Code, to the same extent as all of our other full-time employees. During 2019, we made discretionary employer matching contributions equal to 50% of elective contributions made by participants in the 401(k) plan, up to 6% of a participant's eligible compensation. These matching contributions are fully vested as of the date on which the contribution is made. We believe that providing a vehicle for tax-deferred retirement savings through our 401(k) plan adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our NEOs, in accordance with our compensation policies. We did not provide any perquisites or special personal benefits to our NEOs for 2019.

		Option Awards						Stock Awards	
Name	Vesting Commencement Date		Number of securities underlying unexercised options: Exercisable	Number of securities underlying unexercised options: Unexercisable	Equity Incentive Plan Awards: Number of Securities underlying unexercised unearned options	Option exercise price	Option expiration date	Number of shares or units of stock that have not vested	Market value of shares or units of stock that have not vested
Eric D. Shaff	2/6/2019	(1)	—	—	286,000	$ 6.15	2/7/2029		
	1/25/2019	(2)	—	275,000		6.01	1/24/2029		
	1/30/2018	(2)	52,500	67,500		10.42	1/29/2028		
	1/26/2017	(2)	72,187	32,813		9.89	1/25/2027		
	1/26/2017	(3)						20,000	$ 69,000
	2/1/2016	(2)	73,593	4,907		26.20	1/31/2026		
	6/26/2015	(4)	100,000	—		18.00	6/25/2025		
	12/9/2014	(4)	233,454	—		7.79	12/8/2024		
Thomas J. DesRosier	2/6/2019	(1)	—	—	84,800	6.15	2/7/2029		
	1/25/2019	(2)	—	84,800		6.01	1/24/2029		
	1/30/2018	(2)	35,000	45,000		10.42	1/29/2028		
	1/30/2018	(5)	33,333	66,667		10.42	1/29/2028		
	1/26/2017	(3)						25,000	86,250
	1/26/2017	(2)	41,250	18,750		9.89	1/25/2027		
	6/1/2016	(2)	87,500	12,500		30.90	5/31/2026		
Matthew R. Henn, Ph.D.	2/6/2019	(1)	—	—	73,500	6.15	2/7/2029		
	1/25/2019	(2)	—	73,500		6.01	1/24/2029		
	1/30/2018	(2)	26,250.0	33,750		10.42	1/29/2028		
	6/19/2017	(7)	70,000.0	—		10.84	6/18/2029		
	1/26/2017	(2)	20,625.0	9,375		9.89	1/25/2027		
	1/26/2017	(3)						7,500	25,875
	2/1/2016	(2)	11,718.0	782		26.20	1/31/2026		
	6/26/2015	(4)	40,000.0	—		18.00	6/25/2025		
	8/7/2014	(4)	26,000.0	—		0.71	8/6/2024		
Roger J. Pomerantz, M.D.	6/13/2019	(6)	—	15,000		2.83	6/12/2029		
	1/26/2017	(2)	114,187	—		9.89	1/25/2027		
	2/1/2016	(2)	121,343	—		26.20	1/31/2026		
	6/1/2014	(4)	797,536	—		0.71	8/6/2024		
	9/9/2013	(4)	82,500	—		0.48	11/5/2023		

(1) Option vests in full upon the day our board of directors determines that the primary endpoint in the SER-287 Phase 2b study has been attained, subject to the holder's continued employment with us through the applicable vesting date.

(2) Option vests as to 25% of the total shares subject to the option on the first anniversary of the vesting commencement date, and as to 6.25% of the shares subject to the option upon each consecutive three months of service during the three-year period thereafter, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting as described in the section titled "Employment Agreements."

(3) The restricted stock units vest as to 20% of the award on the first anniversary of the vesting commencement date, 30% on the second anniversary of the vesting commencement date and 50% on the third anniversary of the vesting commencement date, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting as described in the section titled "Employment Agreements."

(4) Option vests as to 25% of the total shares subject to the option on the first anniversary of the vesting commencement date, and as to 6.25% of the shares subject to the option on the last day of each calendar quarter during the three-year period thereafter, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting as described in the section titled "Employment Agreements."

(5) Option vests as to one-third of the total shares subject to the option on each of the first three anniversaries of the vesting commencement date, subject to the holder's continued employment with us through the applicable vesting date and potential accelerated vesting as described in the section titled "Employment Agreements."

(6) Option vests in full on the earlier of June 13, 2020 or the day before the Company's 2020 Annual Meeting of Shareholders, subject to the holder's continued service as a board advisor to the Company through the vesting date.

(7) Option vests as to 50% of the award upon the filing of a biologics license application for SER-109 with the United States Food and Drug Administration ("FDA") and as to an additional 50% of such shares upon the FDA's approval of SER-109, subject to the holder's continued employment with us through the applicable vesting date.

Employment, Separation and Advisory Agreements

We have entered into employment agreements with each of our NEOs. Certain key terms of these agreements are described below.

Eric D. Shaff

In January 2019, in connection with Mr. Shaff's appointment as the Company's President and Chief Executive Officer and as a member of our board of directors, we entered into an employment agreement with Mr. Shaff that superseded the terms of his prior employment agreement with us. The employment agreement entitles Mr. Shaff to receive an annual base salary of $540,000, subject to periodic review and adjustment by our board of directors or its compensation committee, and an annual target bonus opportunity of 55% of his annual base salary. In connection with his appointment as the Company's President and Chief Executive Officer, we also granted Mr. Shaff a stock option under our 2015 Incentive Award Plan to purchase 275,000 shares of our common stock, which will vest in accordance with our standard four-year vesting schedule, subject to Mr. Shaff's continued service.

Under the terms of his employment agreement, if we terminate Mr. Shaff's employment without cause or he resigns for good reason, subject to his timely executing a release of claims in our favor, Mr. Shaff is entitled to receive 12 months of continued base salary and up to 12 months of Company-paid continued medical, dental or vision coverage pursuant to COBRA, if elected. If the termination occurs within 60 days prior to or 12 months following a change in control, in lieu of the foregoing, he is entitled to receive 18 months of continued base salary, up to 18 months of Company-paid continued medical, dental or vision coverage pursuant to COBRA, if elected, and accelerated vesting of time-based equity awards that he holds.

For purposes of the employment agreement:

- "Cause" generally means Mr. Shaff's (i) failure to substantially perform his duties with us (other than due to disability) or materially comply with our policies; (ii) material failure to carry out or comply with any lawful and reasonable directive of our board of directors; (iii) breach of a material provision of his employment agreement; (iv) conviction, plea of no contest or imposition of unadjudicated probation for any felony or crime involving moral turpitude; (v) unlawful use (including being under the influence) or possession of illegal drugs on our (or our affiliate's) premises or while performing his duties and responsibilities under his employment agreement; or (vi) commission of an act of fraud, embezzlement, misappropriation, willful misconduct or breach of fiduciary duty against us or any of our affiliates.
- "Good reason" generally means, subject to certain notice requirements and cure rights, without Mr. Shaff's consent, (i) a reduction in his base salary (except for a reduction of less than 10% contemporaneously affecting other senior executives); (ii) a material reduction in his authority or areas of responsibility; or (iii) a relocation of his primary office more than 50 miles outside of the Boston metropolitan area.

Mr. Shaff has also agreed to refrain from disclosing our confidential information during or at any time following his employment with us and from competing with us or soliciting our employees or consultants for 12 months following termination of his employment.

Thomas J. DesRosier

Under the terms of our employment agreement with Mr. DesRosier, if we terminate Mr. DesRosier's employment without cause or he resigns for good reason, subject to his timely executing a release of claims in our favor, he is entitled to receive 12 months of continued base salary and up to 12 months of Company-paid continued medical, dental or vision coverage pursuant to COBRA, if elected. If the termination occurs within 60 days prior to or 12 months following a change in control, Mr. DesRosier is also entitled to accelerated vesting of his time-based equity awards.

For purposes of the employment agreement, "cause" and "good reason" have the same meanings as in Mr. Shaff's employment agreement. Mr. DesRosier has also agreed to refrain from disclosing our confidential information during or at any time following his employment with us and from competing with us or soliciting our employees or consultants for 12 months following termination of his employment.

Matthew R. Henn, Ph.D.

Under the terms of our employment agreement with Dr. Henn, if we terminate Dr. Henn employment without cause or he resigns for good reason, subject to his timely executing a release of claims in our favor, he is entitled to receive 12 months of continued base salary and up to 12 months of Company-paid continued medical, dental or vision coverage pursuant to COBRA, if elected. If the termination occurs within 60 days prior to or 12 months following a change in control, Dr. Henn is also entitled to accelerated vesting of his time-based equity awards.

For purposes of the employment agreement, "cause" and "good reason" have the same meanings as in Mr. Shaff's employment agreement. Dr. Henn has also agreed to refrain from disclosing our confidential information during or at any time following his employment with us and from competing with us or soliciting our employees or consultants for 12 months following termination of his employment.

Roger J. Pomerantz, M.D.

Dr. Pomerantz's employment with us terminated on January 14, 2019. In connection with his resignation, we and Dr. Pomerantz entered into a separation agreement and release that provides for Dr. Pomerantz to receive 12 months of continued base salary, his full 2018 annual cash bonus amount and up to 12 months of continued medical, dental or vision coverage pursuant to COBRA, if elected.

Dr. Pomerantz continued to serve as a director and as Chairman of our board of directors following his employment termination and was eligible to receive compensation in accordance with and subject to the terms of our Non-Employee Director Compensation Program described below until his resignation from our board of directors effective December 12, 2019.

Following Dr. Pomerantz's resignation from our board of directors, we entered into an advisory agreement with Dr. Pomerantz under which he will continue to serve as an advisor to our board of directors through the agreement's initial term, which will expire on the date the Company publicly announces the top-line results of the SER-287 Phase 2b clinical study, unless the agreement is earlier terminated. The advisory agreement provides for Dr. Pomerantz to receive during the advisory period quarterly fees of $8,750, prorated for any partial quarter of service, continued vesting of the stock option granted to Dr. Pomerantz in June 2019 for his service as a non-employee director and continued exercisability of his outstanding company stock options. If we terminate the advisory agreement prior to expiration of its initial term other than due to Dr. Pomerantz's material breach of the agreement, the agreement provides for Dr. Pomerantz to receive the payments and benefits, including continued vesting of the June 2019 stock options and continued exercisability of his company stock options, provided under the agreement as if he had continued providing services under the agreement until the expiration of its initial term.

Director Compensation

Directors who are also our employees do not receive compensation for their service on our board of directors. Mr. Shaff served as a director and executive officer of our company during 2019, and Dr. Pomerantz served as a non-employee director and executive officer of our company during 2019. Refer to the 2019 Summary Compensation Table and related narrative disclosure above for information regarding the compensation each received from us during 2019.

We maintain a compensation program for our non-employee directors providing for each non-employee director to receive the following amounts for serving on our board of directors:

- option to purchase 30,000 shares of our common stock upon the director's initial election or appointment to our board of directors;
- if the director has served on our board of directors for at least six months as of the date of an annual meeting of stockholders, an option to purchase 15,000 shares of our common stock on the date of the annual meeting;
- an annual director fee of $35,000, and if the director serves as chairman of our board of directors or lead independent director, an additional annual director fee of $20,000; and
- if the director serves on a committee of our board of directors, an additional annual fee as follows:
- chairman of the audit committee—$15,000;
- audit committee member other than the chairman—$7,500;
- chairman of the compensation committee—$10,000;
- compensation committee member other than the chairman—$5,000;
- chairman of the nominating and corporate governance committee—$7,000; and
- nominating and corporate governance committee member other than the chairman—$3,500.

Stock options granted to our non-employee directors under the program have an exercise price equal to the fair market value of our common stock on the grant date. The stock options granted upon a director's initial election or appointment vest in four annual installments following the grant date. The stock options granted annually to directors vest in a single installment on the earlier of the day before the next annual meeting of stockholders or the first anniversary of the grant date. In addition, all unvested stock options vest in full immediately prior to a change in control.

Each member of our board of directors is entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

Name	Fees Earned or Paid in Cash	Option Awards (1)	Total
Noubar B. Afeyan, Ph.D.	$ 62,000	$ 33,152	$ 95,152
Stephen Berenson (2)	14,097	48,663	62,760
Willard H. Dere, M.D.	42,500	33,152	75,652
Lorence H. Kim, M.D.	43,500	33,152	76,652
Richard N. Kender	55,000	33,152	88,152
Grégory Behar	38,500	33,152	71,652
Dennis A. Ausiello, M.D.	36,074	33,152	69,226
Kurt C. Graves	45,000	33,152	78,152
Meryl S. Zausner	42,500	33,152	75,652

(1) Represents the aggregate grant date fair value of the option awards granted during 2019 computed in accordance with FASB ASC Topic 718. For a description of the assumptions used in valuing these awards, see Notes [2] and [8] to our audited consolidated financial statements included in this Annual Report on Form 10-K for the fiscal year ended December 31, 2019. The table below shows the number of option awards held as of December 31, 2019 by each of our directors who are not NEOs. None of our directors held unvested stock awards as of that date.

Name	Option Awards
Noubar B. Afeyan, Ph.D.	75,000
Stephen Berenson (2)	30,000
Willard H. Dere, M.D.	60,000
Lorence H. Kim, M.D.	150,000
Richard N. Kender	150,000
Grégory Behar	45,000
Dennis A. Ausiello, M.D.	135,000
Kurt C. Graves	90,000
Meryl S. Zausner	45,000

(2) Mr. Berenson began serving on our board of directors on August 5, 2019 and was appointed Chairman of our board of directors effective December 12, 2019.

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

Securities Authorized For Issuance under Equity Compensation Plans

The following table provides information on our equity compensation plans as of December 31, 2019.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants, and Rights	Number of Securities Available for Future Issuance Under Equity Compensation Plans (excludes securities Reflected in first column) (1)
Equity compensation plans approved by security holders (2)	8,440,683 (3)	$ 10.36 (4)	4,001,934 (5)
Equity compensation plans not approved by security holders	—	—	—
Total	8,440,683	$ 10.36	4,001,934

(1) Pursuant to the terms of the 2015 Incentive Award Plan, or the 2015 Plan, the number of shares of common stock available for issuance under the 2015 Plan automatically increases on each January 1 until and including January 1, 2025, by an amount equal to the lesser of: (a) 4% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as is determined by our board of directors. Pursuant to the terms of the 2015 Employee Stock Purchase Plan, or the 2015 ESPP, the number of shares of common stock available for issuance under the 2015 ESPP automatically increases on each January 1 until and including January 1, 2025, by an amount equal to the least of: (a) 400,000 shares, (b) 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (c) such smaller number of shares as is determined by our board of directors.

(2) Consists of the 2012 Stock Incentive Plan, or the 2012 Plan, the 2015 Plan, and the 2015 ESPP.

(3) Includes 1,989,391 outstanding options to purchase stock under the 2012 Plan, 6,321,292 outstanding options to purchase stock under the 2015 Plan, and 130,000 restricted stock units under the 2015 Plan.
(4) As of December 31, 2019, the weighted-average exercise price of outstanding options under the 2012 Plan was $4.92 and the weighted-average exercise price of outstanding options under the 2015 Plan was $12.07.
(5) As of December 31, 2019, a total of 4,001,934 shares of common stock were available for issuance, consisting of 1,847,474 shares under the 2015 ESPP and 2,154,460 shares of common stock were available for future issuance under the 2015 Plan.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information with respect to holdings of our common stock by (i) stockholders who beneficially owned more than 5% of the outstanding shares of our common stock, and (ii) each of our directors, each of our named executive officers and all directors and executive officers as a group as of February 26, 2020, unless otherwise indicated. The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which a person has sole or shared voting power or investment power. Applicable percentage ownership is based on 71,071,068 shares of common stock outstanding as of February 26, 2020. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, shares of common stock subject to options, or other rights held by such person that are currently exercisable or will become exercisable within 60 days of February 29, 2020 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed below is 200 Sidney Street, Cambridge, MA 02139. We believe, based on information provided to us, that each of the stockholders listed below has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

NAME OF BENEFICIAL OWNER	NUMBER	PERCENTAGE
5% or Greater Stockholders		
Entities affiliated with Flagship Pioneering [1]	21,571,764	30.4%
Nikko Asset Management Americas, Inc. [2]	8,273,223	11.7%
ARK Investment Management LLC [3]	7,273,840	10.3%
Nestlé Health Science US Holdings, Inc. [4]	6,918,888	9.8%
FMR LLC [5]	6,499,118	9.2%
BlackRock, Inc. [6]	4,003,353	5.6%
Named Executive Officers and Directors		
Noubar B. Afeyan, Ph.D. [1, 7]	21,646,905	30.5%
Dennis A. Ausiello, M.D. [8]	120,000	*
Grégory Behar [9]	30,000	*
Stephen Berenson	—	—
Matthew Henn [10]	167,843	*
Willard H. Dere, M.D. [11]	30,000	*
Thomas DesRosier [12]	316,720	*
Kurt C. Graves [13]	75,000	*
Richard N. Kender [14]	135,000	*
Lorence H. Kim, M.D. [15]	135,000	*
Roger J. Pomerantz, M.D. [16]	1,329,542	*
Eric D. Shaff [17]	676,045	*
Meryl S. Zausner [18]	7,500	*
All executive officers and directors as a group (15 persons) [19]	25,080,905	34.0%

* Less than 1%

1 Based solely on a Schedule 13D filed with the SEC on June 28, 2019 by Flagship VentureLabs IV, LLC, or VentureLabs IV, Flagship Ventures Fund IV, L.P., or Flagship Fund IV, Flagship Ventures Fund IV-Rx, L.P., or Flagship Fund IV-Rx (and, together with VentureLabs IV and Flagship Fund IV, the Flagship IV Funds), Flagship Ventures Fund IV General Partner LLC, or Flagship Fund IV GP, Nutritional Health LTP Fund, L.P., or Nutritional LTP, Nutritional Health LTP Fund General Partner LLC, or Nutritional LTP GP, Flagship Pioneering Fund VI, L.P., or Flagship Fund VI (and, together with the Flagship IV Funds and Nutritional LTP, the Flagship Funds), Flagship Pioneering Fund VI General Partner LLC, or Flagship Fund VI GP, Flagship Pioneering, Inc., or Flagship Pioneering, Noubar B. Afeyan, Ph.D. and Edwin M. Kania, Jr. VentureLabs IV, Flagship Fund IV, Flagship Fund IV-Rx, Flagship Fund IV GP, Nutritional LTP, Nutritional LTP GP, Flagship Fund VI, Flagship Fund VI GP, Flagship Pioneering, Dr. Afeyan and Mr. Kania are collectively referred to herein as the Flagship Reporting Persons. VentureLabs IV, Flagship Fund IV and Flagship Fund IV-Rx have shared voting and dispositive power over the 2,734,994 shares, 8,022,420 shares, and 1,925,462 shares of common stock directly held by them, respectively. Flagship Fund IV, as the manager of VentureLabs IV, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by VentureLabs IV. Flagship Fund IV GP, as the general partner of the Flagship Fund IV Funds, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by the Flagship Fund IV Funds. Nutritional LTP directly holds and has shared voting and dispositive power over 4,444,444 shares of common stock. Nutritional LTP GP, as the general partner of Nutritional LTP, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by Nutritional LTP. Flagship Fund VI directly holds and has shared voting and dispositive power over 4,444,444 shares of Common Stock. Flagship Fund VI GP, as the general partner of Flagship

Fund VI, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by Flagship Fund VI. Flagship Pioneering, as the general partner of Flagship Fund VI GP, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by Flagship Fund VI. Dr. Afeyan and Mr. Kania, as the managers of Flagship Fund IV GP, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by the Flagship Fund IV Funds. While Mr. Kania is retired from Flagship Pioneering, he continues to serve as a manager of Flagship Fund IV GP. Dr. Afeyan, as the sole member and manager of Nutritional LTP GP and as CEO and sole shareholder of Flagship Pioneering, may be deemed to beneficially own and share voting and dispositive power over the shares directly held by each of Nutritional LTP and Flagship Fund VI. The address for the Flagship Reporting Persons is c/o Flagship Pioneering, Inc., 55 Cambridge Parkway, Suite 800E, Cambridge, Massachusetts 02142.

2 Based solely on a Schedule 13G/A filed with the SEC on February 12, 2020 by Sumitomo Mitsui Trust Holdings, Inc., or SMTH, and Nikko Asset Management Co., Ltd., or NAM. Each of SMTH and NAM are parent holding companies of Nikko Asset Management Americas, Inc., or Nikko Americas. Nikko Americas has shared dispositive power over all 8,273,223 shares and shared voting power over 5,434,478 shares. All of the shares of common stock are owned, or may be deemed to be beneficially owned, by Nikko Americas. The address for SMTH is 1-4-1 Marunouchi, Chiyoda-ku, Tokyo 100-8233, Japan. The address for NAM is Midtown Tower, 9-7-1 Akasaka, Minato-ku, Tokyo 107-6242, Japan.

3 Based solely on a Schedule 13G/A filed on February 14, 2020 by ARK Investment Management LLC, or ARK. ARK is an investment adviser and has sole dispositive power over all 7,273,840 shares, sole voting power over 5,983,163 shares and shared voting power over 445,694 shares. The address for Ark Investment Management LLC is 3 East 28th Street, 7th Floor, New York, NY 10016.

4 Based on a Schedule 13D filed with the SEC on April 11, 2018 by Nestlé Health Science US Holdings, Inc., or NHS, NIMCO US, Inc., or NIMCO and Nestlé S.A., or Nestlé. NHS is a wholly owned subsidiary of NIMCO, which is a wholly owned subsidiary of Nestlé, a publicly traded company, and other information known to the us. Each of these entities may be deemed to share voting and investment power with respect to all shares of common stock held by NHS. Each of NHS, NIMCO and Nestlé disclaims beneficial ownership of such shares of common stock except to the extent of its pecuniary interest therein. The address for NHS and NIMCO is 383 Main Ave., 5th Floor, Norwalk, CT 06851. The address for Nestlé is Avenue Nestlé 55, CH-1800, Vevey Switzerland.

5 Based solely on a Schedule 13G/A filed on February 7, 2020 by FMR LLC and Abigail P. Johnson. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or the Fidelity Funds, advised by Fidelity Management & Research Company, or FMR Co, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR LLC has sole voting power over 2,079,689 shares and sole dispositive power over 6,499,118 shares. Abigail P. Johnson has sole dispositive power over 6,499,118 shares. The address for FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

6 Based solely on a Schedule 13G filed on February 7, 2020 by BlackRock, Inc., or Blackrock, on behalf of itself and its wholly owned subsidiaries, BlackRock Advisors, LLC, BlackRock Investment Management (UK) Limited, BlackRock Asset Management Canada Limited, BlackRock Fund Advisors, BlackRock Asset Management Ireland Limited, BlackRock Institutional Trust Company, National Association, BlackRock Financial Management, Inc., BlackRock Japan Co., Ltd. and BlackRock Investment Management, LLC. BlackRock reported that as of December 31, 2019, it had sole voting power with respect to 3,863,749 shares of common stock and sole dispositive power with respect to all 4,003,353 shares, and that the shares are beneficially owned by BlackRock and its wholly owned subsidiaries identified above. The address of each of the foregoing is 55 East 52nd Street, New York, NY 10055.

7 Based solely on a Schedule 13D filed with the SEC on June 28, 2019 by VentureLabs IV. Includes 60,000 shares of common stock which Dr. Afeyan has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

8 Includes 120,000 shares of common stock which Dr. Ausiello has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

9 Includes 30,000 shares of common stock which Mr. Behar has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

10 Includes 155,843 shares of common stock which Mr. Henn has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

11 Includes 30,000 shares of common stock which Dr. Dere has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

12 Includes 275,666 shares of common stock which Mr. DesRosier has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

13 Includes 75,000 shares of common stock which Mr. Graves has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

14 Includes 135,000 shares of common stock which Mr. Kender has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

15 Includes 135,000 shares of common stock which Dr. Kim has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

16 Includes 1,115,566 shares of common stock which Dr. Pomerantz has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

17 Includes 643,203 shares of common stock which Mr. Shaff has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

18 Includes 7,500 shares of common stock which Ms. Zausner has the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

19 Consists of (a) 22,000,627 shares of common stock and (b) 3,080,278 shares of common stock which the holders have the right to acquire pursuant to outstanding stock options which are or will be immediately exercisable within 60 days of February 29, 2020.

Item 13. Certain Relationships and Related Transactions and Director Independence

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written Related Person Transaction Policy and Procedures, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy covers, with certain exceptions set forth in Item 404 of Regulation S-K, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we (including any of our subsidiaries) are, were or will be a participant, where the amount involved exceeds $120,000 in any fiscal year and a related person has, had or will have a direct or indirect material interest. Our finance team is primarily responsible for developing and implementing procedures to obtain information regarding potential related person transactions and for determining whether a related person transaction requiring compliance with our policy exists. Our Chief Executive Officer then presents the related person transaction to our Audit Committee. In reviewing and approving any such transaction, our Audit Committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction, the extent of the related person's interest in the transaction and the conflicts of interest and corporate opportunity provisions under our Code of Business Conduct and Ethics. No director may participate in approval of a related person transaction in which he or she is a related person. Our Audit Committee may also ratify related person transactions that were entered into by management because pre-approval was not feasible and transactions that were not initially recognized as related person transactions. If these transactions are not ratified, our management must make all reasonable efforts to cancel or annul such transactions. Our management must update our Audit Committee on material changes to any approved or ratified related person transaction and provide an annual status report on all then-current related person transactions. The following are certain transactions, arrangements and relationships with our directors, executive officers and stockholders owning 5% or more of our outstanding common stock.

Transactions with Nestle Health Science

In January 2016 we entered into the License Agreement with NHS, an affiliate of Nestlé Health Science US Holdings, Inc., which holds approximately 9.7% of our common stock as of February 25, 2020, for the development and commercialization of certain of our product candidates in development for the treatment and management of CDI and IBD, including ulcerative colitis and Crohn's disease. The License Agreement supports the development of our portfolio of products for CDI and IBD in markets outside of the Licensed Territory and is expected to provide substantial financial support for our ongoing worldwide research and development. We have retained full commercial rights to our entire portfolio of product candidates with respect to the United States and Canada, where we plan to build our own commercial organization.

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

The License Agreement sets forth our and NHS' respective obligations for development, commercialization, regulatory and manufacturing and supply activities for the NHS Collaboration Products with respect to the licensed fields and the Licensed Territory. In exchange for the license, NHS paid us an upfront cash payment of $120 million in February 2016 and has 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 million milestone payment in 2016 associated with the initiation of our Phase 1b study for SER-262 in CDI and a $20 million milestone payment in 2017 associated with the initiation of our Phase 3 study of SER-109 in multiply recurrent CDI.

In November 2018, we executed the Letter Agreement, modifying certain terms of the License Agreement. Under the Letter Agreement, NHS agreed to accelerate the payment of the $20.0 million Phase 3 commencement milestone to be payable upon the commencement of the Phase 2b study for SER-287. Further, based on the results of the Phase 2b study, the Letter Agreement modifies certain terms and conditions related to the extent and timing of expense reimbursement associated with the ongoing SER-287 clinical trials. The Phase 2b study was initiated and the $40.0 million of milestone payments were received in December 2018.

To date, we have received $70.0 million in development milestones under the License Agreement and the Letter Agreement.

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

2019 Follow-On Offering

In June 2019, we completed a registered public offering pursuant to which we issued and sold an aggregate of 28,818,578 shares of our common stock (including 2,151,911 shares sold pursuant to the underwriters' partial exercise of their option to purchase additional shares) at a public offering price of $2.25 for aggregate net proceeds to us of approximately $60.5 million. The following table sets forth the number of shares of common stock purchased in our registered public offering by directors (and related parties thereto) and holders of more than 5% of our common stock:

Name (1)	Shares of Common Stock Purchased	Total Purchase Price
Entities affiliated with Flagship Pioneering (affiliate of Noubar Afeyan, Ph.D.) (2)	8,888,888	$ 19,999,998
Nikko Asset Management Co., Ltd.	380,000	$ 855,000
Entities affiliated with ARK Investment Management LLC	1,130,000	$ 2,542,500
Entities affiliated with FMR LLC	3,357,300	$ 7,553,925

(1) Additional details regarding these stockholders and their equity holdings are provided in this Annual Report under the caption "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."
(2) Represents shares acquired by Flagship Pioneering Fund VI, L.P. and Nutritional Health LTP Fund, L.P.

Employment Agreements

We have entered into employment agreements with our named executive officers. For more information regarding these agreements, see Part III, Item 11. "Executive and Director Compensation—Employment Agreements."

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Director Independence

All of our directors, other than Eric D. Shaff, qualify as "independent" in accordance with the listing requirements of The Nasdaq Global Select Market or Nasdaq. Roger J. Pomerantz, M.D., who served on our board of directors until his resignation on December 12, 2019, did not qualify as "independent" in accordance with Nasdaq listing requirements. The Nasdaq independence definition includes a series of objective tests, including that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In

addition, as required by Nasdaq rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. Mr. Shaff is not independent because he is the President and Chief Executive Officer of our Company. Dr. Pomerantz was not independent because he served as President and Chief Executive Officer of our Company until January 2019. There are no family relationships among any of our directors or executive officers.

For additional information regarding our board of directors and their committee memberships see Part III, Item 10, "Directors, Executive Officers, and Corporate Governance."

Item 14. Principal Accountant Fees and Services

The following table summarizes the fees of PricewaterhouseCoopers LLP, our independent registered public accounting firm, billed to us for each of the last two fiscal years for audit services and billed to us in each of the last two fiscal years for other services:

Fee Category	2019	2018
Audit fees	$ 695,000	$ 488,000
Audit-related fees	50,000	20,000
Tax fees	—	—
All other fees	900	900
Total fees	$ 745,900	$ 508,900

Audit Fees

Audit fees consist of fees billed for the audit of our annual consolidated financial statements, the review of the interim consolidated financial statements, related services that are normally provided in connection with registration statements, and services performed in connection with the public offering of our common stock in June 2019.

Audit-Related Fees

Audit-related fees in 2019 consist of fees in connection with an audit of our grant from CARB-X. Audit-related fees in 2018 consist of fees for services performed related to our adoption of the new lease accounting standard in the first quarter of 2019.

Tax Fees

There were no tax fees incurred in 2019 or 2018.

All Other Fees

All other fees in 2019 and 2018 represent non-audit fees in connection with access to the PricewaterhouseCoopers LLP on-line accounting research and disclosures database.

Audit Committee Pre-Approval Policy and Procedures

The Audit Committee has adopted a policy, or the Pre-Approval Policy, which sets forth the procedures and conditions pursuant to which audit and non-audit services proposed to be performed by the independent registered accounting firm may be pre-approved. The Pre-Approval Policy generally provides that we will not engage PricewaterhouseCoopers LLP to render any audit, audit-related, tax or permissible non-audit service unless the service is either (i) explicitly approved by the Audit Committee, or specific pre-approval, or (ii) entered into pursuant to the pre-approval policies and procedures described in the Pre-Approval Policy, or general pre-approval. Unless a type of service to be provided by PricewaterhouseCoopers LLP has received general pre-approval under the Pre-Approval Policy, it requires specific pre-approval by the Audit Committee or by a designated member of the Audit Committee to whom the committee has delegated the authority to grant pre-approvals. Any proposed services exceeding pre-approved cost levels or budgeted amounts will also require specific pre-approval. For both types of pre-approval, the Audit Committee will consider whether such services are consistent with the SEC's rules on auditor independence. The Audit Committee will also consider whether the

independent auditor is best positioned to provide the most effective and efficient service, for reasons such as its familiarity with our business, people, culture, accounting systems, risk profile and other factors, and whether the service might enhance our ability to manage or control risk or improve audit quality. All such factors will be considered as a whole, and no one factor should necessarily be determinative. On an annual basis, the Audit Committee reviews and generally pre-approves the services (and related fee levels or budgeted amounts) that may be provided by PricewaterhouseCoopers LLP without first obtaining specific pre-approval from the Audit Committee. The Audit Committee may revise the list of general pre-approved services from time to time, based on subsequent determinations.

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.

The following is a list of all exhibits filed as a part of this Annual Report on Form 10-K.

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	
4.3	Description of Capital Stock					*
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#	2012 Stock Incentive Plan, as amended and form of option agreement thereunder	S-1	333-204484	10.1	5/27/15	
10.4#	Non-Employee Director Compensation Program	S-1/A	333-204484	10.4	6/16/15	
10.5	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	
10.6	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	
10.7	Sublease Agreement dated July 1, 2019, by and between the Registrant and Flagship VL56, Inc., and Flagship VL58, Inc.	10-Q	001-37465	10.3	11/5/19	
10.8#	Amended and Restated Employment Agreement, dated January 14, 2019, by and between the Registrant and Eric D. Shaff	8-K	001-37465	10.2	1/15/19	
10.9#	Employment Agreement, dated August 10, 2015, by and between the Registrant and John G. Aunins	10-Q	001-37465	10.10	8/10/15	
10.10#	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	
10.11#	Employment Agreement, dated April 26, 2016 by and between the Registrant and Thomas J. DesRosier	10-Q	001-37465	10.1	8/11/16	
10.12#	Amended and Restated Employment Agreement, dated March 25, 2019, by and between the Registrant and Matthew Henn	10-Q	001-37465	10.1	8/6/19	
10.13#	Employment Agreement, dated July 11, 2019, by and between the Registrant and Marcus Chapman	10-Q	001-37465	10.1	11/5/19	

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.14#	Advisory Agreement, dated December 12, 2019, by and between the Registrant and Roger Pomerantz					*
10.15	Loan and Security Agreement, dated October 29, 2019, between the Registrant and Hercules Capital, Inc.	8-K	001-37465	10.1	11/4/19	
10.16^	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	
10.17	Amendment No 1 to the Collaboration and License Agreement, dated August 10, 2016, by and between the Registrant and Nestec Ltd.	10-K	001-37465	10.22	3/6/19	
10.18^	Letter Agreement dated October 30, 2018, by and between the Registrant and Nestec Ltd.	10-K	001-37465	10.23	3/6/19	
10.19^^	Research Collaboration and Option Agreement, dated March 11, 2019, by and between the Registrant and MedImmune, LLC	10-Q	001-37465	10.1	5/2/19	
10.20	Loan and Security Agreement dated October 29, 2019 between the Registrant and Hercules Capital, Inc.	8-K	001-37465	10.1	11/4/19	
21.1	Subsidiaries of Seres Therapeutics, Inc.					*
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 Principal Financial Officer					*
32.1	Section 1350 Certification of Chief Executive Officer					**
32.2	Section 1350 Certification of Principal 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.

^^ Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10). Such omitted information is not material and would likely cause competitive harm to the registrant if publicly disclosed. Additionally, schedules and attachments to this exhibit have been omitted pursuant to Regulation S-K, Items 601(a)(5).

Item 16. Form 10-K Summary

None.

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 2, 2020

By: /s/ Eric D. Shaff
Eric D. Shaff
President, Chief Executive Officer and Director

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/ Eric D. Shaff Eric D. Shaff	President, Chief Executive Officer and Director (Principal Executive Officer)	March 2, 2020
/s/ Marcus Chapman Marcus Chapman	Vice President, Finance (Principal Financial and Accounting Officer)	March 2, 2020
/s/ Stephen Berenson Stephen Berenson	Chairman of the Board	March 2, 2020
/s/ Noubar B. Afeyan Noubar B. Afeyan, Ph.D.	Director	March 2, 2020
/s/ Dennis Ausiello Dennis Ausiello, M.D.	Director	March 2, 2020
/s/ Willard Dere Willard Dere	Director	March 2, 2020
/s/ Grégory Behar Grégory Behar	Director	March 2, 2020
/s/ Kurt C. Graves Kurt C. Graves	Director	March 2, 2020
/s/ Richard N. Kender Richard N. Kender	Director	March 2, 2020
/s/ Lorence H. Kim Lorence H. Kim, M.D.	Director	March 2, 2020
/s/ Meryl Zausner Meryl Zausner	Director	March 2, 2020

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 (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations and comprehensive loss, of stockholders' equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred losses and negative cash flows from operations since its inception, that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Change in Accounting Principles

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019 and the manner in which accounts for revenues from contracts with customers in 2018.

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 audits. 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 audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits 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 audits 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 audits 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 audits 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 audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 2, 2020

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, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 65,126	$ 85,820
Investments	29,690	—
Prepaid expenses and other current assets	3,588	6,845
Accounts receivable	1,785	—
Total current assets	100,189	92,665
Property and equipment, net	19,495	26,294
Operating lease assets	11,356	—
Restricted investments	1,400	1,400
Restricted cash	—	113
Total assets	$ 132,440	$ 120,472
Liabilities and Stockholder's Deficit		
Current liabilities:		
Accounts payable	$ 4,859	$ 6,415
Accrued expenses and other current liabilities	10,884	15,207
Operating lease liabilities	4,456	—
Deferred revenue - related party	20,960	20,419
Deferred revenue	4,834	—
Total current liabilities	45,993	42,041
Note payable, net of discount	24,648	—
Operating lease liabilities, net of current portion	15,676	—
Lease incentive obligation, net of current portion	—	6,776
Deferred rent	—	2,216
Deferred revenue, net of current portion - related party	89,111	116,840
Deferred revenue, net of current portion	4,834	—
Other long-term liabilities	502	644
Total liabilities	180,764	168,517
Commitments and contingencies (Note 14)		
Stockholders' (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2019 and 2018; no shares issued and outstanding at December 31, 2019 and 2018	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2019 and 2018; 70,143,252 and 40,936,735 shares issued and outstanding at December 31, 2019 and 2018	70	41
Additional paid-in capital	411,255	341,284
Accumulated other comprehensive income (loss)	—	—
Accumulated deficit	(459,649)	(389,370)
Total stockholders' deficit	(48,324)	(48,045)
Total liabilities and stockholders' deficit	$ 132,440	$ 120,472

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

SERES THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,		
	2019	2018	2017
Revenue:			
Collaboration revenue - related party	$ 27,188	$ 26,917	$ 32,100
Grant revenue	1,102	1,350	—
Collaboration revenue	6,215	—	—
Total revenue	34,505	28,267	32,100
Operating expenses:			
Research and development expenses	$ 80,141	$ 95,955	$ 89,455
General and administrative expenses	24,748	32,596	34,040
Restructuring expenses	1,492	—	—
Total operating expenses	106,381	128,551	123,495
Loss from operations	(71,876)	(100,284)	(91,395)
Other income (expense):			
Interest income	1,033	1,172	1,590
Interest expense	(502)	—	—
Other income	1,066	170	425
Total other income (expense), net	1,597	1,342	2,015
Net loss	$ (70,279)	$ (98,942)	$ (89,380)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.24)	$ (2.43)	$ (2.21)
Weighted average common shares outstanding, basic and diluted	56,649,220	40,743,492	40,449,410
Other comprehensive income (loss):			
Unrealized gain (loss) on investments, net of tax of $0	—	146	3
Total other comprehensive income (loss)	—	146	3
Comprehensive loss	$ (70,279)	$ (98,796)	$ (89,377)

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

SERES THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity (Deficit)
	Shares	Par Value				
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, net of tax withholdings	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
Issuance of common stock upon exercise of stock options	212,240	$ 1	$ 146	$ —	$ —	$ 147
Issuance of common stock upon vesting of RSUs, net of tax withholdings	138,048	—	61	—	—	61
Repurchase of common stock for employee tax withholdings	(17,900)	—	(197)	—	—	(197)
Issuance of common stock under ESPP plan	33,332	—	257	—	—	257
Stock-based compensation expense	—	—	16,641	—	—	16,641
Unrealized gain on investments	—	—	—	146	—	146
Adoption of new revenue standard (ASC 606)	—	—	—	—	(26,857)	(26,857)
Net loss	—	—	—	—	(98,942)	(98,942)
Balance at December 31, 2018	40,936,735	$ 41	$ 341,284	$ —	$ (389,370)	$ (48,045)
Issuance of common stock from public offering, net of commissions, underwriting discounts and offering costs	28,818,578	$ 29	$ 60,498	$ —	$ —	$ 60,527
Issuance of common stock from at the market equity offering	128,400	—	512	—	—	512
Issuance of common stock upon exercise of stock options	90,125	—	145	—	—	145
Issuance of common stock upon vesting of RSUs, net of tax withholdings	94,400	—	176	—	—	176
Issuance of common stock under ESPP plan	75,014	—	296	—	—	296
Stock-based compensation expense	—	—	8,344	—	—	8,344
Net loss	—	—	—	—	(70,279)	(70,279)
Balance at December 31, 2019	70,143,252	$ 70	$ 411,255	$ —	$ (459,649)	$ (48,324)

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

SERES THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2019	2018	2017
Cash flows from operating activities:			
Net loss	$ (70,279)	$ (98,942)	$ (89,380)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Stock-based compensation expense	8,344	16,641	17,362
Depreciation and amortization expense	7,603	7,862	7,259
Non-cash operating lease cost	2,227	—	—
Non-cash interest expense	281	—	3
Accretion of discount on investments	(172)	(214)	(216)
Loss on disposal of property and equipment	103	—	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	3,257	(2,056)	31
Accounts receivable	(1,785)	—	—
Deferred revenue	(17,520)	13,476	(11,888)
Accounts payable	(1,460)	(353)	(856)
Operating lease liabilities	(4,211)	—	—
Accrued expenses and other liabilities	(2,908)	732	2,162
Net cash (used in) operating activities	(76,520)	(62,854)	(75,523)
Cash flows from investing activities:			
Purchases of property and equipment	(1,002)	(1,937)	(4,676)
Purchases of investments	(46,420)	(21,832)	(97,934)
Sales and maturities of investments	16,904	136,087	158,312
Net cash (used in) provided by investing activities	(30,518)	112,318	55,702
Cash flows from financing activities:			
Proceeds from public offering of common stock, net of commissions, underwriting discounts and offering costs	60,527	—	—
Proceeds from issuance of note payable	25,000	—	—
Proceeds from at the market equity offering	512	—	—
Payments of debt issuance costs	(425)	—	—
Proceeds from exercise of stock options	145	147	116
Proceeds from issuance of common stock and restricted common stock	176	61	—
Payments for repurchase of common stock for employee tax withholdings	—	(197)	(33)
Issuance of common stock under ESPP plan	296	257	—
Net cash provided by financing activities	86,231	268	83
Net (decrease) increase in cash, cash equivalents and restricted cash	(20,807)	49,732	(19,738)
Cash, cash equivalents and restricted cash at beginning of year	85,933	36,201	55,939
Cash, cash equivalents and restricted cash at end of year	$ 65,126	$ 85,933	$ 36,201
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 221	$ —	$ 1
Supplemental disclosure of non-cash investing and financing activities:			
Property and equipment purchases included in accounts payable and accrued expenses	$ 62	$ 157	$ 877
Reduction of operating lease assets and operating lease liabilities from operating lease modifications or reassessments	154	—	—

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

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. SER-287 is being developed by the Company to treat ulcerative colitis ("UC"). 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 is also developing product candidates to treat diseases where the microbiome is implicated, including SER-301, a rationally designed, fermented inflammatory bowel disease ("IBD"), candidate, and SER-401, a microbiome therapeutic candidate for use with checkpoint inhibitors ("CPI's") in patients with metastatic melanoma. The Company continues to evaluate microbiome pharmacokinetic and pharmacodynamic data from their SER-262 Phase 1b study and other completed clinical trials, in addition to insights gained from research efforts with their other rationally designed Ecobiotic microbiome therapeutic candidates, in order to determine next steps in the development of both SER-262 to treat an initial recurrence of CDI and SER-155 to modulate the microbiome and dysbiosis in patients following allogeneic hematopoietic stem cell 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 and cancer.

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 preclinical 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.

Under Accounting Standards Update ("ASU") 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40) ("ASC 205-40"), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. As required by ASC 205-40, this evaluation shall initially not take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued.

As of December 31, 2019, the Company had an accumulated deficit of $459,649 and cash, cash equivalents and investments of $94,816. For the year ended December 31, 2019, the Company incurred a loss of $70,279 and used $76,520 of cash in operations. Management has assessed the Company's ability to continue as a going concern in accordance with the requirements of ASC 205-40 and determined that the Company's accumulated deficit, history of losses, and future expected losses meet the ASC 205-40 standard for raising substantial doubt about the Company's ability to continue as a going concern.

The Company's current financial resources and currently forecasted operating plan would allow the Company to operate into the second quarter of 2021. The Company has developed plans to mitigate this risk, which primarily consist of raising additional capital through some combination of equity or debt financings, and/or potentially new collaborations and reducing cash expenditures. If the Company is not able to secure adequate additional funding, the Company plans to make reductions in spending. In that event, the Company may have to delay, scale back, or eliminate some or all of the Company's planned clinical trials and research stage programs. The actions necessary to reduce spending under this plan at a level that mitigates the factors described above is not considered probable, as defined in the accounting standards and therefore, the full extent to which management may extend the Company's funds through these actions may not be considered in management's assessment of the Company's ability to continue as a going concern. As a result, management has concluded that substantial doubt exists about the Company's ability to continue as a going concern.

The Company is eligible to receive contingent milestone payments under its license and collaboration agreement with Nestec Ltd. ("NHS"), an affiliate of Nestlé Health Science US Holdings, Inc. ("Nestlé Health Science"), a significant stockholder of the Company, 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 may require the Company to delay, reduce or eliminate certain research and development activities and reduce or eliminate discretionary operating expenses, 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.

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 and the accrual of research and development expenses. 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 and corporate bonds purchased with original maturities of less than 90 days from the date of purchase, are stated at fair value.

Investments

The Company classifies its available-for-sale marketable debt securities 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 marketable debt securities as available-for-sale securities. Accordingly, these marketable debt securities are recorded at fair value and unrealized gains and losses are reported as a separate component of accumulated other comprehensive income (loss) in 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.

Restricted Investments

The Company held investments of $1,400 as of December 31, 2019 and December 31, 2018 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 investments on its balance sheet.

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 preclinical and clinical testing. These programs could be adversely affected by a significant interruption in the supply of such drug substance products.

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. The carrying values of the Company's accounts receivable, prepaid expense and other current assets, accounts payable, accrued expenses and variable interest rate note payable are recorded at cost, which approximates fair value due to their short-term nature of these assets and liabilities.

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.

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 preclinical 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.

Following the Company's adoption of ASU 2018-07, Compensation—Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting ("ASU 2018-07"), on January 1, 2019, for stock-based awards issued to non-employees, the Company no longer revalues non-employee awards at each reporting date and instead calculates the fair value of the awards as of the grant date using the Black-Scholes option-pricing model. Compensation expense for these awards is recognized over the related service period.

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 accounts for forfeitures of stock-based awards as they occur rather than applying an estimated forfeiture rate to stock-based compensation expense.

The fair value of each stock option grant is estimated on the date of grant using the Black- Scholes option-pricing model. The Company lacks sufficient 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 Company uses 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. 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.

Revenue Recognition

The Company adopted ASC 606 on January 1, 2018, using the modified retrospective method for all contracts not completed as of the date of adoption. The reported results for 2019 and 2018 reflect the application of ASC 606 while the reported results for 2017 were prepared under ASC 605, Revenue Recognition ("ASC 605").

The adoption of ASC 606 changed the pattern and timing of revenue recognition under the Collaboration and License Agreement ("License Agreement") with NHS. Under ASC 605, the upfront fee of $120,000 received by the Company in the first quarter of 2016 was deferred and recognized on a straight-line basis over the estimated performance period of ten years. In addition, the Company recognized revenue associated with substantive development milestones not considered probable at the inception of the License Agreement in their entirety in the period in which the milestone was achieved, in accordance with ASC 605-28, Revenue Recognition-Milestone Method. Under ASC 606, the Company recognizes revenue using the cost-to-cost method over the remaining performance period as described in Note 12. The cumulative effect of applying ASC 606 as of the adoption date of January 1, 2018 of $26,857 was recorded as an adjustment to accumulated deficit in the statement of stockholders' equity (deficit).

The Company recognizes revenue in accordance with the guidance under ASC 606, *Revenue from Contracts with Customers*. ASC 606 applies to all contracts with customers, except those contracts that are within the scope of other guidance, such as leases, insurance, and financial instruments. The Company enters into agreements that are within the scope of ASC 606, under which the Company licenses certain of the Company's product candidates and performs research and development services in connection with such arrangements. The terms of these arrangements typically include payment of one or more of the following: nonrefundable up-front fees, reimbursement of research and development costs, development, clinical, regulatory and commercial sales milestone payments, and royalties on net sales of licensed products. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. When determining the timing and extent of revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps:

(vi) identify the contract(s) with a customer;

(vii) identify the performance obligations in the contract;

(viii) determine the transaction price;

(ix) allocate the transaction price to the performance obligations in the contract; and

(x) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services transferred to the customer.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within the contract to determine whether each promised good or service is a performance obligation. The promised goods or services in the Company's arrangements typically consist of a license to the Company's intellectual property and/or research and development services. The Company may provide options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promises in a contract to transfer a distinct good or service to the customer that (i) the customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised goods or services until such combined group of promises meet the requirements of a performance obligation.

The Company determines transaction price based on the amount of consideration the Company expects to receive for transferring the promised goods or services in the contract. Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, the Company estimates the probability and extent of consideration it expects to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. The Company then considers any constraints on the variable consideration and includes in the transaction price variable consideration to the extent it is deemed probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

The Company then allocates the transaction price to each performance obligation based on the relative standalone selling price and recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company records amounts as accounts receivable when the right to consideration is deemed unconditional. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded for deferred revenue.

The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. Incremental costs of obtaining a contract are expensed as and when incurred if the expected period over which the Company would have amortized the asset is one year or less, or the amount is immaterial.

Collaboration Revenue

Arrangements with collaborators may include licenses to intellectual property, research and development services, manufacturing services for clinical and commercial supply, and participation on joint steering committees. The Company evaluates the promised goods or services to determine which promises, or group of promises, represent performance obligations. In contemplation of whether a promised good or service meets the criteria required of a performance obligation, the Company considers the stage of development of the underlying intellectual property, the capabilities and expertise of the customer relative to the underlying intellectual property, and whether the promised goods or services are integral to or dependent on other promises in the contract. When accounting for an arrangement that contains multiple performance obligations, the Company must develop judgmental assumptions, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success to determine the stand-alone selling price for each performance obligation identified in the contract.

When the Company concludes that a contract should be accounted for as a combined performance obligation and recognized over-time, the Company must then determine the period over which revenue should be recognized and the method by which to measure revenue. The Company generally recognizes revenue using a cost-based input method.

Licenses of intellectual property

If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue associated with the bundled performance obligation. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes developmental and regulatory milestone payments, the Company evaluates whether the achievement of each milestone specifically relates to the Company's efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. If the achievement of a milestone is considered a direct result of the Company's efforts to satisfy a performance obligation or transfer a distinct good or service and the receipt of the payment is based upon the achievement of the milestone, the associated milestone value is allocated to that distinct good or service, otherwise it will be allocated to all performance obligations of the arrangement based on the initial allocation.

The Company evaluates each milestone to determine when and how much of the milestone to include in the transaction price. The Company first estimates the amount of the milestone payment that the Company could receive using either the expected value or the most likely amount approach. The Company primarily uses the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, the Company considers whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty). The Company updates the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any revenue related to sales-based royalties or milestone payments based on the level of sales.

Manufacturing supply services

For arrangements that include a promise of supply of clinical or commercial product, the Company determines if the supply is a promise in the contract or a future obligation at the customer's option. If determined to be a promise at inception of the contract, the Company evaluates the promise to determine whether it is a separate performance obligation or a component of a bundled performance obligation. If determined to be an option, the Company determines if the option provides a material right to the customer and if so, accounts for the option as a separate performance obligation. If determined to be an option but not a material right, the Company accounts for the option as a separate contract when the customer elects to exercise the option.

Grant Revenue

The Company generates revenue from government contracts that reimburse the Company for certain allowable costs for funded projects. For contracts with government agencies, when the Company has concluded that it is the principal in conducting the research and development expenses, and where the funding arrangement is considered central to the Company's ongoing operations, the Company classifies the recognized funding received as revenue.

The Company has concluded to recognize funding received as revenue, rather than as a reduction of research and development expenses, because the Company is the principal in conducting the research and development activities and these contracts are central to its ongoing operations. Revenue is recognized as the qualifying expenses related to the contracts are incurred. Revenue recognized upon incurring qualifying expenses in advance of receipt of funding is recorded in the Company's consolidated balance sheet as accounts receivable. The related costs incurred by the Company are included in research and development expense in the Company's consolidated statements of operations and comprehensive loss.

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.

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 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.

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 agreements with its collaborators, 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, 2019, 2018 and 2017, 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 unvested restricted stock. The Company applies the two-class method to calculate its basic and diluted net loss per share attributable to common stockholders. 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.

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

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting ("ASU 2018-07"). This ASU is intended to simplify aspects of share-based compensation issued to non-employees by making the guidance consistent with the accounting for employee share-based compensation. For public entities, this guidance was effective for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The Company adopted ASU 2018-07 as of January 1, 2019. The adoption of ASU 2018-07 had no material impact on the Company's consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. In addition, a lessee is required to record (i) a right-of-use asset and a lease liability on its balance sheet for all leases with accounting lease terms of more than 12 months regardless of whether it is an operating or financing lease and (ii) lease expense on its statement of operations for operating leases and amortization and interest expense on its statement of operations for financing leases. Leases with a term of 12 months or fewer may be accounted for similar to prior guidance for operating leases. In July 2018, the FASB issued ASU No. 2018-11, Leases (Topic 842), which added an optional transition method that allows companies to adopt the standard as of the beginning of the year of adoption as opposed to the earliest comparative period presented. In November 2019, the FASB issued guidance delaying the effective date for all entities, except for public business entities. For public entities, this guidance was effective for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The Company adopted ASC 842 effective January 1, 2019 using the modified retrospective transition method. Under this method, financial statements for periods after the adoption date are presented in accordance with ASC 842 and prior-period financial statements continue to be presented in accordance with ASC 840, the accounting standard originally in effect for such periods. See Note 7 "Leases" for discussion of the impact of adoption of this standard.

Recently Issued Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework— Changes to the Disclosure Requirements for Fair Value Measurement ("ASU 2018-13"), which modifies the existing disclosure requirements for fair value measurements. The new disclosure requirements include disclosure related to changes in unrealized gains or losses included in other comprehensive income (loss) for recurring Level 3 fair value measurements held at the end of each reporting period and the explicit requirement to disclose the range and weighted average of significant unobservable inputs used for Level 3 fair value measurements. The other provisions of ASU 2018-13 include eliminated and modified disclosure requirements. An entity is permitted to early adopt any removed or modified disclosures upon issuance of ASU No. 2018-13 and delay adoption of the additional disclosures until their effective date. For all entities, this guidance is required to be adopted for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2018-13 will have on its disclosures.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model. It also eliminates the concept of other-than-temporary impairment and requires credit losses related to available-for-sale debt securities to be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. These changes will result in the earlier recognition of credit losses, if any. In May 2019, the FASB issued ASU No. 2019-05, Financial Instruments—Credit Losses (Topic 326): Targeted Transition Relief ("ASU 2019-05"), which provides additional implementation guidance on the previously issued ASU 2016-13. For public entities, this guidance is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted as of the fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is currently evaluating the impact that the adoption of ASU 2016-13 and ASU 2019-05 will have on its consolidated financial statements.

In November 2018, the FASB issued ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606 ("ASU 2018-18"). ASU 2018-18 makes targeted improvements to GAAP for collaborative arrangements, including (i) clarification that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account, (ii) adding unit-of-account guidance in ASC 808, Collaborative Arrangements, to align with the guidance in ASC 606 and (iii) a requirement that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. For public entities, this guidance is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company is currently evaluating the impact that the adoption of ASU 2018-18 will have on its consolidated financial statements.

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

3. Fair Value of Financial Assets and Liabilities

The following tables present the Company's fair value hierarchy for its assets and liabilities that are measured at fair value on a recurring basis:

	Fair Value Measurements as of December 31, 2019 Using:			
	Level 1	Level 2	Level 3	Total
Cash Equivalents:				
Money market funds	$ 25,510	$ —	$ —	$ 25,510
Commercial paper	—	4,243	—	4,243
Corporate bonds	—	4,900	—	4,900
Investments:				
Commercial paper	$ —	$ 11,957	$ —	$ 11,957
Corporate bonds	—	17,733	—	17,733
	$ 25,510	$ 38,833	$ —	$ 64,343

	Fair Value Measurements as of December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
Cash Equivalents:				
Money market funds	$ 39,982	$ —	$ —	$ 39,982
	$ 39,982	$ —	$ —	$ 39,982

Money market funds were valued by the Company based on quoted market prices, which represent a Level 1 measurement within the fair value hierarchy. Commercial paper and corporate bonds were valued by the Company using quoted prices in active markets for similar securities, which represent a Level 2 measurement within the fair value hierarchy. There were no transfers between Level 1 or Level 2 during the years ended December 31, 2019 and 2018.

As of December 31, 2019 and 2018 the Company held a restricted investment of $1,400, which represents a certificate of deposit that is classified as Level 2 in the fair value hierarchy.

4. Investments

Investments by security type consisted of the following at December 31, 2019:

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Commercial Paper	$ 11,957	$ —	$ —	$ 11,957
Corporate Bonds	17,732	3	(2)	17,733
	$ 29,689	$ 3	$ (2)	$ 29,690

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 twelve months are considered current assets and those investments with maturities greater than twelve months are considered non-current assets.

Excluded from the table above is a restricted investment of $1,400 as the cost approximates current fair value.

As of December 31, 2018, the Company had no investments.

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

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31, 2019	December 31, 2018
Laboratory equipment	$ 15,140	$ 14,695
Computer equipment	2,874	2,864
Furniture and office equipment	1,033	1,033
Leasehold improvements	27,977	27,977
Construction in progress	213	26
	47,237	46,595
Less: Accumulated depreciation and amortization	(27,742)	(20,301)
	$ 19,495	$ 26,294

Depreciation and amortization expense was $7,603, $7,862 and $7,259 for the years ended December 31, 2019, 2018 and 2017, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2019	December 31, 2018
Development and clinical manufacturing costs	$ 5,605	$ 7,046
Payroll and payroll-related costs	4,609	5,020
Facility and other	670	3,141
	$ 10,884	$ 15,207

7. Leases

The Company adopted ASC 842 on January 1, 2019 using the modified retrospective approach with no restatement of prior periods or cumulative adjustment to accumulated deficit. The reported results for 2019 reflect the application of ASC 842 while the reported results for 2018 and 2017 were prepared under ASC 840. Upon adoption, the Company elected the package of transition practical expedients, which allowed the Company to carry forward prior conclusions related to whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases and initial direct costs for existing leases. The Company also made an accounting policy election not to recognize leases with an initial term of 12 months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations and comprehensive loss over the lease term. Upon adoption of the new leasing standards, the Company recognized an operating lease asset of approximately $13,737 and a corresponding operating lease liability of approximately $24,497, which are included in the Company's consolidated balance sheet. The adoption of the new leasing standards did not have any impact on the Company's consolidated statements of operations and comprehensive loss. The impact to the consolidated balance sheets for the opening balances is as follows:

	December 31, 2018	Impact of adoption of ASC 842	January 1, 2019
Operating lease assets	$ —	$ 13,737	$ 13,737
Accrued expenses and other current liabilities	$ 15,207	$ (1,768)	$ 13,439
Operating lease liabilities	$ —	$ 4,285	$ 4,285
Lease incentive obligation, net of current portion	$ 6,776	$ (6,776)	$ —
Deferred rent	$ 2,216	$ (2,216)	$ —
Operating lease liabilities, net of current portion	$ —	$ 20,212	$ 20,212

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

The Company leases real estate, primarily laboratory, office and manufacturing space. The Company's leases have remaining terms ranging from less than 1 year to 5 years. Certain leases include one or more options to renew, exercised at the Company's sole discretion, with renewal terms that can extend the lease from one year to five years. The Company evaluated the renewal options in its leases to determine if it was reasonably certain that the renewal option would be exercised, and therefore should be included in the calculation of the operating lease assets and operating lease liabilities. Given the Company's current business structure, uncertainty of future growth, and the associated impact to real estate, the Company concluded that it is not reasonably certain that any renewal options would be exercised. Therefore, the operating lease assets and operating lease liabilities only contemplate the initial lease terms. All of the Company's leases qualify as operating leases.

In July 2019, the Company entered into a sublease agreement with a related party to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the sublease agreement commenced in July 2019 and ends on the last day of the 24th calendar month following commencement, with no option to extend. The annual rent for the subleased premises will be approximately $1,200 in the first year and $1,300 in the second year, which is greater than the annual rent owed by the Company to the landlord for the leased premises. The sublessee is obligated to pay all real estate taxes and costs related to the subleased premises, including cost of operations, maintenance, repair, replacement and property management.

As of December 31, 2019, future undiscounted cash inflows under the sublease are as follows:

Year Ending December 31,	
2020	$ 1,248
2021	633
Total	$ 1,881

The Company concluded that the sublease is an operating lease. Consistent with the Company's policy election for lessor operating leases, each lease component and its associated non-lease components is accounted for as a single lease component.

The following table summarizes the presentation in the Company's consolidated balance sheets of its operating leases:

	As of December 31, 2019
Assets:	
Operating lease assets	$ 11,356
Liabilities:	
Operating lease liabilities	$ 4,456
Operating lease liabilities, net of current portion	15,676
Total operating lease liabilities	$ 20,132

The following table summarizes the effect of lease costs in the Company's consolidated statement of operations and comprehensive loss:

	For the Year Ended December 31, 2019
Operating lease costs	$ 4,532
Short-term lease costs	1,878
Variable lease costs	3,022
Sublease income	(890)
Total lease costs	$ 8,542

During the year ended December 31, 2019, the Company recognized $4,322 of rental expense related to office, laboratory, and manufacturing space. During the year ended December 31, 2019, the Company made cash payments of $6,514 for operating leases.

As of December 31, 2019, future payments of operating lease liabilities are as follows (in thousands):

	As of December 31, 2019
2020	6,302
2021	6,461
2022	6,390
2023	5,157
2024 and thereafter	—
Total future payments of operating lease liabilities	$ 24,310
Less: imputed interest	(4,178)
Present value of operating lease liabilities	$ 20,132

As of December 31, 2019, the weighted average remaining lease term was 3.88 years and the weighted average incremental borrowing rate used to determine the operating lease liability was 11%.

ASC 840 Disclosures

The future minimum lease payments under the Company's operating leases as of December 31, 2018, were as follows (in thousands):

	As of December 31, 2018
2019	$ 6,342
2020	6,120
2021	6,221
2022	6,372
2023	5,158
2024 and thereafter	—
Total future minimum lease payments	$ 30,213

During the years ended December 31, 2018 and 2017, the Company recognized $4,377 and 4,458, of rental expense, respectively, related to office, laboratory, and manufacturing space.

8. Restructuring

In February 2019, the Company implemented corporate changes to focus its resources on advancing its clinical-stage therapeutic candidates. As a result, the Company is concentrating on completing the SER-287 Phase 2b study in mild-to-moderate UC, obtaining results from the ongoing SER-109 Phase 3 study for recurrent CDI, advancing the SER-401 Phase 1b study, to evaluate augmenting checkpoint inhibitor response in patients with metastatic melanoma and advancing SER-301 into clinical development. In connection with the prioritization of these therapeutic candidates, the Company made changes to its management team and reduced headcount by approximately 30 percent.

During the year ended December 31, 2019 the Company recorded charges of $1,492, related to severance and other termination benefits. No restructuring charges were recorded during the years ended December 31, 2018 and 2017. During the year ended December 31, 2019 the Company paid $1,299 related to the restructuring and it expects to pay approximately $193 in 2020.

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

The outstanding restructuring liabilities are included in accrued expenses and other current liabilities on the consolidated balance sheets. As of December 31, 2019, the components of the outstanding restructuring liabilities included in accrued expenses and other current liabilities were as follows:

	Employee Severance and Other Benefits
Restructuring expenses	$ 1,492
Cash payments	$ (1,299)
Liability included in accrued expenses and other current liabilities at December 31, 2019	$ 193

9. Notes Payable

On October 29, 2019 (the "Closing Date"), the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Hercules Capital, Inc. ("Hercules") pursuant to which a term loan in an aggregate principal amount of up to $50,000 (the "Term Loan Facility") is available to the Company in three tranches, subject to certain terms and conditions. The first tranche of $25,000 was advanced to the Company on the Closing Date. Upon satisfaction of certain milestones, the second tranche is available under the Term Loan Facility which allows the Company to borrow an additional amount up to $12,500 through March 15, 2021. The third tranche, which allows the Company to borrow an additional $12,500, will be available upon Hercules' approval on or prior to June 30, 2021.

Advances under the Term Loan Facility will bear interest at a rate equal to the greater of either (i) the Prime Rate (as reported in The Wall Street Journal) plus 4.40%, and (ii) 9.65%. The Company will make interest only payments through December 1, 2021. The interest only period may be extended to June 1, 2022 upon satisfaction of certain milestones. Following the interest only period, the Company will repay the principal balance and interest of the advances in equal monthly installments through November 1, 2023.

The Company may prepay advances under the Loan Agreement, in whole or in part, at any time subject to a prepayment charge (the "Prepayment Premium") equal to: (a) 3.0 % of amounts so prepaid, if such prepayment occurs during the first year following the Closing Date; (b) 2.0% of the amount so prepaid, if such prepayment occurs during the second year following the Closing Date, and (c) 1.0% of the amount so prepaid, if such prepayment occurs after the second year following the Closing Date.

Upon prepayment or repayment of all or any of the term loans under the Term Loan Facility, the Company will pay (in addition to any Prepayment Premium) an end of term charge of 4.85% of the aggregate funded amount under the Term Loan Facility. With respect to the first tranche, an end of term charge of $1,213 will be payable upon any prepayment or repayment. To the extent that the Company is provided additional advances under the Term Loan Facility, the 4.85% end of term charge will be applied to any such additional amounts.

The Term Loan Facility is secured by substantially all of the Company's assets, other than the Company's intellectual property. The Company has agreed to not pledge or secure its intellectual property to others.

Upon issuance, the first tranche was recorded as a liability with an initial carrying value of $24,575, net of debt issuance costs. The initial carrying value will be accreted to the repayment amount, which includes the outstanding principal plus the end of term charge, through interest expense using the effective interest rate method over the term of the debt. As of December 31, 2019, the carrying value of the debt is $24,648 which is classified as a non-current liability on the Company's consolidated balance sheet.

As of December 31, 2019, the future principal payments due under the arrangement, excluding interest and the end of term charge, are as follows:

Year Ending December 31,	Principal
2020	$ -
2021	949
2022	11,970
2023	12,081
Total	$ 25,000

During the year ended December 31, 2019, the Company recognized $502 of interest expense related to the Loan Agreement, which is reflected in other income (expense), net on the consolidated statements of operations and comprehensive loss.

10. Convertible Preferred Stock

On July 1, 2015, in connection with the closing of the initial public offering of the Company's common stock ("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.

11. Stockholders' Equity Common 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 200,000,000 shares of common stock, $0.001 par value per share.

On June 18, 2019, the Company completed an underwritten public offering, in which the Company sold 26,666,667 shares of its common stock at a price to the public of $2.25 per share. The aggregate net proceeds received by the Company from the offering were approximately $55,976, after deducting underwriting discounts and commissions and offering expenses payable by the Company. In addition, the Company granted the underwriters a 30-day option to purchase up to an additional 2,666,666 shares of common stock at the public offering price, less underwriting discounts and commissions.

On June 21, 2019, the Company sold an additional 2,151,911 shares of its common stock at a price to the public of $2.25 per share. The aggregate net proceeds received by the Company were approximately $4,551, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

On November 27, 2019, the Company entered into a Sales Agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen") to sell shares of the Company's common stock, par value $0.001 per share (the "Common Stock"), with aggregate gross sales proceeds of up to $25,000, from time to time, through an "at the market" equity offering program under which Cowen will act as sales agent. As of December 31, 2019, The Company has sold 128,400 shares under the Sales Agreement.

2012 Stock Incentive Plan

The Company's 2012 Stock Incentive Plan, as amended, (the "2012 Plan") provided 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 granted 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, 2019, 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 was 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.

Stock options granted under the 2015 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, 2019, there were 2,154,460 shares available for future grant under the 2015 Plan.

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

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 automatically increase on the first day of each calendar year, beginning in 2016 and ending in 2025, by an amount equal to the lesser 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 the Company's board of directors. Offering periods under the ESPP will commence when determined by the plan administrator. As of December 31, 2019, there were 108,346 shares issued under the ESPP and 1,847,474 shares were reserved and available for issuance under the ESPP.

The ESPP provides that eligible employees may contribute up to 15% of their eligible earnings toward the semi-annual purchase of the Company's common stock. The ESPP is qualified under Section 423 of the Internal Revenue Code. The employee's purchase price is derived from a formula based on the closing price of the common stock on the first day of the offering period versus the closing price on the date of purchase (or, if not a trading day, on the immediately preceding trading day). The offering period under the ESPP has a duration of six months, and the purchase price with respect to each offering period beginning on or after such date is, until otherwise amended, equal to 85% of the lesser of (i) the fair market value of the Company's common stock at the commencement of the applicable six-month offering period or (ii) the fair market value of the Company's common stock on the purchase date. The Company estimates the fair value of common stock under the ESPP using a Black-Scholes valuation model. The fair value was estimated on the date of grant using the Black-Scholes option valuation model and the straight-line attribution approach with the following weighted-average assumptions: risk-free interest rate (1.73%); expected term (0.5 years); expected volatility (75.9%); and an expected dividend yield (0%). The Company recorded $109 and $145 of stock-based compensation expense under the ESPP for the twelve months ended December 31, 2019 and December 31, 2018, respectively. There was no stock-based compensation expense under the ESPP for the twelve months ended December 31, 2017.

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,		
	2019	2018	2017
Risk-free interest rate	2.64%	2.39%	2.20%
Expected term (in years)	6.0	6.0	6.0
Expected volatility	88.4%	76.0%	80.9%
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, 2019:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2018	7,561,719	$ 12.26	7.23	$ 4,958
Granted	2,456,850	5.79		
Exercised	(90,125)	1.61		
Forfeited	(1,617,761)	12.82		
Outstanding as of December 31, 2019	8,310,683	$ 10.36	7.01	$ 3,427
Options vested and expected to vest as of December 31, 2019	8,310,683	$ 10.36	7.01	$ 3,427
Options exercisable as of December 31, 2019	4,815,001	$ 12.47	5.78	$ 3,296

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

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2019, 2018 and 2017 was $4.13, $6.53, and $7.07 per share, respectively. The total intrinsic value of stock options exercised during the years ended December 31, 2019, 2018, and 2017 was $244, $1,801, and $1,912, respectively.

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.

During the year ended December 31, 2019, the Company granted performance-based stock options to employees for the purchase of an aggregate of 1.1 million shares of common stock with a grant date fair value of $4.58 per share. These stock options are exercisable only upon achievement of specified performance targets. As of December 31, 2019, none of these options were exercisable because none of the specified performance targets had been achieved. Because achievement of the specified performance targets was not deemed probable as of December 31, 2019, the Company did not record any expense for these stock options from the dates of issuance through December 31, 2019.

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, 2019:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested restricted stock units as of December 31, 2018	226,900	$ 9.64
Granted	20,000	$ 2.69
Forfeited	(22,500)	$ 8.77
Vested	(94,400)	$ 9.46
Unvested restricted stock units as of December 31, 2019	130,000	$ 8.86

The aggregate intrinsic value of restricted stock units that vested during the years ended December 31, 2019, 2018 and 2017 was $517, $1,206, and $445, 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,		
	2019	2018	2017
Research and development expenses	$ 4,613	$ 8,388	$ 8,115
General and administrative expenses	3,731	8,253	9,247
	$ 8,344	$ 16,641	$ 17,362

As of December 31, 2019, the Company had an aggregate of $9,387 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.30 years.

12. Collaboration Revenue

NHS Collaboration Agreement

Summary of Agreement

In January 2016, the Company entered into the License Agreement 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 supports 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.

Under the License Agreement, NHS agreed to pay the Company an upfront cash payment of $120,000, which the Company received in February 2016. 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. 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.

Under the License Agreement, the Company was entitled to receive a $20,000 milestone payment from NHS following initiation of a SER-287 Phase 2 study and a $20,000 milestone payment from NHS following the initiation of a SER-287 Phase 3 study. In November 2018, the Company entered into a letter agreement with NHS which modified the License Agreement to address the current clinical plans for SER-287. Through the letter agreement, the Company and NHS agreed that following initiation of the SER-287 Phase 2b study, the Company will receive $40,000 in milestone payments from NHS which represents the milestone due to the Company for the initiation of the SER-287 Phase 2 and Phase 3 studies. The SER-287 Phase 2b study was initiated and the $40,000 of milestone payments were received in December 2018. The letter agreement also provides scenarios under which NHS' reimbursement to the Company for certain Phase 3 development costs would be reduced or delayed depending on the outcomes of the SER-287 Phase 2b study.

Accounting Analysis

The Company assessed the License Agreement in accordance with ASC 606 and concluded that NHS is a customer. The Company identified the following promises under the contract: (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. In addition, the Company identified a contingent obligation to perform manufacturing services to provide commercial supply if commercialization occurs, which is contingent upon regulatory approval. This contingent obligation is not a performance obligation at inception and has been excluded from the initial allocation as it represents a separate buying decision at market rates, rather than a material right in the contract. The Company assessed the promised goods and services to determine if they are distinct. Based on this assessment, the Company determined that NHS cannot benefit from the promised goods and services separately from the others as they are highly interrelated and therefore not distinct. Accordingly, the promised goods and services represent one combined performance obligation and the entire transaction price will be allocated to that single combined performance obligation.

At contract inception, the Company determined that the $120,000 non-refundable upfront amount constituted the entirety of the consideration to be included in the transaction price as the development, regulatory, and commercial milestones were fully constrained. 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. 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. During the year ended December 31, 2018, the Company received $40,000 from NHS in connection with the initiation of the Phase 2b study for SER-287.

Therefore, as of December 31, 2019, the aggregate amount of the transaction price allocated to the remaining performance obligation of the License Agreement was approximately $190,000.

During the year ended December 31, 2018, the Company received $40,000 from NHS in connection with the initiation of the Phase 2b study for SER-287. In the third quarter of 2018, the Company increased the transaction price by $20,000 associated with the Phase 2 milestone for SER-287. The Company estimated the $20,000 of variable consideration by using the most likely amount method which best predicts the amount of consideration to which the Company will be entitled. The Company included the $20,000 in the transaction price because it is probable that a significant reversal in the amount of cumulative revenue recognized would not occur when the uncertainty associated with the variable consideration was subsequently resolved.

In the fourth quarter of 2018, the Company entered into a letter agreement with NHS which modified the License Agreement to address the current clinical plans for SER-287. As a result of this modification, the Company and NHS agreed that the $20,000 milestone payment due to the Company from NHS following the initiation of a Phase 3 study for SER-287 would now be due to the Company upon initiation of the SER-287 Phase 2b study. The Letter Agreement constituted a contract modification under ASC 606. The Company accounted for the contract modification through a cumulative catch-up adjustment of approximately $5,517 because the contract modification did not add any additional goods or services and the remaining goods and services are not distinct. The SER-287 Phase 2b study was initiated in December 2018 and the Company included the $20,000 in the transaction price as of December 31, 2018. The transaction price as of December 31, 2018 was approximately $190,000.

In April 2019, the Company, with the approval of the Seres/NHS Joint Steering Committee, as provided for in the License Agreement, modified the SER-109 clinical trial. As a result of this modification, the Company and NHS agreed, and informed the FDA, that the target study enrollment would be reduced from 320 subjects to 188 subjects. This modification to the SER-109 clinical trial constituted a contract modification under ASC 606. The Company accounted for the contract modification through a cumulative catch-up adjustment because the contract modification did not add any additional goods or services and the remaining goods and services are not distinct. The modification reduced the total estimated costs in the Company's cost-to-cost model for the License Agreement and resulted in the Company recognizing $6,830 of collaboration revenue – related party in the twelve months ended December 31, 2019.

During the twelve months ended December 31, 2019, 2018, and 2017 using the cost-to-cost method, which best depicts the transfer of control to the customer, the Company recognized $27,188, $26,917, and $32,100 of Collaboration revenue – related party, respectively.

As of December 31, 2019 and December 31, 2018, there was $110,071, and $137,259 of deferred revenue related to the unsatisfied portion of the performance obligation under the License Agreement. As of December 31, 2019, deferred revenue 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 which is determined by the cost-to-cost method which measures the extent of progress towards completion based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the performance obligation. All costs associated with the License Agreement are recorded in research and development expense in the consolidated statements of operations and comprehensive loss.

AstraZeneca Research Collaboration and Option Agreement

Summary of the Agreement

In March 2019, the Company entered into a Research Collaboration and Option Agreement (the "Research Agreement") with MedImmune, LLC, a wholly owned subsidiary of AstraZeneca Inc. ("AstraZeneca"), to advance the mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy. Under the Research Agreement, the Company and AstraZeneca will conduct certain research and development activities as set forth on a research plan focused on the role of the microbiome in certain cancers and cancer immunotherapies, including furthering the research program for SER-401, in combination with AstraZeneca compounds targeting various cancers.

Pursuant to the Research Agreement, the Company agreed not to conduct research or development on any microbiome products specifically designed by the Company during the term of the Research Agreement for the treatment of cancer ("Microbiome Oncology Products"), with or on behalf of any third-party without the prior approval of the joint steering committee for the Research Agreement for at least three years after the effective date (the "Exclusivity Period"). Additionally, AstraZeneca will pay to the Company a total of $20,000 in three equal installments, the first of which the Company received in April 2019, the second of which the Company

received in December 2019, and the third of which become due on January 4, 2021. Such payments are payable even if the Research Agreement is terminated in accordance with its terms, unless the Research Agreement is terminated by AstraZeneca for the Company's uncured material breach. Additionally, AstraZeneca will bear its costs of conducting activities under the research plan and will reimburse the Company for all activities performed under the research plan based on actual full-time employee ("FTE") time and certain third-party costs incurred by the Company in connection therewith.

Under the Research Agreement, the Company granted to AstraZeneca an exclusive option to negotiate a worldwide, sublicensable exclusive license under relevant intellectual property rights controlled by the Company to exploit Microbiome Oncology Products for the treatment of cancer. Additionally, the Company granted to AstraZeneca an additional exclusive option to obtain a worldwide, sublicensable, license under certain intellectual property rights arising out of the Agreement or coming into the control of the Company during the term of the Agreement, to exploit AstraZeneca's oncology and other assets which are the subject of the research plan. AstraZeneca may exercise each option at any point prior to 90 days after the end of the Exclusivity Period (the "Option Exercise Period") by delivering an option exercise notice to the Company. If AstraZeneca exercises an option during the Option Exercise Period, the parties will enter into exclusive, good faith negotiations for a period of six months (the "Negotiation Period") regarding the terms of the definitive license agreement contemplated by such option. If no definitive agreement is reached during the Negotiation Period, subject to certain other terms and conditions applicable for a one (1) year period, the Company is free to license, further develop or otherwise exploit its assets that were the subject of the option without further obligation to AstraZeneca.

The term of the Research Agreement continues in effect until the Research Agreement is terminated by the parties in accordance with its terms by mutual written agreement. Either party may terminate the Research Agreement for the other party's uncured material breach or bankruptcy or insolvency-related events. AstraZeneca may terminate the Research Agreement for convenience.

Accounting Analysis

The Company assessed the Research Agreement in accordance with ASC 606 and concluded that AstraZeneca is a customer. The Company identified the following promises under the contract: (i) a research license, (ii) an obligation to perform research and development services, and (iii) participation on a joint steering committee. The Company assessed the promised goods and services to determine if they are distinct. Based on this assessment, the Company determined that AstraZeneca cannot benefit from the promised goods and services separately from the others as they are highly interrelated and therefore not distinct. Accordingly, the promised goods and services represent one combined performance obligation and the entire transaction price will be allocated to that single combined performance obligation.

Each exclusive option granted to AstraZeneca provides AstraZeneca with the right to negotiate a license agreement in the future at fair value. Therefore, the Company concluded that each option does not constitute a performance obligation at inception and has been excluded from the initial allocation since each option represents a separate buying decision at market rates, rather than a material right in the contract.

At contract inception, the Company determined that the transaction price is comprised of: (i) the $20,000 fee, which represents fixed consideration, and (ii) the estimated reimbursement of research and development costs incurred, which represents variable consideration. The Company included the estimated reimbursement of research and development costs, approximately $13,900, in the transaction price at the inception of the arrangement because the Company is required to perform research and development services and the contract requires AstraZeneca to reimburse the Company for costs incurred. Also, since the related revenue would be recognized only as the costs are incurred, and the contract precludes the joint steering committee from changing the research plan without mutual agreement, the Company determined it is not probable that a significant reversal of cumulative revenue would occur.

The Company determined that revenue under the Research Agreement should be recognized over time as AstraZeneca simultaneously receives the benefit from the Company as the Company performs under the single performance obligation over time. The Company will recognize revenue for the single performance obligation using a cost-to-cost input method as the Company has concluded it best depicts the research and joint steering committee participation services performed prior to AstraZeneca's ability to negotiate a license. Under this method, the transaction price is recognized over the contract's entire performance period, using costs incurred relative to total estimated costs to determine the extent of progress towards completion.

For the twelve months ended December 31, 2019, the Company recognized collaboration revenue of $6,215 based on the measured progress under the Research Agreement. The transaction price as of December 31, 2019 was approximately $33,900.

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

As of December 31, 2019, there was $9,668 of deferred revenue associated with the Research Agreement, with $4,834 presented as current and $4,834 as non-current in the consolidated balance sheets based on the Company's estimate of revenue that will be recognized within the next 12 months. All costs associated with the Research Agreement are recorded in research and development expense in the consolidated statements of operations and comprehensive loss.

Contract Balances from Contracts with Customers

The following tables present changes in the Company's contract liabilities during the twelve months ended December 31, 2019 and 2018:

	Balance as of December 31, 2018	Additions	Deductions	Balance as of December 31, 2019
Year ended December 31, 2019				
Contract liabilities:				
Deferred revenue - related party	137,259	—	(27,188)	110,071
Deferred revenue	—	15,883	(6,215)	9,668

	Balance as of January 1, 2018	Additions	Deductions	Balance as of December 31, 2018
Year ended December 31, 2018				
Contract liabilities:				
Deferred revenue - related party	123,783	40,393	(26,917)	137,259

During the twelve months ended December 31, 2019 the Company recognized the following revenues as a result of changes in the contract liability balances in the respective periods:

	Year Ended December 31,	
	2019	2018
Revenue recognized in the period from:		
Amounts included in the contract liability at the beginning of the period	27,188	15,774

When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded. Revenue is recognized from the contract liability over time using the cost-to-cost method.

13. Net Loss per Share

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

	Year Ended December 31,		
	2019	2018	2017
Numerator:			
Net loss attributable to common stockholders	$ (70,279)	$ (98,942)	$ (89,380)
Denominator:			
Weighted average common shares outstanding, basic and diluted	56,649,220	40,743,492	40,449,410
Net loss per share attributable to common stockholders, basic and diluted	$ (1.24)	$ (2.43)	$ (2.21)

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

The Company's potential dilutive securities, which include stock options, unvested restricted common stock and shares issuable under the ESPP, 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,		
	2019	2018	2017
Stock options to purchase common stock	8,310,683	7,561,719	6,125,692
Unvested restricted stock units	130,000	226,900	356,778
Shares issuable under employee stock purchase plan	89,821	49,495	—
	8,530,504	7,838,114	6,482,470

14. Commitments and Contingencies

Leases

Refer to Note 7 "Leases" for discussion of the commitments associated with the Company's lease portfolio.

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, 2019 or 2018.

15. Income Taxes

During the years ended December 31, 2019, 2018 and 2017, 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.

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,		
	2019	2018	2017
Federal statutory income tax rate	(21.0)%	(21.0)%	(34.0)%
Research and development tax credits	(5.8)	(7.2)	(7.7)
State taxes, net of federal benefit	(6.8)	(7.2)	(4.8)
Stock-based compensation	(1.7)	2.0	1.2
Revaluation of preferred stock warrant liability	—	—	33.1
Other	(0.7)	0.8	(0.3)
Change in deferred tax asset valuation allowance	36.0	32.6	12.5
Effective income tax rate	—%	—%	—%

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

Net deferred tax assets as of December 31, 2019 and 2018 consisted of the following:

	December 31, 2019	December 31, 2018
Deferred tax assets:		
Net operating loss carryforwards	$ 72,752	$ 50,723
Research and development tax credit carryforwards	36,602	32,522
Capitalized organization costs	244	275
Stock-based compensation expense	12,783	9,178
Lease Liability	5,500	—
Charitable Contributions	13	11
Deferred Revenue	32,713	37,499
Accrued expenses	1,251	4,279
Capitalized research and development expenses	58	66
Total deferred tax assets	$ 161,916	$ 134,553
Deferred tax liabilities:		
Depreciation and amortization	(1,467)	(2,544)
Right of use assets	(3,103)	—
Total deferred tax liabilities	(4,570)	(2,544)
Valuation allowance	$ (157,346)	$ (132,009)
Net deferred tax assets	$ —	$ —

As of December 31, 2019, the Company had net operating loss carryforwards (“NOLs”) for federal and state income tax purposes of $266,485 and $265,671, respectively. Federal NOLs of $119,781, generated before 2018, will begin expiring in varying amounts in 2035 unless utilized. The remaining federal NOLs of $146,704, generated after 2017, will be carried forward indefinitely and could be used to offset up to 80% of taxable income of each future tax year. Massachusetts does not follow federal time periods for NOLs and as such the Company’s Massachusetts NOLs of $265,671 will expire in at various times starting in 2035. As of December 31, 2019, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $31,828 and $6,043, respectively, which begin to expire in 2031 and 2028, respectively. The federal research and development tax credits include an orphan drug credit carryforward of $18,817. Utilization of the NOLs and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 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 its formation, the Company has 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 or could result in a change of control in the future upon subsequent disposition. The Company conducted an analysis to determine if historical changes in ownership through August 31, 2015 would limit or otherwise restrict its ability to utilize these NOLs and research and development credit carryforwards. As a result of this analysis, the Company does not believe there are any significant limitations on its 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 NOLs or research and development 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, 2019 and 2018. Management reevaluates the positive and negative evidence at each reporting period.

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

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2019, 2018 and 2017 related primarily to the increases in NOLs, research and development tax credit carryforwards, stock-based compensation and decrease of the deferred rate due to tax reform were as follows:

	Year Ended December 31,		
	2019	2018	2017
Valuation allowance at beginning of year	$ (132,009)	$ (94,126)	$ (82,994)
Decreases recorded as benefit to income tax provision	—	—	29,546
Increases recorded to income tax provision	(25,337)	(37,883)	(40,678)
Valuation allowance as of end of year	$ (157,346)	$ (132,009)	$ (94,126)

As of December 31, 2019, 2018, and 2017, 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.

16. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2019 and 2018. 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.

	2019				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue - related party	$ 6,615	$ 10,454	$ 4,840	$ 5,279	$ 27,188
Grant revenue	446	260	85	311	1,102
Collaboration revenue	260	1,817	2,106	2,032	6,215
Total operating expenses	31,874	23,479	24,214	26,814	106,381
Loss from operations	(24,553)	(10,948)	(17,183)	(19,192)	(71,876)
Net loss	(24,333)	(10,759)	(16,409)	(18,778)	(70,279)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.59)	$ (0.24)	$ (0.23)	$ (0.27)	$ (1.24)

	2018				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Collaboration revenue - related party	$ 3,766	$ 4,271	$ 8,684	$ 10,196	$ 26,917
Grant revenue	205	341	371	433	1,350
Total operating expenses	32,237	32,748	31,266	32,300	128,551
Loss from operations	(28,266)	(28,136)	(22,211)	(21,671)	(100,284)
Net loss	(27,919)	(27,787)	(21,949)	(21,287)	(98,942)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.69)	$ (0.68)	$ (0.54)	$ (0.52)	$ (2.43)

17. Related Party Transactions

As described in Note 12, in January 2016 the Company entered into a License Agreement and, in November 2018, a letter 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 years ended December 31, 2019, 2018, and 2017, the Company recognized $27,188, $26,917, and $32,100, respectively, of related party revenue associated with the License Agreement. As of December 31, 2019 and 2018, there was $110,071 and $137,259, respectively, 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, 2019. There is no amount due from NHS as of December 31, 2019.

In July 2019, the Company entered into a sublease agreement with Flagship Pioneering, one of the Company's significant stockholders, to sublease a portion of its office and laboratory space in Cambridge, Massachusetts. The term of the sublease agreement commenced in July 2019 and ends on the last day of the 24th calendar month following commencement, with no option to extend (see Note 7). Under this agreement, the Company recorded other income of $890 during the twelve months ended December 31, 2019. The Company received cash payments of $890 during the twelve months ended December 31, 2019.

18. 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 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, 2019, 2018, and 2017 the Company recorded expense of $542, $604, and $484, respectively, for 401(k) match contributions.

DESCRIPTION OF CAPITAL STOCK

The following description of the capital stock of Seres Therapeutics, Inc. (the "Company," "we," "us," and "our") and certain provisions of our restated certificate of incorporation and amended and restated bylaws are summaries and are qualified in their entirety by reference to the applicable provisions of our restated certificate of incorporation and amended and restated bylaws, which have been publicly filed with the Securities and Exchange Commission. We encourage you to read our restated certificate of incorporation, our amended and restated bylaws and the applicable provisions of the General Corporation Law of the State of Delaware for more information.

Our authorized capital stock consists of:

- 200,000,000 shares of common stock, par value $0.001 per share; and
- 10,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our restated certificate of incorporation and amended restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our restated certificate of incorporation. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

Rights Upon Liquidation. In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock.

Other Rights. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Dividend

Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock. We have never declared or paid any cash dividends on our capital stock. We do not intend to pay cash dividends for the foreseeable future. We currently expect to retain all future earnings, if any, for use in the development, operation and expansion of our business. Any determination to pay cash dividends in the future will depend upon, among other things, our results of operations, plans for expansion, tax considerations, available net profits and reserves, limitations under law, financial condition, capital requirements and other factors that our board of directors considers to be relevant.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our restated certificate of incorporation and our amended and restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interest, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock. The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to effect a change in control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings. Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals. Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent. Our restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board. Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors. Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting. Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this law may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum. Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or amended and restated bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Restated Certificate of Incorporation. The amendment of any of the above provisions in our restated certificate of incorporation, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interest.

SERES THERAPEUTICS, INC.
ADVISORY AGREEMENT

THIS AGREEMENT is made and effective as of December 12, 2019 (the "**Effective Date**") by and between Roger J. Pomerantz, M.D. an individual ("**Advisor**"), whose address is set forth on the signature page below and SERES THERAPEUTICS, Inc., a Delaware corporation (along with its affiliated companies, the "**Company**") (collectively referred to as the "**Parties**" or individually referred to as a "**Party**").

WHEREAS, the Parties have previously entered into that certain Separation Agreement and Release dated as of January 14, 2019 (the "**Separation Agreement**"), which sets forth certain terms and conditions of Advisor's resignation of employment with the Company and continued service on the Company's board of directors (the "**Board**");

WHEREAS, Advisor's service on the Board terminated effective as of the Effective Date; and

WHEREAS, the Company seeks to retain Advisor's services on and following the Effective Date on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, the Company and Advisor hereby agree as follows:

1. Services. The Company hereby engages Advisor to provide to the Company, and Advisor agrees to provide to the Company under the terms and conditions of this Agreement, board advisory services as reasonably requested by the Company from time to time (hereinafter the "**Services**").

2. Compensation. As consideration for Advisor's Services, the Company will pay to Advisor a quarterly retainer in the amount of $8,750 per quarter (and pro-rated for partial quarters) due at the end of each calendar quarter. The retainer will give the Company access to the Advisor's Services for up to 15 hours per quarter. In addition, the Parties agree that notwithstanding their contrary terms, with respect to those outstanding options to purchase shares of the Company's common stock held by Advisor on the Effective Date, which options are set forth on Exhibit A to this Agreement, Advisor's service under this Agreement shall constitute continued service to the Company such that (i) with respect to the option to purchase 15,000 shares of the Company's common stock granted to Advisor on June 13, 2019, such option will continue to vest during the Term (as defined below), and (ii) with respect to all such outstanding options, such options will remain exercisable during the Term and the post-termination exercise period of such options will not commence until the expiration of the Term. For the avoidance of doubt, effective as of the Effective Date, Advisor will no longer be eligible to receive compensation for service on the Board under the Company's Non-Employee Director Compensation program.

3. Expenses. The Company will reimburse Advisor for reasonable and necessary out-of-pocket expenses incurred by Advisor in the performance of the Services, provided such out-of-pocket expenses are approved in advance by an officer of the Company and further are supported by reasonable documentation. Such expenses will include reasonable travel expenses of Advisor to the Company's offices.

4. Independent Contractor. Advisor is not, nor will Advisor be deemed to be at any time during the term of this Agreement, an employee of the Company, and therefore Advisor will not be entitled to any benefits provided by the Company to its employees (including such items as health and disability benefits, but except as otherwise provided in the Separation Agreement with respect to continued medical, dental or vision coverage pursuant to COBRA), even if it is later determined that Advisor is a common law employee of Company or any of its affiliates for any purpose. Advisor's status and relationship with the Company will be that of an independent contractor and consultant. Advisor will not state or imply, directly or indirectly, that Advisor is empowered to bind the Company without the Company's prior written consent. Nothing herein will create, expressly or by implication, a partnership, joint venture or other association between the parties. Advisor will be solely responsible for payment of all charges and taxes arising from his or her relationship to the Company.

5. Term of Agreement. The term of this Agreement and Advisor's Services hereunder will commence as of the Effective Date of this Agreement and, unless terminated earlier as a result of the death, physical incapacity or mental incompetence of Advisor, which will result in automatic termination, or unless terminated pursuant to Section 6, it will continue in effect until the date on which the Company publicly announces the top-line results of the SER-287 Phase 2b clinical study (the "**Initial Term**"). The term of this Agreement may be extended beyond the Initial Term for additional periods upon mutual written agreement of the parties. Upon expiration or termination of this Agreement all obligations of the parties hereunder shall cease except that the provisions of Sections 7 through 13 will survive the termination or expiration of this Agreement for any reason. The period from the Effective Date through the expiration or termination of this Agreement, regardless of the time or reason for such termination, shall be referred to herein as the "**Term**".

6. Termination. Either Party may, without prejudice to any right or remedy it may have due to any failure of the other Party to perform its obligations under this Agreement, terminate the Term immediately by written notice to the other Party in the event of a material breach of this Agreement by such other Party. The Company may terminate the Term at any time by ten (10) days' written notice to Advisor. If prior to the expiration of the Initial Term the Company terminates the Term other than due to Advisor's material breach of this Agreement, Advisor shall be entitled to the payments and benefits (including, for the avoidance of doubt, continued vesting and exercisability of Advisor's options to purchase shares of the Company's common stock) set forth in Section 2 of this Agreement as if Advisor had continued providing the Services until the expiration of the Initial Term. In the event of termination under this Section 6 at any time, the Advisor shall be entitled to payment for Services performed and expenses paid or incurred prior to the effective date of termination and shall have no further rights under this Agreement. Such payments shall constitute full settlement of any and all claims of the Advisor of every description against the Company under this Agreement.

7. Representations and Warranties of Advisor. Advisor represents and warrants to the Company that (i) with respect to any information, know-how, knowledge or data disclosed by Advisor to the Company or any other third party in the performance of this Agreement, Advisor has the full and unrestricted right to disclose the same; and (ii) Advisor is free to undertake the Services required by this Agreement, and there is, and will be, no conflict of interest between Advisor's performance of this Agreement and any obligation Advisor may have to other parties.

8. Covenants of Advisor. Notwithstanding anything herein to the contrary, Advisor agrees to continue to abide by the terms of the Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement previously entered into between Advisor and the Company (the "**Proprietary Information Agreement**"), which are hereby incorporated by reference into this Agreement and which shall apply in addition to the other covenants set forth in this Agreement.

9. Confidentiality. Advisor agrees to hold all Confidential Information (as hereinafter defined) of the Company (or other parties whose Confidential Information the Company has in its possession under obligations of confidentiality) in trust and strict confidence and, except as may be authorized by the Company in writing, will not use for any purpose other than the performance of the Services under this Agreement, nor disclose such Confidential Information to any person, association, company, entity or other organization (whether for profit or not for profit).

As used herein, "**Confidential Information**" means all knowledge and information which Advisor has acquired or may acquire as a result of, or related to his or her relationship with the Company, including but not limited to, Works (as defined below) information concerning the Company's business, finances, operations, strategic planning, research and development activities, products, molecules, organisms, laboratory materials, prototypes, cell lines, inventions, research developments, improvements, processes, trade secrets, services, cost and pricing policies, formulae, diagrams, schematics, notes, data, memoranda, methods, know-how, techniques, inventions, and marketing strategies. Confidential Information will also include information received by the Company from third parties under an obligation of confidentiality. Notwithstanding the foregoing sentence, such Confidential Information does not include (i) information which is or becomes publicly available (except as may be disclosed by Advisor in violation of this Agreement), (ii) information acquired by Advisor from a third-party source other than the Company or any of its employees, advisors or shareholders, which source legally acquired such information under no obligation of confidentiality, or (iii) information of a general nature and specifically information regarding the microbiome therapeutics field known to Advisor prior to advising the Company or acquired by Advisor during the term hereof by reason of his or her other business activities. This Agreement shall not prohibit Advisor from disclosing Confidential Information to the extent required for Advisor to comply with a court or governmental order, provided that Advisor provides prior written notice of such required disclosure to the Company and cooperates in reasonable and lawful actions by the Company to avoid and/or minimize the extent of such disclosure.

10. Ownership of Work Product. Advisor will communicate in writing and disclose to the Company promptly and fully all concepts, inventions, formulae, molecules, organisms, trade secrets, know-how, technical or business innovations, writings or other works of authorship and patents or patent rights created, reduced to practice, or conceived by Advisor (whether or not patentable or copyrightable and whether made solely by Advisor or jointly with others), which result from the Services that Advisor performs for the Company or which result from use of Confidential Information (along with all patent, copyright and other proprietary rights arising therefrom, collectively the "**Works**").

Advisor will make and maintain adequate and current written records of all Works, which records will be available to and remain the property of the Company at all times. The Works will be and remain the sole and exclusive property of the Company or its nominees whether or not patented or copyrighted and without regard to any termination of this Agreement. The Works are being created at the instance of the Company and will be deemed to be "works made for hire" under the United States copyright laws. Advisor hereby assigns and, to the extent any such assignment cannot be made at present, hereby agrees to assign to the Company, without further compensation, all right, title and interest in and to all Works. Advisor will assist the Company in any reasonable manner to obtain for its own benefit patents, copyrights and other proprietary rights in any and all countries with respect to the Works, and Advisor will execute and deliver, when requested, patent and other applications and assignments thereof. In the event Advisor’s signature on any assignment of the Works or patent or other application or assignment thereof with respect to the Works cannot be obtained within five (5) days after the Company’s request therefor, Advisor hereby designates the Company as his agent for, and grants to the Company a power of attorney, which power of attorney shall be deemed coupled with an interest, solely for the purpose of effecting the execution of such documents. Advisor will further assist the Company at the Company’s expense, and including compensation at Advisor’s then current hourly consulting rate, in every proper way to enforce any patents, copyrights and other legal protections obtained, including testifying in any suit or proceeding.

11. Company Data. Any data or other materials furnished by the Company for use by Advisor in connection with the Services will remain the sole property of the Company and will be held in trust and confidence by Advisor in accordance with Section 9 as Confidential Information. The Company may obtain the return of the Company data or other materials furnished to Advisor upon written notice to Advisor requesting such return, and in any event Advisor will promptly return such data or materials upon termination of this Agreement.

12. Advertising. Advisor will not in any way or in any form publicize or advertise in any manner the fact that Advisor is performing the services called for by this Agreement without the prior written consent of the Company.

13. Restriction on Solicitation. During the Term and for one year thereafter, Advisor will not recruit or otherwise solicit, entice and induce any employee of the Company to terminate their employment with, or otherwise cease their relationships with the Company.

14. Trade Secrets. In accordance with 18 U.S.C. §1833, notwithstanding anything to the contrary in this Agreement, the Proprietary Information Agreement or any other agreement between Advisor and the Company or any of its subsidiaries in effect as of the Effective Date (together, the "**Subject Documents**"): (a) Advisor will not be in breach of the Subject Document, and shall not be held criminally or civilly liable under any federal or state trade secret law (i) for the disclosure of a trade secret that is made in confidence to a federal, state, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, or (ii) for the disclosure of a trade secret that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal; and (b) if Advisor files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Advisor may disclose the trade secret to Advisor's attorney, and may use the trade secret information in the court proceeding, if Advisor files any document containing the trade secret under seal, and does not disclose the trade secret, except pursuant to court order.

15. Assignment. The rights and liabilities of the parties hereto shall bind and inure to the benefit of their respective successors, heirs, executors and administrators, as the case may be; provided that, as the Company has specifically contracted for Advisor's Services, Advisor may not assign or delegate Advisor's obligations under this Agreement either in whole or in part without the prior written consent of the Company. The Company may assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of the Company's business. Any assignment not in accordance with this Section 15 shall be void.

16. Section 409A. The intent of the Parties is that the payments and benefits under this Agreement comply with or be exempt from Section 409A of the Internal Revenue Code of 1986, as amended ("**Section 409A**"), and, to the maximum extent permitted, this Agreement will be interpreted accordingly. Notwithstanding anything in this Agreement to the contrary, any compensation or benefits payable under this Agreement upon termination of the Term and that constitutes "non-qualified deferred compensation" under Section 409A shall be payable only upon Advisor's "separation from service" with the Company within the meaning of Section 409A (a "**Separation from Service**"). If Advisor is deemed by the Company at the time of Advisor's Separation from Service to be a "specified employee" for purposes of Section 409A, to the extent delayed commencement of any portion of the benefits to which Advisor is entitled under this Agreement is required in order to avoid a prohibited distribution under Section 409A, such portion of Advisor's benefits shall not be provided to Advisor prior to the earlier of (i) the expiration of the six-month period measured from the date of Advisor's Separation from Service with the Company or (ii) the date of Advisor's death. Upon the first business day following the expiration of the applicable Section 409A period, all payments deferred pursuant to the preceding sentence will be paid in a lump sum to Advisor (or Advisor's estate or beneficiaries), and any remaining payments due to Advisor under this Agreement will be paid as otherwise provided herein. Advisor's right to receive any installment payments under this Agreement will be treated as a right to receive a series of separate payments for purposes of Section 409A.

17. Miscellaneous. This Agreement (together with all exhibits hereto), the Separation Agreement and the Proprietary Information Agreement, contain the entire understanding of the parties with respect to the matters contained herein, and supersedes all proposals and agreements, written or oral, and all other communications between the parties relating to the subject matter of this Agreement. This Agreement will be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts without regard to its conflict of laws rules that would result in the application of the laws of another jurisdiction. Advisor and the Company each hereby submits to the exclusive personal jurisdiction of the federal and state courts located in Massachusetts in connection with any disputes as to the meaning, effect, performance or validity of this Agreement or arising out of, related to, or in any way connected with, this Agreement or Advisor's relationship with the Company. This Agreement may not be modified or amended except in writing signed or executed by Advisor and the Company. In the event any provision of this Agreement is held to be unenforceable or invalid because it is overbroad or too far reaching, such provision will be deemed to be revised so that it applies to the maximum extent permitted by law.

[remainder of this page intentionally left blank]

IN WITNESS WHEREOF, the parties have caused this Agreement to be duly executed as of the date first set forth above.

ADVISOR

/s/ Roger J. Pomerantz
Name: Roger J. Pomerantz, M.D.
Address:

SERES THERAPEUTICS, INC.

By: /s/ Eric D. Shaff
Name: Eric D. Shaff
Title: President and CEO

EXHIBIT A
Equity Awards

Date of Grant	Total Shares Subject to Option	Exercise Price per Share	Vested Shares as of Effective Date	Vested and Unexercised as of Effective Date	Unvested Shares as of Effective Date
Nov. 6, 2013	220,000	$0.48	220,000	82,500	-
Aug. 7, 2014	1,675,751	$0.71	1,675,751	797,536	-
Feb. 1, 2016	176,500	$26.20	121,343*	121,343	-
Jan. 26, 2017	261,000	$9.89	114,187*	114,187	-
Jun. 13, 2019	15,000	$2.83	-	-	15,000

*Balance of grant was unvested and therefore canceled as of the separation date

EXHIBIT 21.1

SUBSIDIARIES OF SERES THERAPEUTICS, INC.

Legal Name of Subsidiary	Jurisdiction of Organization
Seres Therapeutics Securities Corporation	Massachusetts
Seres Therapeutics UK Limited	United Kingdom
Seres Therapeutics Netherlands B.V.	The Netherlands

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-230092, 333-223514, 333-210171 and 333-205253) and Form S-3 (No. 333-216735) of Seres Therapeutics, Inc. of our report dated March 2, 2020 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 2, 2020

Exhibit 31.1

CERTIFICATIONS

I, Eric D. Shaff, certify that:

1. I have reviewed this Annual Report on Form 10-K of Seres Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: March 2, 2020

By: /s/ Eric D. Shaff
Eric D. Shaff
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Marcus Chapman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Seres Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: March 2, 2020

By: /s/ Marcus Chapman
Marcus Chapman
Vice President, Finance and Principal Financial and Accounting Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Eric D. Shaff, President and Chief Executive Officer of Seres Therapeutics, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Annual Report on Form 10-K of the Company for the period ended December 31, 2019 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

March 2, 2020

/s/ Eric D. Shaff
Eric D. Shaff
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Marcus Chapman, Vice President, Finance and Principal Financial and Accounting Officer of Seres Therapeutics, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Annual Report on Form 10-K of the Company for the period ended December 31, 2019 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

March 2, 2020

/s/ Marcus Chapman
Marcus Chapman
Vice President, Finance and Principal Financial and Accounting Officer
(Principal Financial Officer)