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

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES**
For the Fiscal Year Ended December 31, 2018
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES AND EXCHANGE ACT OF 1934**
For the transition period from _____ to _____
Commission File Number: 001-38473

Evelo Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**46-5594527**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification No.)**

620 Memorial Drive,
Cambridge, Massachusetts 02139
(617) 577-0300
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	**NASDAQ Global Select Market**

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "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	x	Smaller reporting company	x
		Emerging growth company	x

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 Exchange Act.) Yes ☐ No x

As of June 30, 2018, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates was approximately $158.0 million based on the closing price of the registrant's common stock on June 30, 2018. The calculation excludes shares of the registrant's common stock held by current executive officers, directors and stockholders that the registrant has concluded are affiliates of the registrant. This determination of affiliate status is not a determination for other purposes.

As of February 8, 2019, there were 31,869,740 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2019 annual meeting of stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, and similar expressions.

Forward-looking statements include, but are not limited to, statements about:

- our status as a development-stage company and our expectation to incur losses in the future;
- our estimates regarding our expenses, future revenues, anticipated future capital requirements 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 and volunteers in clinical trials, timely and successfully complete those trials and receive necessary regulatory approvals;
- the timing of the progress and receipt of data from our clinical trials of EDP-1066, EDP-1815, EDP-1503 and the potential use of those candidates to treat various indications;
- our ability to establish our own manufacturing facilities and to receive or manufacture sufficient quantities of our product candidates;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- our ability to protect and enforce our intellectual property rights;
- federal, state, and foreign regulatory requirements, including FDA regulation of our product candidates;
- the timing of clinical trials and the likelihood of regulatory filings and approvals;
- our ability to obtain and retain key executives and attract and retain qualified personnel;
- our ability to successfully manage our growth; and
- developments relating to our competitors and our industry.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A. "Risk Factors," below and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions. Given these uncertainties, you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, our information may be incomplete or limited and we cannot guarantee future results. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs and consumer products, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources and we have not independently verified the data from third party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

In this Annual Report on Form 10-K, unless otherwise stated or as the context otherwise requires, references to "Evelo," "the Company," "we," "us," "our" and similar references refer to Evelo Biosciences Inc. and its wholly owned subsidiaries. This Annual Report on Form 10-K also contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PART I

Item 1. Business

Overview

Evelo Biosciences is discovering and developing potential therapies designed to engage immune cells in the small intestine to drive therapeutic immune effects throughout the body for the treatment of inflammatory diseases and cancers. The action of our therapies is based upon the observation that immune cells in the small intestine have a central role in controlling immune and biological activity throughout the body. We refer to this relationship as the gut-body network, which represents the connections of the gut to all organs and tissues. The centrality of the gut-body network to the immune system has only recently become appreciated, and modern medicine and research have largely overlooked the potential role of the gut-body network in treating disease. We believe that we have the potential to use the unexplored biology of the gut-body network to develop novel therapies that could transform the treatment of many major diseases, potentially driving profound benefits to patients and society.

The gut, and specifically the small intestine, is the largest part of the immune system. The small intestine is networked to almost all parts of the body by the lymphatic and nervous systems. As part of this connected network, which we call the gut-body network, the body's immune cells regularly traffic through the small intestine. The natural biology of the small intestine acts as an important regulator of the human immune system. Specific types of immune cells, such as dendritic cells and macrophages, are resident in the tissue of the small intestine. They sample specific contents in the interior of the small intestine, which is called the lumen. These immune cells then migrate to lymph nodes where they condition other important immune cells, including T-cells. These conditioned T-cells then travel throughout the body via the lymphatic system to impact disease. Microbes, in particular, have the ability to condition immune cells in the small intestine.

We are developing monoclonal microbials, a potential new modality of oral biologic medicines. Monoclonal microbials are orally-delivered pharmaceutical compositions of naturally-occurring, specific single strains of microbes. Our monoclonal microbials engage immune cells in the small intestine and drive changes in systemic biology without systemic exposure and without colonizing the gut in preclinical models. We and our collaborators have observed in preclinical studies that specific monoclonal microbials can downregulate or upregulate immune responses throughout the body by acting on the gut-body network with naturally-evolved pharmacology. We believe that monoclonal microbials exert their effects through interactions with immune cells in the small intestine. Based on our preclinical studies, we believe that our product candidates could improve the treatment of many diseases.

We have built a proprietary platform designed to develop monoclonal microbials as therapeutics. Our platform integrates tools and capabilities necessary to source, select, formulate, develop and manufacture monoclonal microbials as therapies. The efficiency of our platform has, in a relatively short period of time, allowed us to advance three product candidates into clinical trials for a range of inflammatory diseases and cancers.

We believe that monoclonal microbials have the potential to address patient need at all stages of disease. We believe this is due to their potentially superior characteristics over current therapies and the advantages of our platform, specifically:

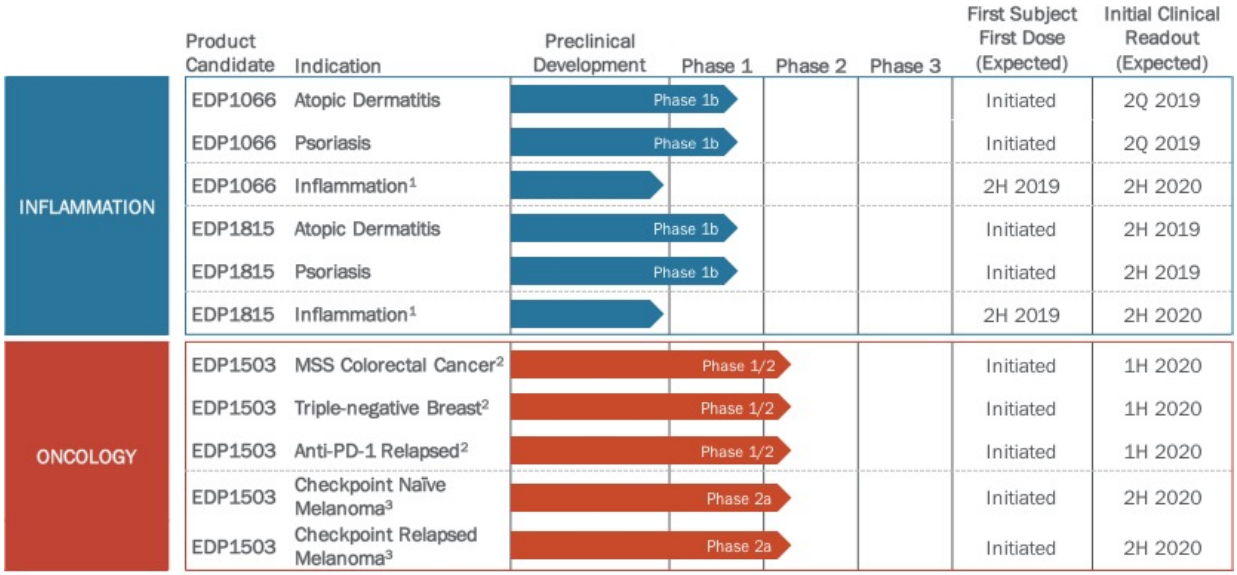
- We have observed activity in preclinical animal models for each of our lead product candidates. Each of our monoclonal microbials acts through multiple clinically relevant and validated biological pathways. By acting on multiple pathways simultaneously, we believe monoclonal microbials can impact disease in ways that are not addressable with current single-target therapies.
- We believe our monoclonal microbials are likely to be well tolerated given that they are naturally occurring, specific single strains of human microbes that engage immune cells in the small intestine and drive changes in systemic biology without systemic exposure and without colonizing the gut. If we validate this profile in clinical trials, we believe monoclonal microbials have the potential to be used at all stages of disease and in many more patients than current immunomodulatory drugs.
- Our development of monoclonal microbials has the potential to be more efficient than those of other therapeutic classes such as cell therapy, monoclonal antibodies and small molecules. We believe that monoclonal microbials do not require the lengthy target validation and compound discovery requirements of conventional drug discovery. Additionally, we believe the manufacture of monoclonal microbials is meaningfully faster than that of certain other biologics and can further accelerate our path to clinical testing and commercialization.

Our product development strategy is to evaluate a range of monoclonal microbials with different pharmacology in clinical trials across multiple diseases. The initial trials for our product candidates are expected to provide information on safety, tolerability, biomarkers of immune response at and beyond the site of disease and activity on exploratory clinical endpoints. This data may enable expansion into a broad range of clinical indications.

We initiated a clinical trial of our first monoclonal microbial candidate in inflammatory diseases, EDP1066, in April 2018, and initiated a clinical trial for our second inflammation candidate, EDP1815, in November 2018. We expect initial safety and tolerability data in the second quarter of 2019 for EDP1066 and the second half of 2019 for EDP1815. These trials are also evaluating exploratory endpoints of biomarkers of immune response and multiple clinical measures of disease.

We are also developing monoclonal microbial therapies in oncology. Our first oncology product candidate is EDP1503. We initiated our clinical trial of EDP1503 in combination with KEYTRUDA® (pembrolizumab) in multiple oncology indications in December 2018 and we expect to obtain initial clinical data during the first half of 2020. The University of Chicago is conducting a clinical trial with EDP1503 in combination with KEYTRUDA in patients with metastatic melanoma who are previously untreated or who have relapsed following treatment with an anti-PD-1 inhibitor. This trial dosed its first patient in January 2019 and initial clinical data is anticipated in the second half of 2020.

Our ongoing and planned clinical trials for our current product candidates are illustrated below.



Notes:

(1) We expect to advance EDP1815 and EDP1066 into additional inflammatory disease indications in the second half of 2019. We intend to finalize the indication selection decisions after data from the ongoing EDP1066 and EDP1815 clinical trials have been analyzed. Potential indications include asthma, psoriatic arthritis, rheumatoid arthritis and inflammatory bowel disease.

(2) The Phase 1/2 study of EDP1503 in combination with KEYTRUDA is being conducted in a clinical collaboration with Merck & Co, Inc, or Merck.

(3) The Phase 2a study of EDP1503 in combination with KEYTRUDA in melanoma is being conducted as an investigator-sponsored study by the University of Chicago.

Beyond our first set of product candidates, we have identified several other potential candidates from our discovery program, and we are continuing to invest in the discovery of additional potential candidates. We believe monoclonal microbials and our platform have broad potential utility beyond our initial therapeutic focus areas of inflammatory diseases and oncology, and we plan to explore many opportunities in which our platform has the potential to transform the treatment of disease.

Our Strategy

Our goal is to create and develop a new class of therapies that has the potential to transform the treatment of a broad range of diseases by focusing on the gut-body network.

Key elements of our strategy to achieve this goal are to:

- ***Explore the full potential of the gut-body network to create an expansive and diversified product portfolio.*** We believe the gut-body network has applicability across a range of disease areas and we are committed to pursuing the many opportunities in which our platform has the potential to transform the treatment of a broad range of diseases. Our initial focus is on inflammatory diseases and oncology, and we intend to expand into other disease areas, such as autoimmune diseases, respiratory diseases, neuro-inflammation and degeneration, liver diseases, type I diabetes, food allergy, neurobehavior, cardiovascular disease and diseases of metabolism.
- ***Develop best-in-class therapies to improve outcomes across various stages of disease.*** We intend to develop best-in-class orally-delivered therapies and intend to explore the potential of monoclonal microbials across the full spectrum of disease severity, not only in patients with severe or advanced disease. We intend to pursue what we believe to be the inherent advantages of monoclonal microbials to enable use in all stages of disease.
- ***Generate early clinical readouts with biomarker-driven validation to efficiently advance our product candidates.*** We have prioritized indications with ease of accessibility to tissue biopsies for biomarker analysis. We intend to use these biomarkers to clinically validate the immunological activity and dose of our monoclonal microbials and to guide subsequent clinical expansion and patient selection.
- ***Industrialize monoclonal microbials to advance and scale our platform.*** We plan to continue to invest in our platform, which integrates microbiology, immunology and computational biology capabilities. We intend to expand the diversity of our monoclonal microbial library and enhance our proprietary *in vitro* and *in vivo* models to optimize selection of our future product candidates. Our manufacturing processes are designed to ensure the quality and scalability of our products. We plan to continue to invest in novel methods for process development, manufacturing and formulation for our monoclonal microbials. Future plans include investment in clinical and commercial scale manufacturing. We plan to leverage the efficiency of our integrated capabilities to accelerate the clinical development of many product candidates.
- ***Strengthen and expand our intellectual property to protect our platform.*** We have exclusive rights to our technologies including issued composition of matter and method of use patents in the United States for our product candidates. We intend to diligently pursue patent protection for our scientific innovations and to maintain a strong and broad estate of patents and trade secrets in the United States and other geographies.
- ***Collaborate to realize the potential of the gut-body network and monoclonal microbials.*** We intend to continue to seek collaborations with academic groups, biotech and pharmaceutical companies to realize the value of our broad platform and extend the range of our development activities and disease areas in a timely and cost-effective manner. We plan to commercialize products in multiple geographies both on our own and with collaborators.

The Immune System and the Use of Immunotherapy in Disease

Immunology and Current Immunotherapy

The immune system consists of many different cell types that act together as a coordinated system constantly scanning for, identifying and responding to both human and microbial signals. Immune cells, including different types of T-cells, circulate throughout the body via the lymphatic system searching for signs of disease or infection. When this immune surveillance is functioning correctly, immune cells recognize and destroy both pathogens and cancer cells. However, when the immune system responds excessively, diseases such as psoriasis, rheumatoid arthritis, asthma, inflammatory bowel disease and multiple sclerosis can result. Conversely, an inadequate immune system response may allow various types of cancer to progress unchecked.

Advances in our understanding of how the immune system affects a broad spectrum of disease has resulted in the development of immunotherapies, which are medicines that reduce, suppress, elicit or amplify specific immune responses. Antibody-based immunotherapies for inflammatory diseases and oncology have fundamentally changed the treatment landscape for patients. For example, anti-TNFa antibodies are widely used to treat moderate to severe stages of many inflammatory diseases. In 2017, three of the five top selling drugs worldwide were anti-TNFa antibodies, with HUMIRA alone generating worldwide annual net sales of $18.4 billion. In oncology, checkpoint inhibitor antibodies, including those targeting the programmed cell death protein/ligand 1, or PD-1/PD-L1 pathways, block the tumor’s ability to suppress the immune response. They have improved the treatment of many cancers and are expected as a class to reach peak annual net sales of $30 billion by 2025. While existing immunotherapies have been successful in treating inflammatory diseases and oncology, there remains a substantial unmet need for a majority of patients.

Emergence of a New Paradigm in Immunotherapy

Until recently, immunotherapeutic approaches have largely ignored one of the body's naturally-evolved routine immunological processes and its associated immune organ—the gut, and specifically the small intestine. Immunomodulation through the small intestine has the potential to address certain limitations of current immunotherapies by acting on multiple naturally-evolved and clinically relevant pathways. We believe this novel approach presents advantages, including potentially minimizing adverse events, enhancing patient convenience and targeting multiple immune pathways simultaneously. We believe that a novel class of therapeutics with these attributes has the potential to be transformative in treating a broad range of immune-mediated diseases. Furthermore, we believe this approach could also expand the use of immunotherapies for the treatment of patients with earlier stages of disease.

The Gut-Body Network is Central to Human Biology and Immunology

The gut, and specifically the small intestine, is the largest part of the immune system. The small intestine is networked to almost all parts of the body by the lymphatic and nervous systems. As part of this connected network, which we call the gut-body network, the body's immune cells regularly traffic through the small intestine. The natural biology of the small intestine acts as an important regulator of the human immune system. Specific types of immune cells, such as dendritic cells and macrophages, are resident in the tissue of the small intestine. They sample specific contents in the interior of the small intestine, which is called the lumen. These immune cells then migrate to lymph nodes where they condition other important immune cells, including T-cells. These conditioned T-cells then travel throughout the body via the lymphatic system to impact disease. We believe the gut-body network provides an opportunity for gut-mediated immunomodulation throughout the body after oral delivery of products that remain physically restricted to the lumen and lymphoid tissues of the gut. As such, immunomodulation via the gut-body network may represent an underappreciated opportunity to condition T-cells to drive therapeutically relevant immune responses throughout the body.

The Gut-Body Network and Microbes

Microbes are single-cell organisms that have co-evolved with the human immune system throughout evolutionary history. Many human immune cells are programmed to sense and respond to microbes that they contact in the gut. Research in mucosal immunology has revealed that microbial interactions in the small intestine can drive activity on the gut-body network.

Multiple mechanisms for direct interactions between microbes and immune cells in the gut have been demonstrated. We believe that dendritic cells and macrophages in the lymphoid tissues of the gut are key target cells of immunomodulatory microbes, especially in the small intestine where the large gut surface area and thin and diffuse mucus layer allow for close contact between microbes and immune cells. Dendritic cells are a specialized type of immune cell that survey the body's tissues and present antigens to T-cells. Macrophages can take on many functional forms depending on the conditioning of their environment in the body and are important for both anti-inflammatory and anti-tumor immunity. Immune cells, such as dendritic cells and macrophages, can extend protrusions through junctions between epithelial cells in the lining of the small intestine. These protrusions come into direct contact with and sample the microbial contents of the gut lumen. These immune cells then migrate to mesenteric lymph nodes where they come into contact with T-cells. Dendritic cells and macrophages that have been primed by exposure to microbes in the gut condition T-cells and push them towards inflammatory or immunoregulatory activities depending on the specific strain of the original microbe. Conditioned T-cells continue to move through the body via the lymphatic system to other parts of the body where they may act in local tissue to modulate an immune response.

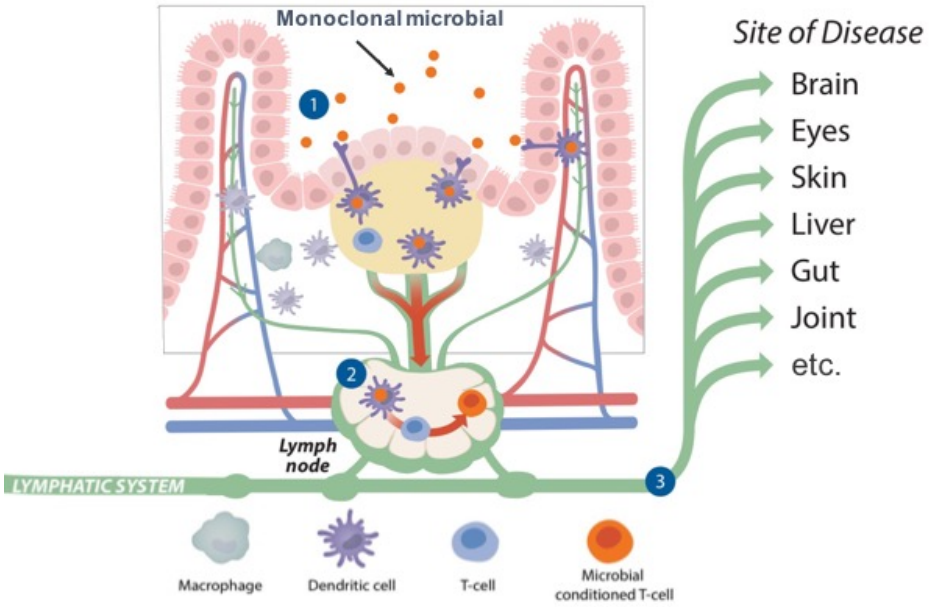


Figure 1: The small intestine and microbes. The small intestine is connected to many other parts of the body via the lymphatic system in green. The cross-section of the small intestine depicts (1) sampling of microbes in the gut by dendritic cells and macrophages, (2) conditioning of T-cells by dendritic cells and macrophages in the lymph node, and (3) migration of conditioned T-cells to other areas of the body.

Several of our academic collaborators have explored the functional consequences of the interactions between immune cells and single strains of microbes in the gut. Veena Taneja, Ph.D. and Joseph Murray M.D. of Mayo Clinic showed that an orally-administered strain of *Prevotella histicola* modulated immune function in mouse models of rheumatoid arthritis and multiple sclerosis. In the field of immuno-oncology, Thomas Gajewski, M.D., Ph.D. and his group at the University of Chicago conducted an experiment in which a single strain of orally-administered *Bifidobacterium* had equivalent activity to an anti-PD-L1 antibody and additive activity in combination in a mouse model of melanoma. We believe these and other examples from the academic literature support our theory that single strains of microbes can act on the gut-body network to suppress or activate immune responses throughout the body.

Monoclonal Microbials as a Potential New Class of Oral Biologic Medicines

Evelo was founded to discover and develop therapies that act on the gut-body network. We aim to develop therapies based on our observations on the central role of the small intestine in modulating immune activity throughout the body and the equally important role of microbes as key modulators of the gut-body network.

We believe that now is an opportune time to translate observations from the naturally-evolved gut-body network into immunotherapies to treat many diseases. While microbes have evolved with humans throughout evolutionary history, until recently, the scientific community lacked the necessary tools to deconstruct and analyze the complex interactions between microbes, the immune system, and the gut-body network. Advances in next-generation sequencing, immunology and computational analyses of large microbial datasets have led to a better understanding of the microbes that live on and inside humans and have provided critical insights into their specific functions and mechanisms. In turn, these insights have allowed us to develop the tools necessary to isolate, select, and develop specific microbes that have historically been difficult to culture. This extends from the initial stages of microbial isolation to the final stages of monoclonal microbial manufacturing. We have developed proprietary insights and tools that enhance our ability to produce pharmaceutical compositions of monoclonal microbials at scale. This allows us to deliver potentially therapeutic doses of our appropriately formulated select strain.

We are developing monoclonal microbials to engage immune cells in the small intestine and drive changes in systemic biology by either downregulating or upregulating immune responses for the treatment of disease. Monoclonal microbials are orally-delivered pharmaceutical compositions of specific strains of microbes derived from a single clone of naturally-occurring microbes that we believe can interact with and modulate the human immune system.

We believe key features and advantages of our monoclonal microbial product candidates are:

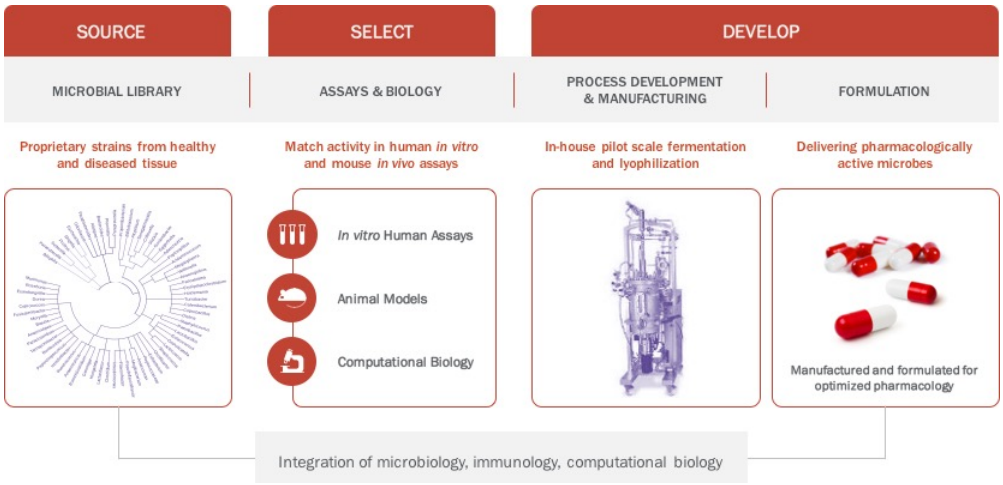
- ***Single strain.*** Our product candidates are pharmaceutical compositions of single strain monoclonal microbials that we have selected for their specific pharmacology. Our preclinical data suggests that various strains of microbes within the same genus or species can have vastly different immunomodulatory properties. We extensively characterize the ability of our product candidates to elicit a desired immunomodulatory effect. We also believe monoclonal microbials have manufacturing advantages over biologics.
- ***Orally-administered formulation.*** We intend to deliver our initial product candidates orally in formulations designed for targeted release of the monoclonal microbials in the small intestine. Patients typically prefer oral administration to intravenous infusion, subcutaneous injection, and topical administration, which we believe will facilitate the adoption of our product candidates, if approved.
- ***Limited systemic exposure.*** In preclinical studies, we observed that monoclonal microbials had limited systemic exposure, that they cleared from the gut within 24 to 48 hours and that colonization was not required for beneficial activity. We believe that these factors suggest that monoclonal microbials may have limited systemic off-target side-effects.
- ***Action on multiple clinically relevant and validated pathways.*** Our preclinical data has shown that monoclonal microbials may act simultaneously on multiple clinically relevant and validated biological pathways. The diseases we intend to treat are multifactorial, and we believe that our potential therapies will be advantageous over single-target treatments.
- ***Manufacturing capabilities.*** Although manufacturing of monoclonal microbials is complex, we believe that we have developed capabilities that will accelerate the process from strain identification to clinical supply. We have been able to manufacture monoclonal microbials in a relatively short timeframe compared to other biologic therapies, which we believe may accelerate our speed into the clinic. Additionally, we believe that we may be able to cost-effectively manufacture monoclonal microbials.

Given these expected features, we believe that monoclonal microbial therapies may have a number of advantages in comparison to other immunotherapies such as antibodies, cell therapies and small molecules.

Our Monoclonal Microbial Platform

We have developed an integrated platform designed to identify individual strains of microbes capable of modulating the immune system by acting on the gut-body network when administered at pharmacologically active doses. We use the process development and formulation capabilities of our platform to develop selected microbes as product candidates.

Our proprietary monoclonal microbial platform is comprised of the following four key areas:



Monoclonal microbial library. We have assembled a proprietary library of diverse strains of microbes. Microbes in our library are isolated from natural sources, including samples from healthy and diseased humans, in order to benefit from the co-evolution of microbes and the human immune system. To increase our probability of finding microbes with potent immunomodulatory activity, we sample from body sites where microbes interact with the immune system, such as gut tissues. We also have bolstered and continue to add to our library through selective licensing agreements and collaborations with academic partners.

***Assays and biology*.** The proprietary tools within our platform are designed to efficiently identify and extensively characterize our monoclonal microbials through a series of *in vitro*, *in vivo* and *ex vivo* assays. We have constructed our proprietary *in vitro* assays to simulate the complex interactions between microbes and the human immune system, allowing us to evaluate the immunological activity of each microbe in a relevant experimental system. Our *in vitro* assays are capable of screening hundreds of microbes in parallel and producing more than 150 data points per strain, including levels of pro-inflammatory and anti-inflammatory cytokines and chemokines. This assists our comprehensive selection process to identify select candidates for testing in disease-relevant animal models. By conducting our *in vitro* assays in both mouse and human immune cells, we add to our mechanistic understanding. We believe this increases the probability of translation of preclinical *in vivo* results to the clinic.

Process development and manufacturing. Process development and manufacturing are critical for the translation of monoclonal microbials into therapies. Our expertise and investments in pilot scale manufacturing have allowed us to mitigate challenges inherent to monoclonal microbial manufacturing at clinical scale. Major challenges include: limited understanding and characterization of applicable microbes; strict anaerobic growth conditions required by certain microbes, many of which have never before been fermented; and temperature and oxygen sensitivities that affect downstream processing. We believe that our approach to these challenges may enable us to accelerate the process from strain identification to clinical supply.

Process development is integrated into our research activities, combining discovery and downstream development. We have achieved control of quality, identity, purity, and potency throughout the process of strain selection, fermentation, formulation, and pharmacology, with high yield. Importantly, our manufacturing processes enable us to produce a drug substance that is pharmacologically active in the form of a lyophilized powder, which is suitable for cGMP production. For each of our three initial clinical product candidates, we have observed therapeutic activity in lyophilized powder form in relevant preclinical mouse models.

Non-replicating monoclonal microbials. The activity of our monoclonal microbials observed in preclinical studies has been driven by engagement with and modification of immune cells in the small intestine. This activity has not been reliant on engraftment (or colonization) as we have observed that our monoclonal microbials passed through the gut and did not distribute around the body or engraft in the gut. Furthermore, the observed preclinical activity of our monoclonal microbials has been independent of their ability to replicate. From this significant observation, we believe that monoclonal microbial activity is likely driven by recognition of structural motifs by immune cells in the small intestine. Our candidate selection process may include an additional manufacturing step for our monoclonal microbial candidates to develop them as non-replicating product candidates.

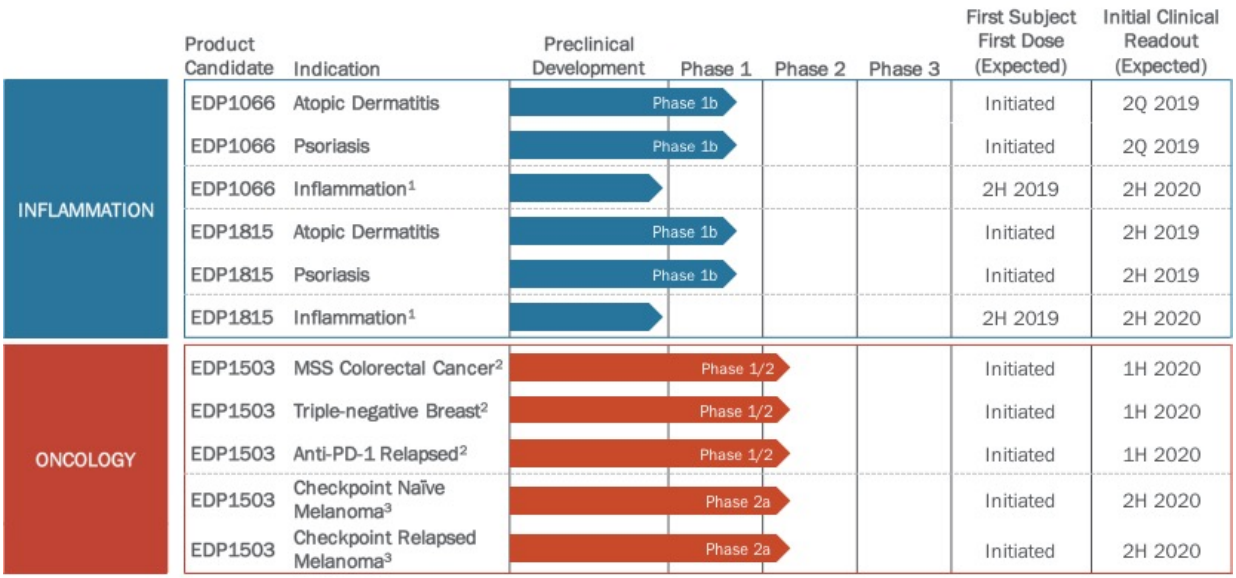
***Formulation*.** Our first clinical product candidates are formulated as capsules containing lyophilized powder for targeted release in the gut. We aim to provide patients with oral therapies with limited off-target effects that preserve the therapeutic activity observed in preclinical studies. We intend to continuously invest in formulation to evaluate optimal delivery of our product candidates and enhance their ability to act on the gut-body network.

Product Development Strategy and Portfolio

We are advancing monoclonal microbials to potentially treat a spectrum of immune-mediated diseases with an initial focus on inflammatory diseases and oncology. We expect our initial clinical trials for our product candidates to provide information on safety, tolerability and biomarkers of immune response in multiple indications with different pathologies and sites of disease. This may allow for expansion into a broad range of clinical indications, which could enable us to capture the breadth of clinical value.

Beyond our first wave of product candidates in inflammatory diseases and oncology, we are continuing to invest in the discovery of new candidates to build a deep pipeline across a wide range of diseases and tissue types to leverage the broad potential of our platform. We also intend to opportunistically collaborate to expand indications and accelerate development of programs where collaborators can contribute further disease-specific expertise to our platform.

Our ongoing and planned clinical trials for our current product candidates are illustrated below.



Notes:

(1) We expect to advance EDP1815 and EDP1066 into additional inflammatory disease indications in the second half of 2019. We intend to finalize the indication selection decisions after data from the ongoing EDP1066 and EDP1815 clinical trials have been analyzed. Potential indications include asthma, psoriatic arthritis, rheumatoid arthritis and inflammatory bowel disease.

(2) The Phase 1/2 study of EDP1503 in combination with KEYTRUDA is being conducted in a clinical collaboration with Merck.

(3) The Phase 2a study of EDP1503 in combination with KEYTRUDA in melanoma is being conducted as an investigator-sponsored study by the University of Chicago.

Inflammatory Diseases Portfolio

We have advanced two monoclonal microbials, EDP1066 and EDP1815, into the clinic for treatment of inflammatory diseases. In December 2018, we nominated a third monoclonal microbial candidate for inflammatory diseases, EDP1867. EDP1867 is the first non-replicating monoclonal microbial in Evelo's pipeline.

Clinical Studies - EDP1066

EDP1066-001 is a Phase 1b placebo-controlled dose-escalating safety and tolerability clinical study of EDP1066 in approximately 36 healthy volunteers and up to 96 patients with psoriasis or atopic dermatitis. It will test a range of daily doses in healthy volunteers over 14 days and in patients over 28 days. We are evaluating safety and tolerability as the primary endpoint, as well as a variety of exploratory endpoints including multiple clinical measures of disease and pharmacodynamic markers, including biomarker signals from paired biopsies of affected skin in patients. We initiated this clinical study in April 2018 and we expect that initial clinical data will be available in the second quarter of 2019.

Dosing of EDP1066 in healthy volunteer cohorts of the Phase 1b trial has been completed, data has been reviewed by the trial's safety review committee and we have proceeded as planned into cohorts of patients with psoriasis or atopic dermatitis.

We plan to initiate an immuno-pharmacology clinical study in healthy volunteers in the first half of 2019. This study is designed to explore additional doses and formulations ahead of potential later stage clinical trials.

Clinical Studies - EDP1815

EDP1815-101 is a similar Phase 1b placebo-controlled dose-escalating safety and tolerability clinical study of our second inflammatory disease candidate, EDP1815, in approximately 24 healthy volunteers and up to 108 patients with mild-to-moderate psoriasis and atopic dermatitis. We are evaluating safety and tolerability as the primary endpoint, as well as a variety of exploratory endpoints including clinical measures of disease and pharmacodynamic markers, including biomarker signals

from paired biopsies of affected skin in patients. We initiated this clinical study in November 2018 and we expect initial clinical data will be available for this trial in the second half of 2019.

We expect that data from these initial studies of EDP1066 and EDP1815, which are both being conducted in the United Kingdom, will be accepted by regulatory agencies in major regions, including the United States, according to guidance from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH. We intend to initiate future additional trials in the United States and other countries.

Inflammation Development Strategy

We selected mild-to-moderate psoriasis and atopic dermatitis as indications for first-in-human studies based upon our preclinical data, need in large patient populations, the ease of access to patient tissue for biomarker analysis and the speed of clinical data readout. Patients with mild-to-moderate disease represent between 80% and 90% of the patient population, which is estimated to represent more than 25 million people in the United States. We believe these patients are underserved by current treatments, including steroids, which either inadequately control inflammation or are not safe for long-term use. The majority of novel therapies, including next generation biologics targeting IL-17, IL-23 or IL4RA, two anti-inflammatory cytokines and a cytokine receptor, are only approved for patients with moderate-to-severe disease. Even in the moderate to severe setting, a large proportion of eligible patients do not receive biologics, instead opting for topicals or oral systemic therapies. These factors suggest a need for a novel therapeutic option that is well tolerated, effective and convenient.

We believe the potential profiles of our monoclonal microbial product candidates may be well suited to treat pediatric patients as well as patients at earlier stages of inflammatory diseases than current therapies. Particularly in atopic dermatitis, many patients are infants or young children who have fewer therapy options than adult patients. If our product candidates demonstrate safety and tolerability and limited adverse events in clinical trials, they could open up a larger market than the one currently treated by biologics. If proof-of-concept in mild-to-moderate patients is established, we also intend to broaden our studies to treat patients with moderate-to-severe inflammation, potentially expanding this market opportunity further.

In preclinical mouse models, our inflammatory disease product candidates reduced systemic inflammation with equal or better activity than current standard of care therapies. We believe that this observation may translate to broad activity across a variety of inflammatory diseases. We have produced preclinical data in distinct mouse models that are representative of different biologies, suggesting that single monoclonal microbials may impact multiple immune pathways.

T-cells of the Th1 or Th17 type are implicated in psoriasis, joint inflammatory diseases and neuroinflammation, while T-cells of the Th2 type are more important for atopies and allergic diseases. With current cytokine-directed therapies, agents are targeted towards a specific cytokine to influence one or more of these pathways. For instance, Th1-driven inflammation can be controlled by TNFa or IL-6 inhibition, Th17-driven inflammation can be controlled by IL-17 or IL-23 inhibition, and Th-2 driven inflammation can be controlled by IL-4 or IL-13 inhibition.

Each of our inflammatory disease monoclonal microbial candidates, EDP1066 and EDP1815, have demonstrated the ability to simultaneously impact multiple of these pathways and associated cytokines in preclinical assays, suggesting that they may have broader applicability than individual cytokine-directed therapies. Separately, there are additional anti-inflammatory cytokines such as IL-10 and IL-27 that can inhibit the production of certain pro-inflammatory cytokines. Certain of our product candidates induced increased production of IL-10 and IL-27 in preclinical assays.

Based on the results of the ongoing Phase 1b clinical trials of EDP1066 and EDP1815 we may advance these product candidates into later stage trials in atopic dermatitis or psoriasis and also expand into new inflammatory disease indications in the second half of 2019. Biomarker data from these initial clinical studies may support expansion to mechanistically similar inflammatory diseases. For example, early proof-of-concept in atopic dermatitis could support expansion to other atopies and Th2-driven diseases, including asthma and food allergy and early proof-of-concept in psoriasis could support expansion into other Th17-driven diseases such as psoriatic arthritis and axial spondylarthritis. We may also study EDP1066 and EDP1815 in diseases such as rheumatoid arthritis and inflammatory bowel disease.

EDP1066 Preclinical Data

EDP1066 is a monoclonal microbial product candidate being developed to treat inflammatory diseases. We selected EDP1066 for its *in vitro* profile in human immune cell assays combined with its anti-inflammatory activity in a range of mouse inflammation models. In preclinical studies, orally-administered EDP1066 acted on the gut-body network to modulate systemic immune responses in multiple mechanistically and anatomically varied *in vivo* models, including the Th1-mediated delayed type hypersensitivity, or DTH, model, which measures skin inflammation after antigen challenge, the Th2-mediated 2,4-dinitrofluorobenzene, or DNFB, skin inflammation model, and the dextran-sodium sulfate, or DSS, model of immune-cell mediated gut inflammation.

In Vitro Assays

Our *in vitro* assays measure the effects of individual strains of bacteria on human immune cells and test several dozen immunomodulatory characteristics. A representative example of a human *in vitro* assay data for EDP1066 is shown in Figure 3. Plotted to show IL-10 and IL-27 cytokines produced, each circle on the plot represents a different individual strain from our microbial library. The size of each circle represents the magnitude of pro-inflammatory chemokine CXCL10. Each strain was co-cultured with human macrophages, an immune cell type that is abundant in the gut and is a known controller of inflammation. In the assay, EDP1066 was a high inducer of anti-inflammatory cytokines, IL-10 and IL-27. Conversely, EDP1066 did not significantly induce CXCL10, a pro-inflammatory mediator, in the assay. We believe these characteristics could be suitable for an anti-inflammatory agent.

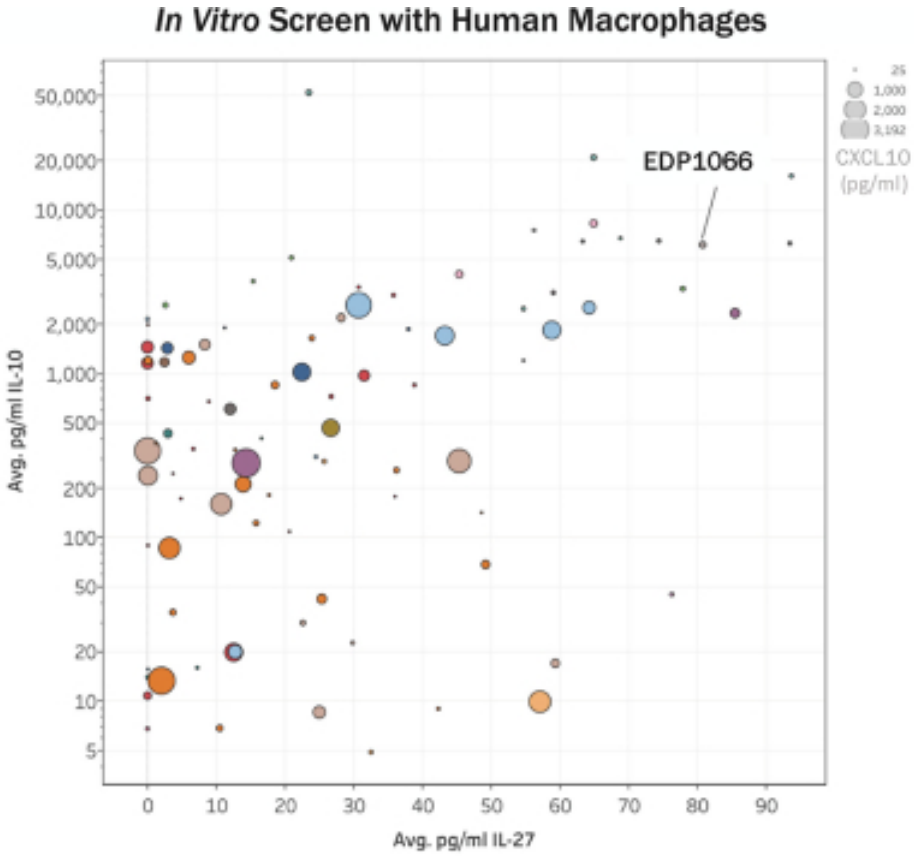


Figure 3: Production of cytokines by human macrophages after co-culture with monoclonal microbials. Macrophages purified from human peripheral blood mononuclear cells were co-cultured with 95 individual monoclonal microbials (each represented by a circle). Cytokines produced by macrophages were measured. EDP1066 induced higher levels of IL-10 and IL-27, relative to other monoclonal microbials screened. EDP1066 also induced relatively lower levels of pro-inflammatory chemokine, CXCL10 (represented by the size of the circle).

Preclinical DTH Mouse Models

DTH in a mouse is a well-established model of Th1-driven inflammation resulting from pro-inflammatory antigen-specific T-cells. In the mouse model depicted in Figure 4, daily oral administration of EDP1066 reduced skin inflammation in response to antigen challenge. In the model, immunomodulation by EDP1066 on the gut-body network was as active as a therapeutic dose of the steroid, dexamethasone. The DTH model also suggests that individual monoclonal microbials may exert differentiated effects on the immune system. For example, a control monoclonal microbial, from the same species as EDP1066 did not reduce inflammation. In the model, orally-delivered and gut-restricted EDP1066 was able to induce certain systemic effects in a mouse as depicted below. We believe this data supports our development of EDP1066 in human diseases with Th1-driven systemic inflammation, starting with psoriasis and arthritides.

P-value is a conventional statistical method for measuring the statistical significance of experimental results. A p-value of less than 0.05 is generally considered to represent statistical significance, meaning that there is a less than five percent likelihood that the observed results occurred by chance. In the figure below and all subsequent figures where p-values are included, a p-value of less than 0.05 is represented by “*”. P-values of less than 0.01 or less than 0.001 are represented by “**”

or "***," respectively, and are considered to have higher statistical significance. Unless otherwise specified, the p-values shown represent a comparison of each treatment group to the vehicle or control group.

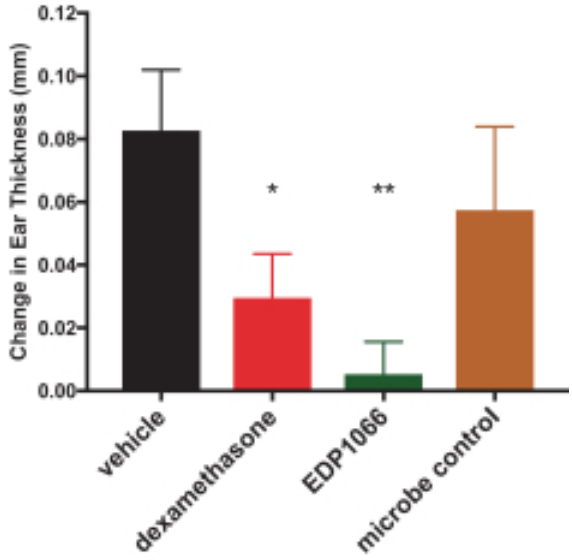


Figure 4: EDP1066 reduced skin inflammation in a DTH mouse model. Mice were sensitized with a foreign antigen, chicken ovalbumin, and Complete Freund's Adjuvant subcutaneously at day zero. Mice were orally-dosed for 10 days from sensitization on day zero with either vehicle, dexamethasone (1 mg/kg), EDP1066, or a microbe control. Eight days after sensitization, mice were given an intradermal ear challenge with ovalbumin. Change in ear thickness, a measure of skin inflammation, was evaluated 48 hours post-challenge. Treatment with EDP1066 resulted in greater reduction in inflammation relative to all other groups. (Significance relative to vehicle: ** = p<0.01, * = p<0.05, ns = not significant)

In a separate preclinical DTH study, we dosed mice with EDP1066 across a range of doses. In this experiment, the activity of EDP1066 was dose-dependent within a 100-fold dose range. Ascending doses varied by a factor of 10. At the two higher doses, change in ear thickness, a measure of skin inflammation, was comparable to treatment with dexamethasone. Because therapeutic activity is not further increased between these two higher doses, we believe that we are at a dose plateau indicative of maximum therapeutic activity in mice. We have used this information to determine the dosing range for our first-in-human clinical study.

Preclinical DNFB Mouse Model

We assessed the therapeutic activity of EDP1066 in an *in vivo* mouse model using DNFB skin challenge. DNFB causes a chronic T-cell and cytokine-dependent skin inflammation resembling atopic dermatitis in human patients. This model is dependent on the Th2 class of T-cells, which is associated with atopic and allergic conditions. In the study, we compared daily oral administration of EDP1066 to daily topical administration of clobetasol, a highly potent steroid cream applied to the skin in patients with atopic dermatitis and psoriasis. In the model, we observed no inflammation in the EDP1066 group eight days after the DNFB challenge, whereas there was not a significant difference between clobetasol and the control. At day 15, inflammation scores for clobetasol and EDP1066 were similar. We believe this activity supports our plan to target Th2-mediated diseases with initial clinical testing in atopic dermatitis.

Preclinical DSS Mouse Model

We also tested EDP1066 in a mouse model of gut inflammation. Dextran sodium sulfate, or DSS, was administered in the drinking water of mice, resulting in immune-mediated gut inflammation and significant weight loss. Anti-IL-12/23 antibodies are often used as a positive control in this model. Daily oral administration of EDP1066 reduced weight loss and signs of inflammation in this model, as shown in Figure 5. Additionally, EDP1066 was more active than anti-IL-12/23, which is a mouse analog that acts on the same pathway as ustekinumab (STELARA), an approved therapy for inflammatory bowel disease. A closely related strain from the same species as EDP1066 was used as a microbe control and demonstrated no therapeutic benefit in this model. We believe the data observed in this model suggests the potential role of EDP1066 in controlling gut inflammation, which is important for IBD.

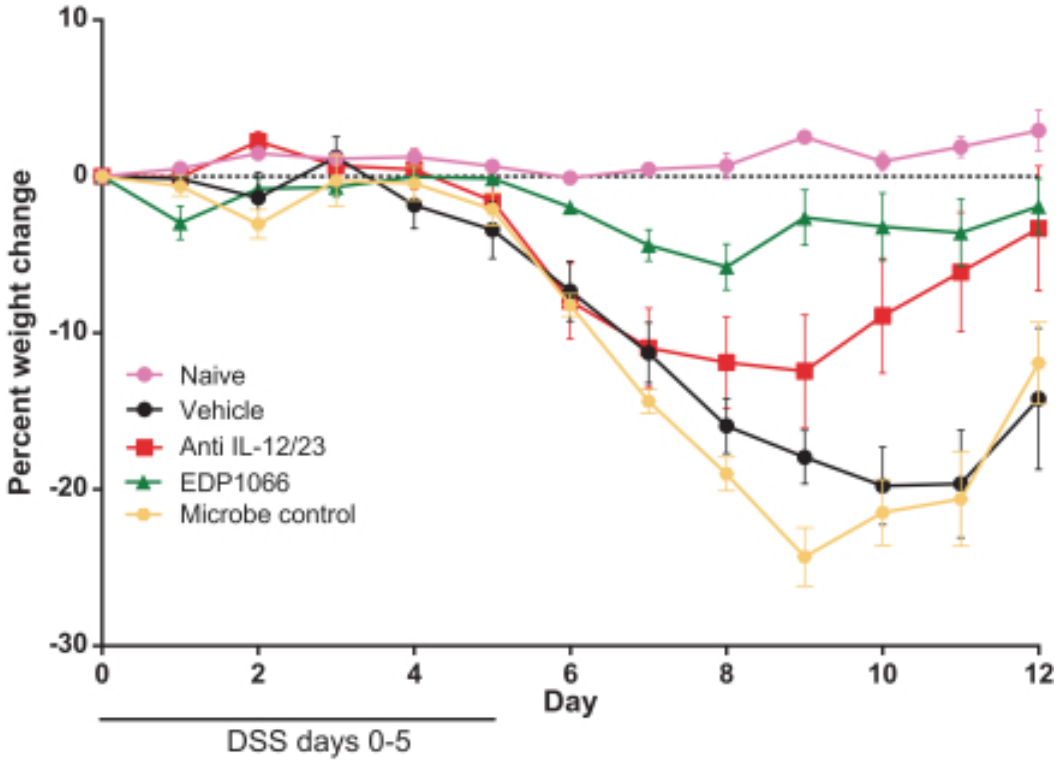


Figure 5: EDP1066 reduced weight loss in a mouse model of colitis. Dextran sodium sulfate (DSS) was administered to mice in drinking water from days 0-5. Mice were dosed daily with oral vehicle, oral EDP1066, oral microbe control, or anti-IL-12/23 (twice weekly intra-peritoneally). Mice treated with EDP1066 exhibited less weight loss compared to mice in vehicle, anti-IL-12/23 and microbe control groups.

EDP1815 Preclinical Data

EDP1815 is our second monoclonal microbial product candidate that is being developed to treat inflammatory diseases. In preclinical testing, EDP1815 has exhibited a different set of biological activities than EDP1066. In preclinical studies, EDP1815 has shown immunomodulatory activity on human immune cells and anti-inflammatory activity in many discrete tissues, including skin, joints, gut and the central nervous system after oral delivery in mouse models.

In Vitro Assays

Data from a representative example of a human *in vitro* assay for EDP1815 are shown in Figure 6. In the *in vitro* assay, human macrophages were pre-conditioned with lipopolysaccharide, or LPS, and interferon gamma, or IFNg, for 24 hours to put them into a strongly pro-inflammatory state. These pre-conditioned human macrophages were then co-cultured with various microbes for another 24 hours to determine their effects on macrophage inflammatory activity. EDP1815 induced production of the anti-inflammatory cytokine IL-10.

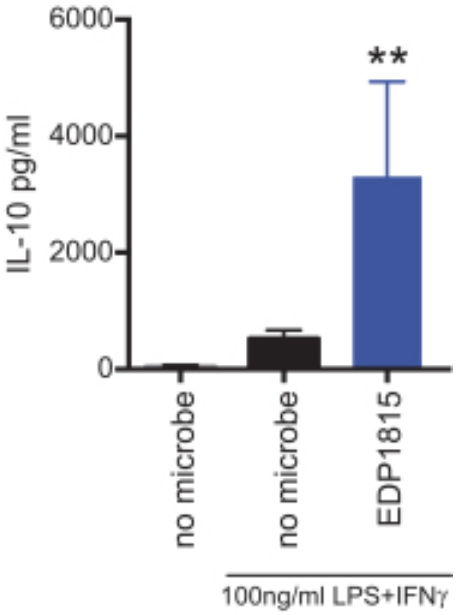


Figure 6: EDP1815 stimulated IL-10 production by human macrophages. Human macrophages were purified from peripheral blood mononuclear cells and pre-conditioned to a pro-inflammatory state with LPS and IFNg. Pre-conditioned macrophages co-cultured with EDP1815 produced significantly higher levels of IL-10 compared to a pre-conditioned control alone (= p<0.01).**

Preclinical DTH Mouse Model

We also tested EDP1815 in a DTH mouse model of Th1-driven skin inflammation relative to dexamethasone, a steroid, and fingolimod (GILENYA), a potent inhibitor of T-cell trafficking which is an approved therapy for multiple sclerosis. Results of the study, represented in Figure 7, show that suppression of inflammation by EDP1815 was comparable to dexamethasone and fingolimod. The dose of fingolimod used in this study was higher than the equivalent dose level in humans that would be used for treatment. Moreover, doses of EDP1815 within a 10-fold range were comparable to fingolimod. Because higher doses of EDP1815 did not further increase therapeutic effect, we believe we achieved a dose plateau for maximum therapeutic activity in mice. We plan to use this information to calculate the dosing range for our first-in-human clinical study. We believe the data from this preclinical study may be supportive of development efforts in human diseases with Th1-driven inflammation, starting with psoriasis and arthritides.

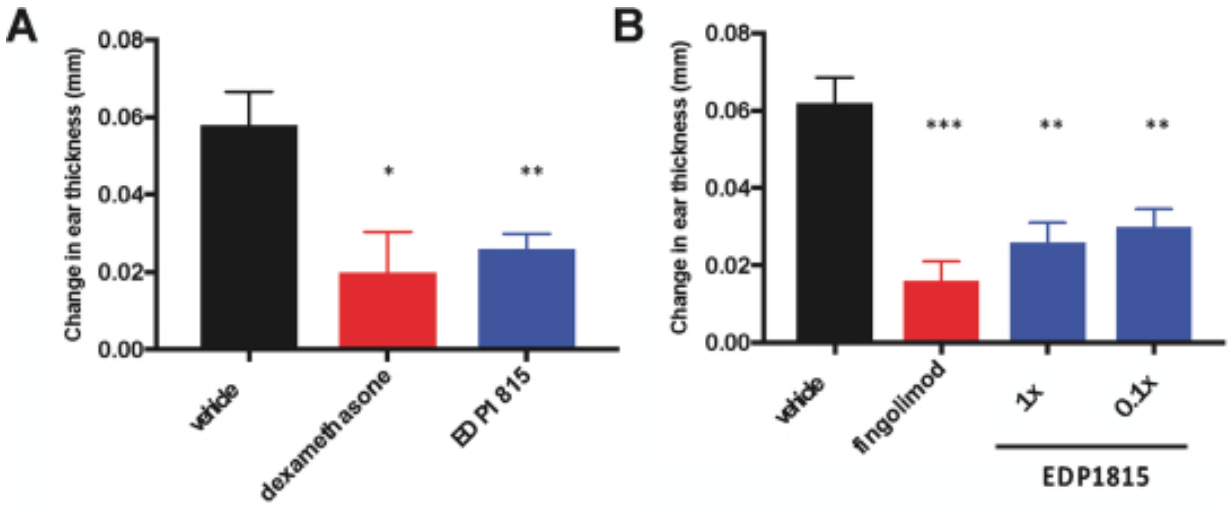


Figure 7: EDP1815 reduced skin inflammation in DTH mouse models. Mice were sensitized with a foreign antigen, keyhole limpet hemocyanin, and Complete Freund's Adjuvant subcutaneously at day zero. Mice were orally-dosed for 10 days from sensitization on day zero with (A) vehicle, dexamethasone (one mg/kg), or EDP1815, or (B) vehicle, fingolimod (supratherapeutic. dose of three mg/kg), or doses of EDP1815 within a 10-fold range. Eight days after sensitization, mice were given an intradermal ear challenge with KLH. Change in ear thickness, a measure of skin inflammation, was evaluated 24 hours post-challenge. Treatment with EDP1815 resulted in greater reduction in inflammation relative to all other groups. (Significance relative to vehicle: *** = p<0.001, ** = p<0.01, * = p<0.05)

Preclinical CIA Mouse Model

Our collaborators at Mayo Clinic observed therapeutic activity of EDP1815 in a mouse model of collagen-induced arthritis, or CIA, which is driven by a Th17 inflammatory response. In this model, CIA mice were conditioned to have autoimmune responses to their own collagen. This is intended to result in the destruction of the joints and mimic human arthritides, including rheumatoid arthritis. In the study, both therapeutic and prophylactic oral administration of EDP1815 significantly reduced disease incidence and severity, as shown in Figure 8 from our collaborators at Mayo Clinic.

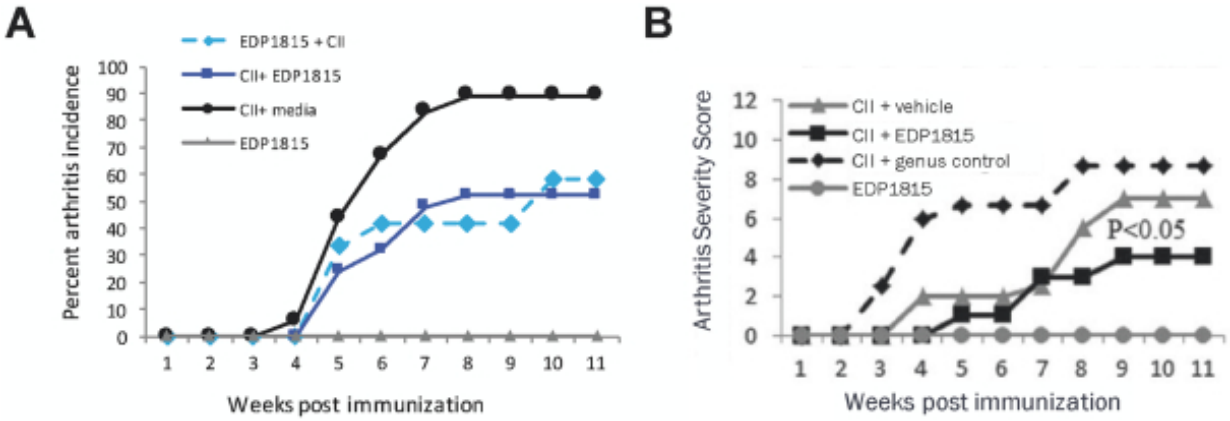


Figure 8: EDP1815 reduced arthritis incidence and severity in a mouse model of rheumatoid arthritis. Inflammatory arthritis was induced in DQ8 mice by immunization with type II collagen, or CII. Mice were treated with 100 microliters of EDP1815 every other day either before or after arthritis induction. Treatment was initiated either 10 days prior (EDP1815 + CII – prophylactic) or two weeks after CIA induction (CII + EDP1815 – therapeutic), and continued for six weeks post-immunization. (A) Both prophylactic and therapeutic dosing of EDP1815 resulted in a lower percentage of arthritis incidence compared to treatment with vehicle. A control using EDP1815 alone, without immunization with CII, showed no arthritis. (B) Arthritis severity score was also measured over time. Therapeutic treatment with EDP1815 (CII + EDP1815) significantly reduced (p<0.05) arthritis severity score relative to control (CII + vehicle). A separate control with a microbe from the same genus as EDP1815 was used (CII + genus control) and did not improve arthritis severity score. Reprinted from Marietta et al. 2016. Arthritis and Rheumatology 68(12): 2878-2888 with permission from Wiley.

Although EDP1815 remained physically restricted to the gut and associated lymphoid tissue in our biodistribution studies, our collaborators at Mayo Clinic observed its immunomodulatory activity throughout the body in mouse models. Blood samples were taken from CIA mice to determine the effects of treatment on circulating levels of immune biomarkers. As shown in Figure 9 from our collaborators at Mayo Clinic, cytokine profiling from serum of treated mice revealed that oral administration of EDP1815 resulted in reduced levels of IL-13 and IL-17, which are relevant to diseases of Th2 and Th17 inflammation, respectively. We believe the data suggests that EDP1815 may be able to treat inflammatory diseases driven by both of these pathways.

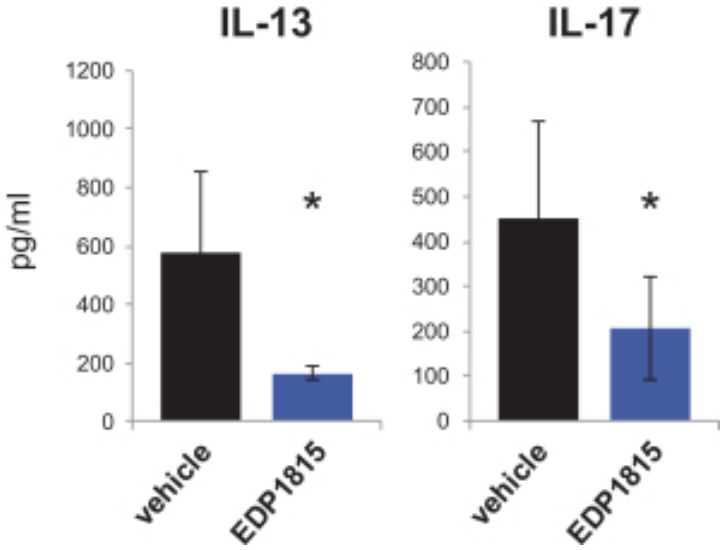


Figure 9: Oral administration of EDP1815 reduced levels of inflammatory serum cytokines. Levels of serum cytokines were evaluated in DQ8 mice immunized with type II collagen and treated with either EDP1815 or with vehicle. IL-13 and IL-17 cytokine levels were significantly reduced in the serum of EDP1815-treated mice compared to mice treated with vehicle. (Significance relevant to vehicle: * = p<0.05) Reprinted from Marietta et al. 2016. Arthritis and Rheumatology 68(12): 2878-2888 with permission from Wiley.

Preclinical EAE Mouse Model

In addition, our collaborators at Mayo Clinic tested EDP1815 in a mouse model of experimental autoimmune encephalomyelitis, or EAE. This is a model of antigen-specific Th17-driven neuro-inflammation. In the study, mice were immunized with myelin peptide. Clinical inflammation was then monitored and scored for a 30-day period. The data from the EAE model in Figure 10 from our collaborators at Mayo Clinic show that oral administration of EDP1815 significantly suppressed disease scores, which is the standard measurement for severity of paralysis in this model. These results were strain dependent—a genus control and two Gram-negative bacterial controls did not result in lower clinical disease scores.

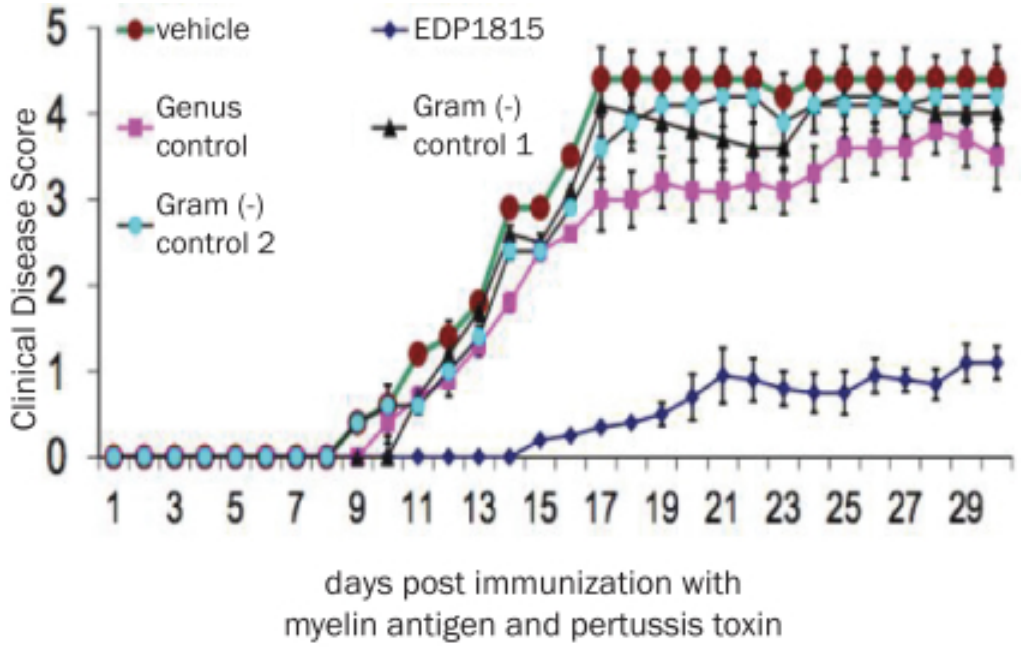


Figure 10: EDP1815 reduced disease scores in a mouse model of experimental autoimmune encephalomyelitis, or EAE. HLA-DR3.DQ8 mice were immunized with myelin peptide PLP91-110 at day zero and were orally-dosed with either vehicle, EDP1815, or other microbe controls starting on day seven. Treatment was continued every other day for a total of seven doses. EDP1815-treated mice exhibited lower daily mean clinical scores compared with mice treated with vehicle or microbe controls.

We believe that data in the above model suggests that EDP1815 anti-inflammatory activity is mediated through the Th17 pathway. Spleen cells were extracted from animals in the study and restimulated *ex vivo* with myelin to recapitulate the inflammatory response that causes disease. The results shown in Figure 11 from our collaborators at Mayo Clinic suggest that EDP1815 treatment induced an anti-inflammatory response in immune cells outside the gut, marked by downregulated IL-17 and IFNg and upregulated IL-10. We believe this further substantiates the potential role of EDP1815 in controlling Th17-driven neuroinflammation, which is relevant to multiple sclerosis. We believe this ability to impact systemic inflammation and inhibit IL-17 outside of the gut may be relevant to other Th17-driven human diseases, such as psoriasis.

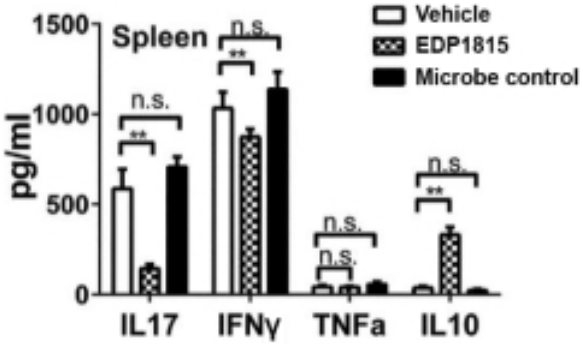


Figure 11: Splenocytes from EAE mice treated with EDP1815 produced an anti-inflammatory cytokine profile. Splenocytes from EDP1815-treated HLA-DR3.DQ8 EAE mice re-stimulated with PLP91-110 had reduced levels of inflammatory cytokines IL-17 and IFNg and increased levels of anti-inflammatory cytokine IL-10, compared with splenocytes from medium-treated mice. Similar observations were noted when compared to mice treated with a microbe control (*E. coli*). (Significance relative to medium: ** = p<0.01, ns = not significant) Reprinted from Mangalam et al. 2017. Cell Reports 20: 1269-1277 with permission from Elsevier.

Preclinical DSS Mouse Model

We also tested EDP1815 in the DSS model of gut inflammation. In this preclinical study, we observed better activity of EDP1815 compared to anti-IL-12/23 with respect to weight loss, as well as bloody stool score and tissue damage as measured by endoscopy. Anti-IL-12/23 is a mouse analog that acts through the same pathway as ustekinumab (STELARA), an approved therapy for inflammatory bowel disease. A microbe control demonstrated no therapeutic benefit in this model. We believe that the observed activity of EDP1815 in this model suggests the potential role of EDP1815 in IBD.

Oncology Portfolio

We have advanced one monoclonal microbial candidate, EDP1503, into two clinical trials in patients with multiple cancer types.

Clinical Studies - EDP1503

In December 2018 we dosed the first patient in our Phase 1/2 trial of EDP1503 in combination with Merck's PD-1 inhibitor KEYTRUDA to evaluate the safety, tolerability, immune response markers and overall response rates achieved in up to 120 patients across three groups: microsatellite stable colorectal cancer; triple-negative breast cancer; and patients across multiple tumor types who have relapsed on prior PD-1/L1 inhibitor treatment. Patients will receive daily EDP1503 monotherapy for two weeks followed by treatment with daily EDP1503 in combination with KEYTRUDA. We will evaluate biomarkers identified from paired biopsies taken before and after the two-week run-in, as well as clinical outcomes observed over the course of this trial. We expect initial clinical data from this trial to be available in the first half of 2020.

In January 2019, the University of Chicago dosed the first patient in its Phase 2a investigator-sponsored clinical study for EDP1503 in metastatic melanoma to evaluate EDP1503 in combination with KEYTRUDA. Both PD-1-naïve and PD-1-relapsed melanoma patients will be recruited into the study. Up to 70 patients will receive daily EDP1503 monotherapy for two weeks followed by treatment with daily EDP1503 in combination with KEYTRUDA. The University of Chicago is evaluating safety, tolerability and overall response rates. In addition, we will evaluate immune response markers from paired biopsies taken before and at the conclusion of the 2-week run in. Initial clinical data is anticipated in the second half of 2020.

EDP1503 Preclinical Data

We have advanced EDP1503 into clinical trials based on our preclinical data, which suggests that EDP1503 is active through different immune mechanisms beyond those targeted by checkpoint inhibitors, such as PD-1/PD-L1, or cytotoxic T-lymphocyte associated protein 4, or CTLA-4, inhibitors. Research suggests that checkpoint inhibition prevents the downregulation of the immune system induced by tumors. In preclinical models, we observed that EDP1503 stimulated upregulation of the immune response to tumors. Oral administration of EDP1503 in preclinical mouse models appeared to delay tumor progression to a similar extent as checkpoint inhibitors using different immune mechanisms. In mouse models, EDP1503 had additive effects when combined with a checkpoint inhibitor.

Multiple clinical studies have demonstrated that checkpoint inhibitor activity is dependent on underlying T-cell infiltration and tumor mutational burden. Consequently, checkpoint inhibitors alone are typically ineffective in tumors without sufficient immune cell infiltration. Furthermore, resistance to checkpoint inhibitors can arise through multiple pathways of immune escape, including downregulation of antigen-presentation pathways (*e.g.*, MHC I, TAP, LMP2, LMP7 proteins), loss of tumor antigens recognized by effector T-cells, upregulation of immunosuppressive cytokines and increased resistance of tumor cells to apoptosis.

We believe that our existing and potential monoclonal microbial product candidates have the potential to broaden the base of cancer immunotherapy. The preclinical data of EDP1503 suggests a variety of effects in mouse tumor models, including upregulation of CD8+ T-cell infiltration, increased intratumoral pro-inflammatory chemokines, upregulation of MHC Class I expression and augmentation of NK cell infiltration. We believe that the ability of a monoclonal microbial to induce these effects across multiple pathways makes it an attractive combination candidate for checkpoint inhibitors relative to other immunotherapies in development that target a single pathway.

Checkpoint inhibitors are projected to generate $30 billion in revenue by 2025. However, efficacy of these therapies has thus far been limited to a subset of patients within select indications. Even in melanoma, where checkpoint inhibition is considered the frontline standard of care, almost half of the patients do not respond to PD-1 + CTLA-4 inhibitor combination and at least a third of responders relapse within two years. Given few additional therapy options, we believe there is high unmet need for the growing population of patients who relapse on PD-1/L1 inhibitors. In approved indications other than melanoma, the majority of patients do not benefit, with response rates ranging from only 10% to 30%. In renal cell carcinoma, PD-1 + CTLA-4 inhibitor combination only demonstrated benefit in a subset of frontline patients with poor to intermediate risk. Lastly, several other tumor types are not responsive to checkpoint inhibition alone. For example, in colorectal cancer, generic chemotherapy continues to be standard-of-care and PD-1 inhibitors have only shown benefit in a small proportion of late-line patients with high microsatellite instability or those who are mismatch repair-deficient. Approximately 95% of colorectal cancer patients are microsatellite stable and do not benefit from checkpoint inhibition alone. These factors suggest a substantial need for non-cytotoxic therapy options.

In all these indications, agents with differentiated immune mechanisms of action may be complementary to checkpoint inhibitors by both augmenting existing effects and testing alternative pathways of immunotherapy in checkpoint inhibitor non-responsive tumor types and patients. However, some combination approaches in oncology have been limited by the toxicity caused by dosing multiple agents concurrently. Because monoclonal microbials may work through differentiated pathways to

modulate systemic immune responses without systemic exposure, we believe they may be well-suited for combination with immuno-oncology agents or other standard-of-care therapies.

In Vitro Assay

Macrophages play an important role in cancer immunity, through both direct and indirect effects on other cells, including T-cells, in the tumor microenvironment. There are two broad classes of macrophages: (1) M1, which are pro-inflammatory and have anti-tumor effects; and (2) M2, which primarily have a tissue repair function and tend to block inflammation and promote tumor growth. Data from an *in vitro* screening assay, depicted in Figure 12, shows the result of co-culture of 37 distinct microbe strains with human macrophages. We assessed the strains based on their ability to polarize macrophages to an M1 or M2 type. We created an M1 control by pre-conditioning macrophages with LPS and IFNg, putting them into a strongly pro-inflammatory state. We created an M2 control by pre-conditioning macrophages with IL-4 and IL-13, inducing an anti-inflammatory, pro-repair state. The aggregate production of pro-inflammatory cytokines, which are characteristic of M1 macrophages, is mapped on the y-axis. EDP1503 is the most M1-polarizing strain in this figure, suggesting that it has the strongest pro-inflammatory properties of the strains evaluated, which we believe is a favorable attribute of an oncology candidate.

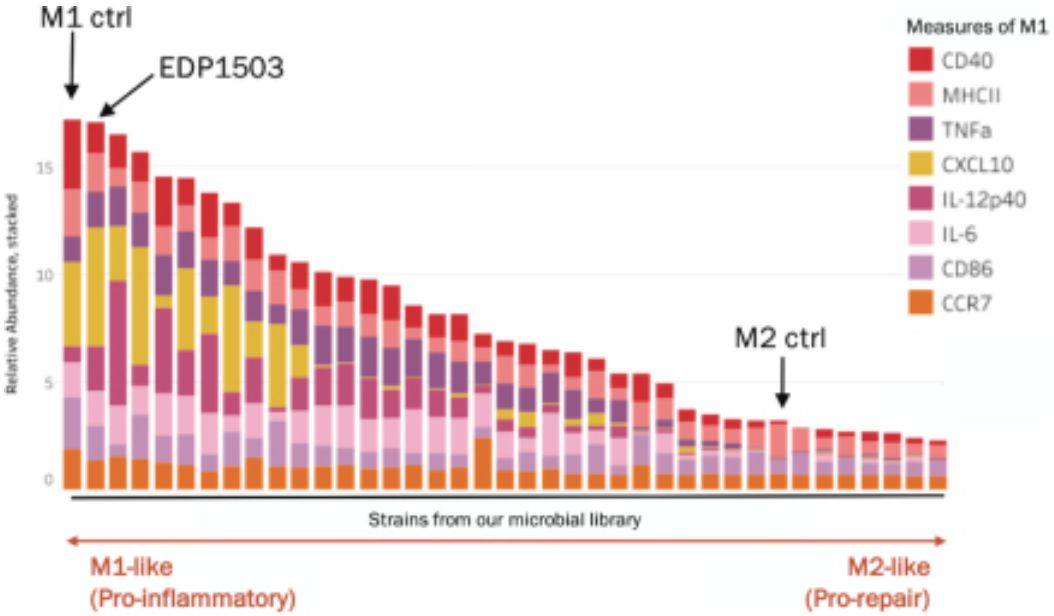


Figure 12: Induction of human macrophage inflammatory responses by EDP1503. Monoclonal microbials candidates and controls were co-cultured with macrophages purified from human peripheral blood mononuclear cells for 24 hours. Controls included LPS and IFNg to push macrophages into a strongly pro-inflammatory state (M1 ctrl) and IL-4 and IL-13 to induce an anti-inflammatory state (M2 ctrl). Cytokine levels were evaluated at the end of the co-culture period. Of all monoclonal microbials tested, EDP1503 induced the highest aggregate level of pro-inflammatory cytokines.

We also tested these strains for their ability to drive antigen-dependent activation of human T-cells. In a separate *in vitro* assay, we co-cultured human dendritic cells with different microbes from our library for 24 hours. We then removed the microbes and tested the ability of respective microbe-conditioned dendritic cells to enhance the inflammatory response of human CD8 T-cells. T-cell response was evaluated through production of IFNg by human CD8 T-cells stimulated by a MHC Class I peptide pool, a marker of T-cell activation. EDP1503 was one of the highest inducers of antigen-specific CD8 T-cell IFNg responses, which we believe suggests it may have the ability to enhance inflammatory T-cell responses in humans.

Preclinical Melanoma and Colon Cancer Mouse Models

We also tested EDP1503 in mouse models of melanoma and colon cancer, as shown in Figure 13. In a melanoma model, we administered EDP1503 daily beginning eight days after tumor implantation in mice, as depicted in Figure 13A below. Reduction in tumor volume was similar to that observed with an anti-PD-L1 antibody, a mouse analog of the current standard of care in melanoma. Furthermore, EDP1503 showed an additive effect with an anti-PD-L1 antibody, further reducing tumor volume. We observed similar results in a colon cancer model shown in Figure 13B. EDP1503 activity was comparable to an anti-PD-1 antibody and showed additive activity in combination with an anti-PD-1 antibody. We believe these models suggest that orally-delivered EDP1503 is able to induce systemic anti-tumor effects in mice, which may support clinical development in a range of solid tumors. Multiple experiments conducted by a variety of contract research organizations reproduced these results, suggesting that the results were not dependent on specific experimental conditions or on the background microbiota of the mice.

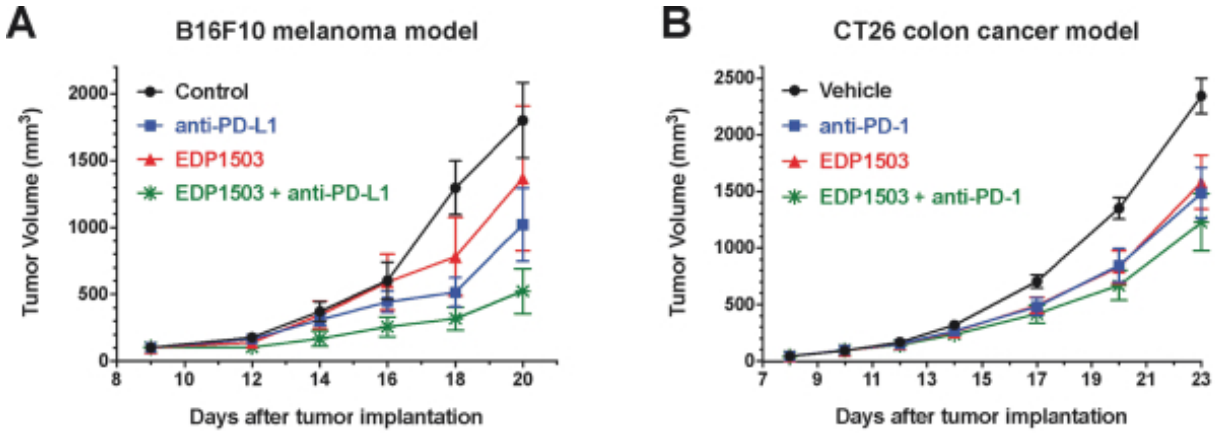


Figure 13: EDP1503 slowed progression of tumors in syngeneic tumor models. (A) B16.F10 melanoma cells were implanted subcutaneously in mice. Treatment was initiated at day nine when tumors reached a volume of 100 mm3. (B) CT26 colon cancer cells were implanted subcutaneously in mice. Treatment was initiated at day seven when tumors reached a volume of 100 mm3. In both models, vehicle and EDP1503 were given orally daily and anti-PD-1/L1 antibodies were administered intra-peritoneally every four days. Mean tumor volumes were recorded at multiple timepoints. EDP1503 demonstrated anti-tumor activity as a monotherapy and in combination with anti-PD-1/L1 antibodies in both tumor models.

Additional testing in the colon cancer model suggested that the anti-tumor activity of EDP1503 was dose-dependent over a 100-fold range. Ascending doses varied by a factor of 10. When we assessed mean tumor volume 12 days post-treatment, activity at higher doses of EDP1503 was comparable to an anti-PD-1 antibody. By showing that the highest dose we evaluated did not significantly increase therapeutic effect over a slightly lower dose, we gained a better understanding of the maximum therapeutic activity in mice. We used this information to calculate the dose for our first-in-human clinical study.

Ex Vivo Analyses of Colon Cancer Mouse Model

Research suggests that T-cell infiltration into tumors is important for immunotherapeutic responses in oncology patients. In an *ex vivo* analysis of a CT26 mouse tumor study, we used a CD3 cell surface marker on dissected tumor sections to identify all T-cells as shown on the left in Figure 14 below. The graphs depicted on the right in Figure 14 plot the total number of CD3 positive T-cells in a defined microscopic view of tumors, treated with EDP1503 or vehicle, respectively. The tumors in mice treated with EDP1503 had increased T-cell infiltration relative to vehicle-treated mice. The increases correlated with therapeutic activity on tumor growth. We have observed in separate preclinical experiments that the majority of these infiltrating T-cells are positive for the T-cell marker CD8, which identifies T-cells thought to be particularly important for killing tumor cells in patients.

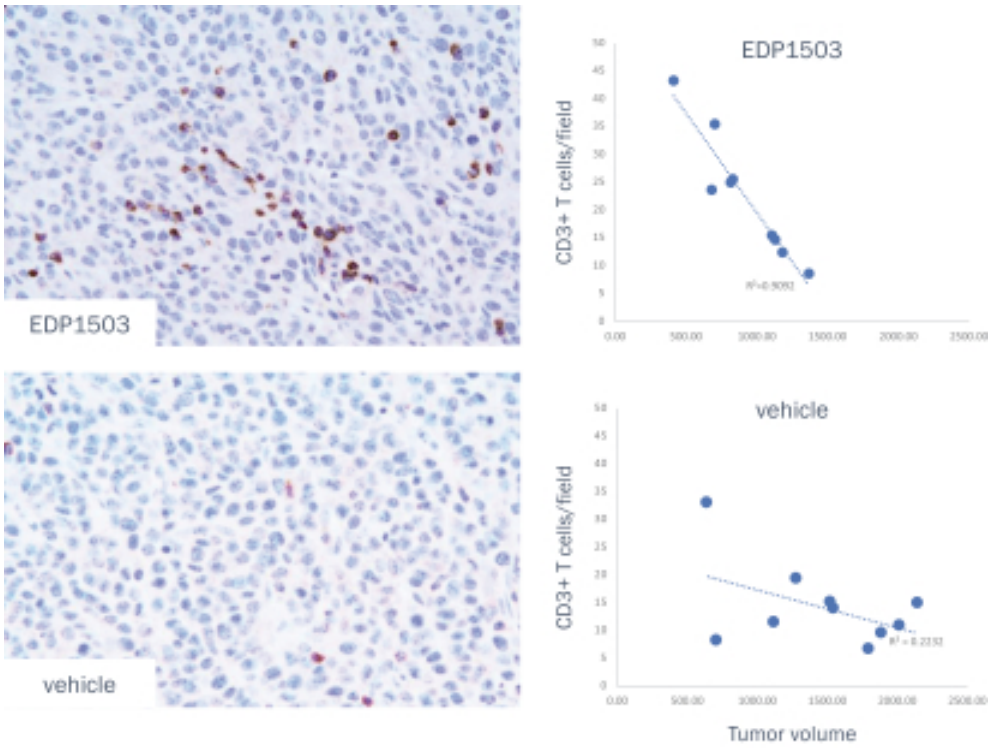


Figure 14: EDP1503 induced T-cell infiltration into tumors. Microscopy images show CD3+ T-cell infiltration in defined microscopic fields of CT26 mouse tumors treated with EDP1503 or vehicle (left). Quantitation of CD3+ T-cell infiltration was plotted against tumor volume. EDP1503 treated mice show greater T-cell infiltration in tumors, with the extent of infiltration being greater in smaller tumors (right).

CXCL10 is a protein hormone of the immune system, or a chemokine, which is produced in response to IFNg. CXCL9 is also produced under similar conditions. Clinical research has demonstrated that melanoma patients that have a high concentration of CXCL10 in their tumors have a significantly better prognosis.

As depicted in Figure 15, we removed colon tumor tissue from a mouse model following treatment with vehicle, anti-PD-1 antibody, EDP1503 or a combination of EDP1503 and anti-PD-1 antibody, and then extracted lymphocytes that had infiltrated the treated tumor. We then tested these lymphocytes for their ability to produce CXCL9 and CXCL10. Lymphocytes from EDP1503-treated tumors induced CXCL9, while those from anti-PD-1 antibody-treated tumors did not. However, we did observe a synergistic effect in combination treated tumors. Lymphocytes from EDP1503-treated tumors more highly induced CXCL10 than those treated with anti-PD-1 antibody and the effect of EDP1503 was greater when used in combination with anti-PD-1.

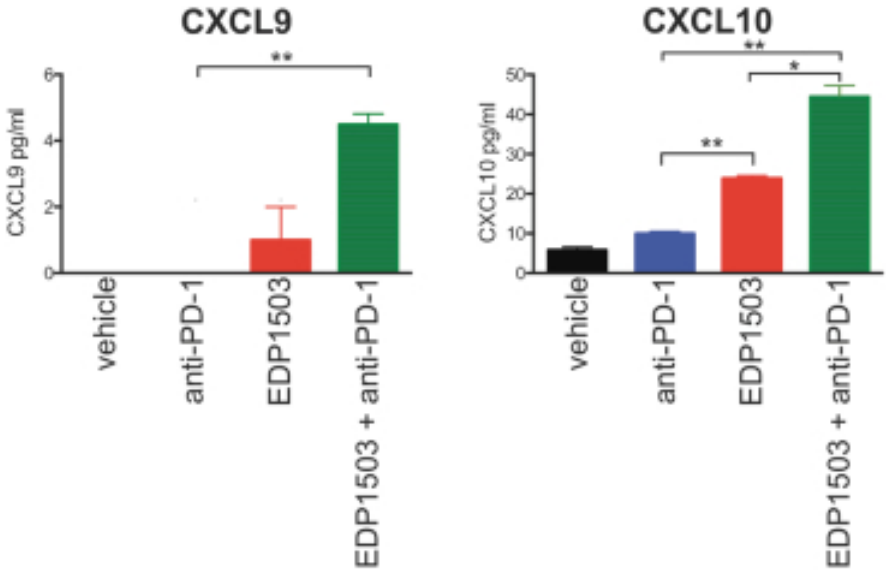


Figure 15: EDP1503 induced production of CXCL9 and CXCL10 in tumors. Secretion of pro-inflammatory chemokines, CXCL9 and CXCL10, by CD8+ T-cells recovered from explanted CT26 tumors in mice treated with anti-PD-1 antibody, EDP1503, or the combination. Compared to anti-PD-1 antibody alone, both EDP1503 monotherapy and combination resulted in greater CXCL9 and CXCL10 secretion by tumor infiltrating lymphocytes. (Significance relative to EDP1503 or anti-PD-1 antibody: ** = p<0.01; * = p<0.05)

In other *ex vivo* analyses of CT26 mouse tumor studies, we have observed that treatment with EDP1503 upregulates MHC Class I expression and augments NK cell infiltration, which are both understood to correlate with improved immune response in cancer patients. Lower MHC Class I expression reduces antigen presentation to immune cells and has been observed in patients with either primary or acquired resistance to checkpoint inhibitors. We believe these data suggest that the action of EDP1503 on the gut-body network enables different immune mechanisms that match the anti-tumor effect of and are potentially complementary to checkpoint inhibitors. We believe this profile offers a range of potential opportunities for improved immuno-oncology treatments.

Biodistribution and Pharmacokinetics

We have used two techniques to determine the pharmacokinetics and biodistribution of EDP1503 *in vivo* in mice: fluorescence microscopy and strain-specific PCR primers.

First, using fluorescence microscopy, we have shown in Figure 16 that labeled EDP1503 reaches the small intestine epithelium, which we believe is the site of action of the gut-body network.

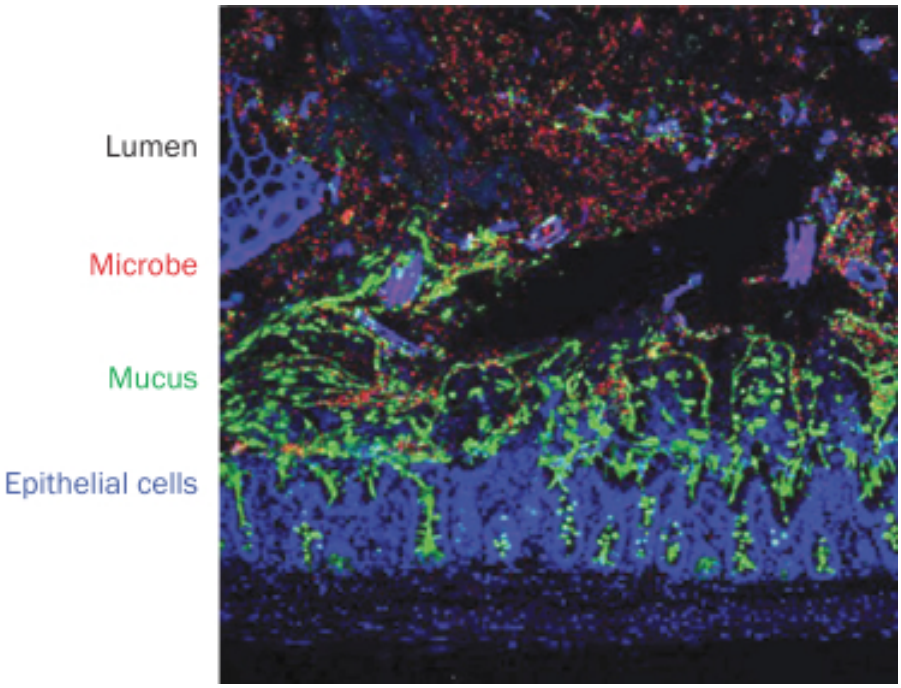


Figure 16: Fluorescence microscopy showing distribution of EDP1503 in the small intestine of a mouse. Mice were treated with a single oral administration of EDP1503, which was covalently labeled with DIBAC-Cy5 (red). A section of small intestine was stained with anti-MUC2 (green), which stains mucus, and DNA-containing epithelial cells were stained with DAPI (blue). EDP1503 (red) is found both free within the lumen, as well as penetrating the mucus layer to the cells of the gut epithelium where it interacts with the gut-body network.

We believe that EDP1503 has an ability to engage with target immune cells *in vivo*. In the experiment plotted in Figure 17, we gave mice oral doses of 108 or 109 fluorescently labeled EDP1503. After three hours, we removed mesenteric lymph nodes. Mesenteric lymph nodes are the lymph nodes that monitor immune activity in the gut. We broke down the lymph nodes into single cells and then assayed them on a fluorescence activated cell analyzer to determine the level of physical engagement between EDP1503 and antigen-presenting cells, or APCs, such as macrophages (CX3CR1+) and dendritic cells (CD103+). Our observations suggest a dose-dependent association of EDP1503 with the target immune cells above the background of vehicle control. We believe this is consistent with the proposed mechanism of action of EDP1503 and its dose-dependent activity in a colon cancer model.

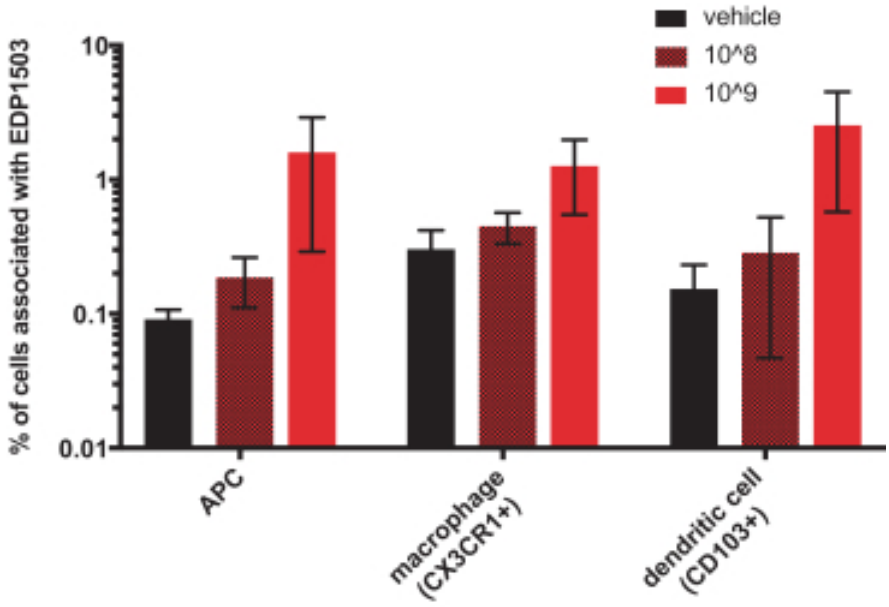


Figure 17: EDP1503 associated with antigen-presenting cells, or APCs, in the mesenteric lymph nodes. Mice were treated with vehicle or 10^8 or 10^9 DIBAC-Cy5 labeled EDP1503. Mesenteric lymph nodes were collected and sorted by flow cytometry, with the proportion of Cy5+ events recorded for each cell type. Increasing proportions of macrophages and dendritic cells show association with EDP1503 with increasing oral dose.

Second, we also used PCR primer pairs specific for EDP1503 to track the passage of EDP1503 through the gut of mice and detected its presence in other tissues. After a single oral dose, EDP1503 cleared from the small intestine within 16 hours and from the colon and stool within 24 to 48 hours. There was no evidence of persistence or colonization either in this model or in the longer-term multi-dose tumor models. The exposure of EDP1503 in other body sites was negligible.

Manufacturing

We have developed proprietary methods for the manufacture of pharmacologically active monoclonal microbials that are scalable and transferable to cGMP manufacturing facilities. Monoclonal microbials are isolated, proliferated and purified in a manner analogous to the manufacture of pharmaceutical drugs. Monoclonal microbials maintain their therapeutic effect through the manufacturing process, which produces drug substance in a powder form that makes our candidates suitable for oral administration, for instance in the form of a capsule, tablet or powder. Additionally, we believe we have established robust analytical methods to assess the identity, strength and purity of monoclonal microbials. We expect that these controlled manufacturing processes and analytical methods will allow us to produce and release cGMP batches of material with consistent quality.

Our internal manufacturing capabilities include production of non-GMP materials for *in vitro* and *in vivo* preclinical assessment of product candidates. We currently rely on third-party manufacturers for the production of materials for clinical studies. Our internal personnel have extensive cGMP manufacturing experience to ensure efficient technology transfer and oversee the development and manufacturing activities conducted by third-party manufacturers. Our agreements with third-party manufacturers include confidentiality and intellectual property provisions to protect our proprietary rights to our monoclonal microbial candidates.

We expect our third-party manufacturers will be able to meet manufacturing requirements and drug supply required by our clinical studies. In some instances, we have reserved resources from third-party manufacturers

for the development and manufacture of our monoclonal microbial candidates for near-term clinical programs. We believe that these relationships are integral to ensuring reliable, high-quality drug supply for clinical development.

While we do not have a current need for commercial manufacturing capacity, we intend to evaluate both building internal capabilities and contracting with third-party manufacturers at the appropriate time.

Process development and manufacturing are critical for translation of monoclonal microbials. We believe our internal expertise and external partnerships have allowed us to address unique challenges associated with monoclonal microbial manufacturing. Some of these major challenges include: limited prior know-how in the field for novel microbes; strict anaerobic growth conditions required by many commensal microbes; and temperature and oxygen sensitivities that affect downstream processing.

Our proprietary methods for the manufacture of pharmacologically active monoclonal microbials address these three major challenges. Many human commensals are strict anaerobes with no prior development precedent. Process development of commensal microbes requires strong technical expertise in microbiology and anaerobic fermentation. We are pioneering strict anaerobic bioprocessing technologies that can allow for rapid development of reproducible manufacturing processes. We continue to optimize our processes across a wide range of parameters including media, temperature, pH, and harvest conditions. By modifying these parameters, we were able to develop a fermentation process for EDP1815, which is an anaerobic microbe with sensitive growth requirements. As depicted in Figure 19, our proprietary fermentation process increased yield, or production of EDP1815 biomass, by 10,000-fold compared to production of EDP1815 biomass produced from an industry standard fermentation process.

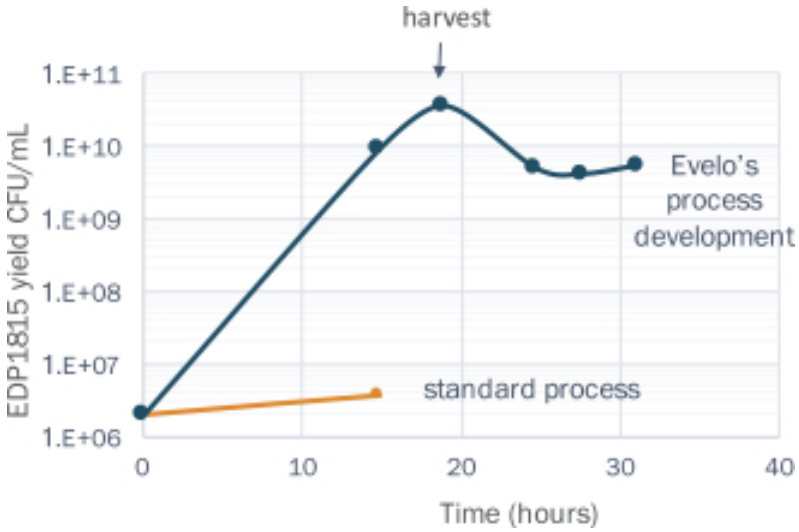


Figure 19. Our process development defines fermentation parameters for EDP1815. Fermentation profile for EDP1815 when grown according to an industry standard fermentation process (orange) and our proprietary process (blue).

Our monoclonal microbial manufacturing processes consist of drug substance and drug product manufacturing. We have established expertise across all aspects of drug substance manufacturing unit operations including cell banking, fermentation, cell separation and lyophilization. We have also advanced knowledge related to drug product manufacturing and our drug product has demonstrated stability under long-term storage conditions. We will continue to advance novel formulation technologies for enhanced delivery and activity in future trials.

Non-replicating Monoclonal Microbials

Our research has shown that the preclinical activity of many monoclonal microbials is independent of their viability - they need to be intact, but growth and cell division are not required. From this observation, we believe that monoclonal microbial activity is likely driven by recognition of structural motifs by immune cells in the small intestine and that this is a formal demonstration that monoclonal microbial activity is not dependent on engraftment or colonization.

As depicted in Figure 20, oral administration of non-replicating EDP1066 reduced inflammation in the preclinical DTH model to the same extent as replication-competent EDP1066. In addition to EDP1066, we have observed that non-replicating forms of EDP1815 and EDP1867 show comparable activity to replication-competent forms.

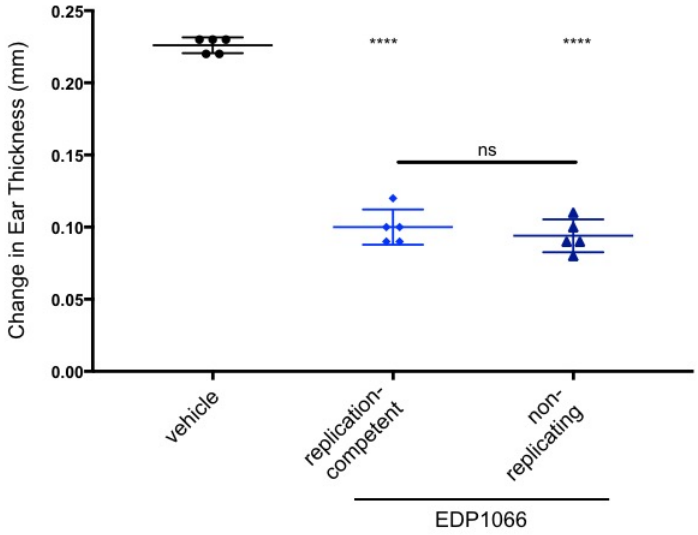


Figure 20. Non-replicating EDP1066 reduced skin inflammation in a DTH mouse model. Mice were sensitized with a foreign antigen, keyhole limpet hemocyanin, and Complete Freund's Adjuvant subcutaneously at day zero. Mice were orally-dosed for 10 days from sensitization on day zero with vehicle, replication-competent EDP1066, or non-replicating EDP1066. Eight days after sensitization, mice were given an intradermal ear challenge with KLH. Change in ear thickness, a measure of skin inflammation, was evaluated 24 hours post-challenge. (Significance relative to vehicle: **** = p<0.0001)

Our candidate selection process may include an additional manufacturing step for our monoclonal microbial candidates to develop them as non-replicating product candidates. EDP1867 is the first non-replicating monoclonal microbial in Evelo's pipeline.

Sales and Marketing

Given the current developmental stage of our product candidates and platform, we have not yet established a commercial organization. We intend to commercialize our products globally and in multiple disease areas. We

intend to do this both through selectively building our own sales and marketing team and partnering or collaborating with third parties.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover both our broad platform and individual product candidates. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions. 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.

We plan to continue to expand our intellectual property estate by filing patent applications directed to pharmaceutical compositions, methods of treatment, methods of manufacture, methods for patient selection created or identified from our ongoing development of our product candidates, as well as discovery based on our proprietary platform. 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.

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, or, if challenged, in courts or administrative proceedings, be determined to be invalid or unenforceable.

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.

Patent Portfolio

Our patent portfolio includes patent applications in varying stages of prosecution in the United States and selected jurisdictions outside of the United States. As of January 31, 2019, our patent portfolio consisted of seven issued patents and 96 pending applications, which include compositions, methods of use, and manufacturing process claims. Of the patents in our portfolio, two are owned by us, four are exclusively licensed from Mayo Clinic and one is exclusively licensed from the University of Chicago. Of the pending applications in our portfolio, 72 are owned by us, 23 are exclusively licensed to us from the University of Chicago and one is exclusively licensed to us from Mayo Clinic. The patent portfolio includes patents and applications covering the following:

- An oral oncology platform exclusively licensed from the University of Chicago, consisting of one issued patent and 23 pending applications. Patents in this family are expected to expire in 2036.
- A translational *in vitro* assay platform developed by us, consisting of one pending provisional application. Any applications claiming priority to this provisional application that issue as patents are expected to expire in 2038.
- A formulation platform consisting of one pending provisional application. Any applications claiming priority to this provisional application that issue as a patent are expected to expire in 2038.
- A modality platform consisting of two pending provisional applications. Any applications claiming priority to these provisional applications that issue as a patent are expected to expire in 2038.
- Inflammation portfolio:
    - EDP1815, consisting of four issued patents in-licensed from Mayo Clinic, covering compositions and methods of use, one pending application in-licensed from Mayo Clinic (the patents and application from Mayo Clinic expected to expire in 2030) and twelve (12) Evelo-owned pending applications directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2038; and
    - EDP1066, consisting of seven (7) pending applications directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2038.
- Oncology portfolio:
    - EDP1503, consisting of protection under the oral oncology platform exclusively licensed from the University of Chicago covering methods of use and four (4) Evelo-owned pending applications directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2038.

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 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. We protect trade secrets and know-how by establishing confidentiality agreements and intellectual property 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.

License and Manufacturing Agreements

We are a party to several license agreements under which we license patents, patent applications and other intellectual property. The licensed intellectual property includes composition of matter and methods of using monoclonal microbials. In some cases, licenses cover physical material in the form of microbial strains. Certain diligence and financial obligations are tied to these agreements. Additionally, we are a party to a manufacturing agreement for committed resources and exclusivity. We consider the following agreements to be material to our business.

University of Chicago License Agreement

In March 2016, we entered into an exclusive license agreement with the University of Chicago. This agreement gives us an exclusive, worldwide, sublicensable license to patent rights related to administration of microbes to treat cancer. Under this agreement, we may make, have made, use, import, have sold, offer to sell, and sell microbial products to treat cancer in combination with checkpoint inhibitors. Many microbial genera are covered by these patent rights, including *Bifidobacterium*, which encompasses our lead oncology candidate, EDP1503. In addition, we have a non-exclusive, worldwide license to use technical information disclosed to us by the University of Chicago for the development and commercialization of microbial products to treat cancer in combination with checkpoint inhibitors. Under this agreement, we must use commercially reasonable efforts to develop and market licensed products. Commercially reasonable efforts can be demonstrated by achieving specific milestones by specific dates.

Pursuant to the terms of the license agreement, we paid the University of Chicago an upfront fee of an amount less than $500,000 and are required to make low five-digit license maintenance fees on an annual basis, creditable against royalties owed in that given year. In addition, we may owe the University of Chicago future milestone payments totaling an aggregate of approximately $60.9 million upon achievement of specific milestones, the vast majority of which are associated with specific regulatory and commercial milestones.

The University of Chicago is entitled to receive low single-digit percentage royalties on annual net sales of products that fall under the licensed patent rights on a country-by-country and product-by-product basis. The royalty percentage depends on the amount of annual net sales and whether the product is covered by valid patent claims, un-published technical information, or published technical information. Our valid claims royalty obligations to the University of Chicago will expire upon the later of (a) expiration of the last-to-expire valid claim covering the product, or (b) the expirations of regulatory exclusivity of a product covered by the patent rights. Technical information royalty obligations will expire upon the earlier of (a) fifteen years from first commercial sale of the applicable product, or (b) when a substantially similar product comes onto the market.

Under the license agreement, we have the right to sublicense licensed rights to third parties, provided that the sublicense agreement is consistent with the terms of the original license and that we hold any sublicensees compliant. Should we enter a sublicense under these patent rights, we are required to pay the University of Chicago a percentage of our sublicense revenue. The University of Chicago is entitled to percentages of sublicense revenue in the low- to mid-teens depending on the stage of development of licensed products at the time the sublicense is entered.

The University of Chicago maintains control of patent prosecution, defense and maintenance on their patent rights. We are responsible for reimbursing the University of Chicago for patent costs incurred. If we cease payment for patent prosecution, our patent rights will terminate and revert to the University of Chicago. We have the first right, but not obligation, to control any post grant proceedings and to take action in the prosecution or prevention of any infringement by a third party to patent rights.

The license granted by the University of Chicago is subject to any retained rights of the U.S. government in the patent rights and to retained rights of the University of Chicago to use the patent rights for non-commercial research purposes. The license agreement will expire on a country-by-country and product-by-product basis on the later of (a) expiration date of the last to expire licensed patents, or (b) a set number of years in the mid-teens from first commercial sale of a licensed product. Prior to the expiration date, we may terminate the license with written notification to the University of Chicago. Prior to the expiration date, the University of Chicago may terminate the agreement in whole or in part if we fail to make payments within thirty days of receiving a written notice of missed payment, if we breach any material obligation of the agreement and do not cure such breach within thirty days, if we become bankrupt or insolvent, or if we are dissolved or liquidated. The University of Chicago may also terminate the license if we fail to show commercially reasonable efforts in meeting diligence milestones.

License Agreement with Mayo Clinic

In August 2017, we entered into an agreement with the Mayo Foundation for Medical Education and Research, an affiliate of Mayo Clinic, or Mayo Clinic, to license intellectual property and microbial strains. This agreement gives us an exclusive, worldwide, sublicensable license to patent rights related to compositions of matter and methods of using microbes from a specific species to treat autoimmune and inflammatory diseases. In addition to patent rights, this agreement also includes an exclusive, worldwide, sublicensable license to an immuno-modulatory microbial strain isolated from a human small intestinal sample by Mayo Clinic. Under the licensed patent rights and/or using the licensed microbial strain, we may make, have made, use, offer for sale, sell, and import products containing microbes of a specific species to treat autoimmune and inflammatory diseases. In addition, we have a non-exclusive, worldwide license to use know-how disclosed to us by Mayo Clinic related to the development and commercialization of products containing microbes of a specific species to treat autoimmune and inflammatory diseases. The licensed patents include four issued U.S. patents and one pending U.S. patent application. Issued claims cover compositions containing microbes from a specified species and methods of using these compositions to treat all autoimmune and inflammatory diseases. EDP1815, one of our lead candidates in the inflammation program, contains the microbial strain licensed from Mayo Clinic and is covered by these patent rights. Under this agreement, we must use commercially reasonable efforts to bring licensed products to the market.

In consideration for the licenses, we paid Mayo Clinic an upfront payment of $225,000. Beginning on the second anniversary of the effective date, we owe Mayo Clinic escalating annual license maintenance fees in the low- to mid–five digits. Annual license maintenance fees count towards milestones and royalties owed in a given year. Mayo Clinic is entitled to future clinical, approval and sales milestones. In addition, we have agreed to pay Mayo Clinic future milestone payments totaling a maximum of $960,000 upon achievement of specific development milestones and $56 million upon achievement of specific regulatory and commercial milestones.

Mayo Clinic is entitled to receive low single-digit percentage royalties on annual net sales of products that fall under the licensed patent rights or contain the licensed microbial strain on a country-by-country and product-by-product basis. The royalty percentage depends on the amount of annual net sales and whether the product is covered by valid patent claims or contains the licensed microbial strain. Royalties on products containing the licensed microbial strain will only be due in countries where licensed products are not covered by valid claims. Our valid claims royalty obligations to Mayo Clinic will terminate on expiration of the last-to-expire valid claim covering the product. Royalty obligations on products containing the licensed microbial strain will expire 15 years from the first commercial sale of the licensed product.

Under the license agreement, we have the right to sublicense licensed patent rights and the licensed microbial strain to third parties through multiple tiers, provided that the sublicense agreement is on substantially the same terms as the original license and that we are responsible for the performance of its sublicensees. We must obtain Mayo Clinic’s permission to grant any fully paid-up, royalty-free or exclusive sublicenses. We have no financial obligations to Mayo Clinic related to sublicenses.

Mayo Clinic has the responsibility to prepare, file, prosecute or abandon its patent rights. We may provide prior comment and advice to Mayo Clinic and we are responsible for reimbursing Mayo Clinic for past and future patent costs. If we cease payment for patent preparation, filing or prosecution, our patent rights will terminate and revert to Mayo Clinic. We have the first right, but not obligation, to control any post grant proceedings and to take action in the prosecution or prevention of any infringement by a third party to patent rights.

The license granted by Mayo Clinic is subject to any retained rights of the US government in the patent rights and to retained rights of Mayo Clinic to use the patent rights and licensed microbial strain for non-commercial research purposes, which excludes human use. The license to patent rights will expire on a country-by-country and product-by-product basis upon the expiration date of the last to expire licensed patents. The license to Mayo Clinic’s microbial strain will expire 15 years from first commercial sale of a product containing the licensed microbial strain. Prior to the expiration date, Mayo Clinic may terminate the license if we fail to make payments within thirty days of receiving a written notice of missed payment, if we breach any material obligation of the agreement and do not cure such breach within thirty days, if we become bankrupt or insolvent, or if we or any sublicensee directly or indirectly brings suit against Mayo Clinic. Upon early termination of our

license, any sublicensee that is not in material breach of the agreement will have the right to retain its sublicense to the patent rights and microbial strain. We do not have the right to terminate the agreement prior to the expiration date.

Biose Committed Resource and Exclusivity Agreement

Effective February 2018, we entered into an exclusivity and commitment agreement with Biose Industrie, or Biose. Under this agreement, Biose reserves sufficient manufacturing resources for the manufacture of our drug substance according to a specified schedule of manufacturing runs over a three-year period. We are required to pay Biose fees in the high five digits to low six digits for each run depending on the type of run being conducted. If we do not use committed manufacturing resources, we are required to pay Biose for these resources unless Biose is able to re-sell unused runs.

In addition to manufacturing resources, this agreement includes exclusivity provisions, which ensure that we are Biose's exclusive customer for the manufacture of certain microbial biotherapeutic products. We are required to pay annual fees in the mid six digits to Biose in consideration for these exclusivity provisions.

The term of the agreement is three years from the effective date. We may terminate at any time with prior notice within a specified period to Biose, or if there is a change of control of Biose that may adversely affect our interest. In the event that we terminate at will, we are obligated to pay Biose a mid-range percentage of the committed manufacturing resource fees for a specified period less than one year following the effective date of termination. In addition, both parties may terminate if the other party materially breaches the agreement and does not cure such breach within a specified period or if either party becomes bankrupt or insolvent, or is dissolved or liquidated.

Collaboration

Merck-MSD International GmbH

In November 2018, we entered into a clinical trial collaboration agreement with MSD International GmbH, an affiliate of Merck, under which we will sponsor and conduct a clinical trial evaluating EDP1503 in combination with KEYTRUDA, Merck's anti-PD-1 therapy, in patients with advanced metastatic colorectal carcinoma, triple-negative breast cancer, and checkpoint inhibitor relapsed tumors. Under the agreement, we retain sole ownership of all rights to EDP1503, and there are no material financial terms or commitments required of either party.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid growth and a dynamic landscape of proprietary therapeutic candidates. While we believe that our monoclonal microbial platform and candidates, coupled with our resources and industry expertise, give us a competitive advantage in the field, we face competition from a variety of institutions, including larger pharmaceutical companies with more resources.

Specialty biotechnology companies, academic research institutions, governmental agencies, as well as public and private institutions are also potential sources of competitive products and technologies.

In both inflammatory diseases and oncology, we anticipate intensifying competition as new therapies are approved and advanced technologies become available. Many of our competitors, either alone or with strategic partners, have considerably greater financial, technical, and human resources than we do. Competitors may also have more experience developing, obtaining approval for, and marketing novel treatments in the indications we are pursuing. These factors could give our competitors an advantage over us in recruiting and retaining qualified personnel, completing clinical development, and commercializing their products. Competitors that are able to obtain FDA or other regulatory approval for their products more rapidly than we can for our products may also establish a stronger market position, diminishing our commercial opportunity. Key considerations that would impact our capacity to effectively compete include the efficacy, safety, ease of use, as well as pricing and reimbursement of our products.

Significant competition exists in the immuno-oncology field, where we are developing our first product candidates in oncology. Although our monoclonal microbial approach is unique from most other existing or investigational therapies in immuno-oncology, we will need to compete with all currently or imminently available therapies within the indications where our development is focused. Although there is a wide range of potentially competitive mechanisms, possible synergies between these and monoclonal microbials will also be evaluated.

The main classes of immunotherapy that are available or are being evaluated by our competitors include:

- ***Checkpoint inhibitors***: Agenus Inc., AstraZeneca plc, Bristol-Myers Squibb, F. Hoffmann-La Roche A.G., Incyte Corporation, Merck, Pfizer Inc., Regeneron Pharmaceuticals Inc.; and
- ***Cell therapy***: Celgene Corporation, Gilead Sciences, Inc., and Novartis International A.G.

In autoimmune or inflammatory diseases, there is also a wide range of competitors that we will be challenged by. In later stages of disease, the majority of competition will stem from companies marketing or developing biologics and novel small

molecule therapies, such as AbbVie Inc., Johnson & Johnson, Pfizer Inc, Novartis International A.G., Regeneron Pharmaceuticals, Inc. and Sanofi S.A. Potentially competing mechanisms of action include TNF, IL-4, IL-17, and JAK inhibitors. Novel delivery of biologics, particularly via oral administration, and the entry of biosimilars will also add to competition within the therapeutic area.

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 licensure, which constitutes 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 investigational new drug application, or 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, and imposes a clinical hold. 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 of 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 and physician labeling.

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.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

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. 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 substantive 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 license 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 license 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. 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.

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.

Post-Approval Requirements

Licensed 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 is also a continuing, annual prescription drug product program user fee.

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.

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

As part of the Patient Protection and Affordable Care Act enacted in 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, the Biologics Price Competition and Innovation Act, or 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 are subject to uncertainty. 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. Furthermore, 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.

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 European Economic Area, or 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 European Medicines Agency, or EMA, 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 or 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 a marketing authorization application, or 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, additional 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.

Similar to the United States, the various phases of non-clinical and clinical research in the European Union are subject to significant regulatory controls.

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation is anticipated to come into application in 2019. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to that third-party payors provide coverage, and establish adequate reimbursement levels for such products.

In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Furthermore, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Research and Development

We have dedicated a significant portion of our resources to our efforts to develop our product candidates. We incurred research and development expenses of $39.9 million, $20.0 million and $9.1 million during the years ended December 31, 2018, 2017 and 2016, respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development in 2019 as we continue to advance our product candidates through clinical development.

Employees

As of February 8, 2019 we have 75 full-time employees, including 34 with M.D. or Ph.D. degrees. Of those full-time employees, 59 are engaged in research and development. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate and Other Information

We were incorporated in Delaware in May 2014. Our principal executive offices are located at 620 Memorial Drive, Cambridge, Massachusetts 02139 and our telephone number is (617) 577-0300. Our website address is *www.evelobio.com*. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only.

We file electronically with the SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. We make available on our website at www.evelobio.com, under "Investors," free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC.

Item 1A. Risk Factors

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

Risks Related to Our Financial Position and Need for Additional Capital

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

Since inception, we have incurred significant operating losses. For the year ended December 31, 2018 our net loss was $56.9 million and as of December 31, 2018 we had an accumulated deficit of $113.4 million. To date, we have financed our operations through private placements of our preferred stock, borrowings under our loan and security agreement with Pacific Western Bank and proceeds from our initial public offering, which was completed in May 2018. We have devoted substantially all of our financial resources and efforts to developing our monoclonal microbial platform, identifying potential product candidates and conducting preclinical studies. We are in the early stages of developing our product candidates, and we have not completed the development of any monoclonal microbial therapies or other drugs or biologics. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- seek to enhance our monoclonal microbial platform and discover and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- seek to establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio; and
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our transition to a public company.

In addition, we anticipate that our expenses will increase substantially if we 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 only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

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

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

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

We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials, build manufacturing capacity and expand into additional therapeutic areas.

We expect that our cash, cash equivalents and short-term investments as of December 31, 2018 will enable us to fund our planned operating expenses and capital expenditure requirements into the second half of 2020. 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 any ongoing and future clinical trials;
- the cost of manufacturing clinical supplies of our product candidates, including EDP1066, EDP1815 and EDP1503;

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any other future product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such transactions.

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

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or product development programs or the commercialization of any product candidates. In addition, we may be unable to make milestone and royalty payments due under our intellectual property license agreements or other payments under our agreements with contract research organizations, or CROs, and academic research collaborators, or 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 2014, we have devoted substantially all of our resources to identifying and developing our product candidates, building our intellectual property portfolio, process development and manufacturing function, planning our business, raising capital and providing general and administrative support for these operations. All of our product candidates are in clinical or preclinical development. We dosed the first subjects in our clinical trial of our first monoclonal microbial candidate in our inflammation portfolio, EDP1066, in April 2018, and commenced initial clinical trials for our second inflammation candidate, EDP1815, and our oncology product candidate, EDP1503, in the fourth quarter of 2018, but have not completed any clinical trials for these or any other product candidates. We have not yet demonstrated our ability to successfully complete any non-clinical toxicology study, Phase 1 clinical study, Phase 2 clinical study or any Phase 3 or other pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control.

Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

We have a $15.0 million term loan credit facility with Pacific Western Bank, or the loan and security agreement, that is secured by a lien covering substantially all of our personal property, excluding intellectual property. As of December 31, 2018,

the outstanding principal balance under the loan and security agreement was $15.0 million. The loan and security agreement contains customary affirmative and negative covenants and events of default applicable to us and our subsidiaries.

The affirmative covenants include, among others, covenants requiring us (and us to cause our subsidiaries) to maintain our legal existence and governmental approvals, deliver certain financial reports and notifications, maintain proper books of record and account, timely file and pay tax returns, maintain inventory and insurance coverage, maintain cash with Pacific Western Bank (subject to exceptions) and in accounts subject to control agreements (subject to exceptions), and protect material intellectual property. The negative covenants include, among others, restrictions on us and our subsidiaries transferring collateral, changing businesses, dissolving, liquidating, engaging in mergers or acquisitions, adding new offices or locations, making certain organizational changes, incurring additional indebtedness, encumbering assets (including a negative pledge on intellectual property), paying cash dividends or making other distributions, making investments, selling assets, making certain capitalized expenditures, undergoing a change in control, and engaging in certain non-ordinary course material transactions with affiliates, in each case subject to certain exceptions. If we default under the loan and security agreement, Pacific Western Bank 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. Pacific Western Bank could declare a default upon the occurrence of any event that they interpret as a material adverse effect as defined under the loan and security agreement, thereby requiring us to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by the lenders of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

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

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

We are using our monoclonal microbial platform, with an initial focus on developing therapies in immunology, specifically inflammatory diseases, and also oncology. While we believe our preclinical studies to date have validated our platform to a degree, we are at an early stage of development and our platform has not yet, and may never lead to, approvable or marketable products. We are developing these product candidates and additional product candidates that we intend to use to treat broader immunological diseases, respiratory diseases, neuro-inflammation and degeneration, liver diseases, type I diabetes, food allergy, neurobehavior, cardiovascular disease and diseases of metabolism. We may have problems applying our technologies to these other areas, and our new product candidates may not demonstrate a comparable ability in treating disease as our initial product candidates. Even if we are successful in identifying additional product candidates, they may not be suitable for clinical development as a result of our inability to manufacture more complex monoclonal microbials, limited efficacy, unacceptable safety profiles 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 the products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology.

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

Our product candidates are intended to act on the gut-body network to produce systemic effects with limited systemic exposure. This biological interaction between the gut and the rest of the body may not function in humans the way we have observed in mice and our drugs may not reproduce the systemic effects we have seen in preclinical data.

We believe our product candidates, including EDP1066, EDP1815 and EDP1503, work by modulating the systemic immune response via the gut-body network. This requires our monoclonal microbials, when dosed, to pass safely through the tissues of the gut, where they can interact with the immune cells in the interior of the small intestine called the lumen. Dosing to achieve sufficient exposure may require an inconvenient dosing regimen. Even with successful formulation and delivery to achieve proper exposure of our microbes to the small intestine, we may not get sufficient or even any immune activity at the site of disease. This may be because our understanding of the mechanisms of the gut-body network do not work in humans the way we believe they do. Despite there being strong academic literature to support the concept of the gut-body network and our observations in preclinical studies in mice, these principles and the ability to use monoclonal microbials to modulate the immune system through the gut-body network has not yet been proven in humans.

Our product candidates are monoclonal microbials, which are an unproven approach to therapeutic intervention.

All of our product candidates are based on monoclonal microbials. We have not, nor to our knowledge has any other company, received regulatory approval for an oral therapeutic based on this approach. We cannot be certain that our approach will lead to the development of approvable or marketable products. In addition, our monoclonal microbial therapies may have different safety profiles and efficacy in various indications. Finally, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of products based on monoclonal microbials, 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 platform relies on third parties for biological materials to expand our microbial library.

Our monoclonal microbial platform relies on third parties for biological materials, including human samples containing bacteria, to expand our microbial library. 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 and ability to build our pipeline of product candidates. For example, if any supplied biological materials are contaminated, we would not be able to use such biological materials. Although we have quality control processes and screening procedures, biological materials are susceptible to damage and contamination. Improper storage of these materials, by us or any third party suppliers, may require us to destroy some of our raw materials or products.

Even if our product candidates do not cause off target adverse events, there may be immunotoxicity associated with the fundamental pharmacology of our product candidates.

Our product candidates, including EDP1066, EDP1815 and EDP1503, are designed to work by modulating the immune system. While we have observed in preclinical studies that our monoclonal microbials have limited systemic exposure, the pharmacological immune effects we induce are systemic. Systemic immunomodulation from taking our monoclonal microbials could lead to immunotoxicity in patients, which may cause us or regulatory authorities to delay, limit or suspend clinical development. Other immunomodulatory agents have shown immunotoxicity. This includes immune suppressive agents, such as HUMIRA or REMICADE, which have shown an increased risk of infection or in rare instances certain types of blood cancer. In the case of immune activating agents, such as YERVOY, induction of adverse auto-immune events has been observed in some patients. Immunotoxicity in one program could cause regulators to view these adverse events as a class effect of our monoclonal microbials which may impact the timing of the development of our pipeline of potential product candidates. Even if the adverse events are manageable, the profile of the drug may be such that it limits or diminishes the possible number of patients who could receive our therapy.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and

prevalence of side effects or unexpected characteristics. For example, some of our product candidates may consist of live biological material that may remain viable in humans, which carries a risk of causing infections in patients. Some infections may require treatment with antibiotics to eliminate the monoclonal microbial. All our product candidates are screened for antibiotic sensitivity but it is possible that if antibiotic therapy does not eliminate the live biological material, a resistant version of our strain could remerge. These events, while unlikely, could cause a delay in our clinical development and/or could increase the regulatory standards for the entire class of monoclonal microbials. In an instance where the infection risk of taking our product candidates is high, this may cause the benefit risk profile of therapy to be non-competitive in the market and may lead to discontinuation of development of the product.

In addition, it is possible that infections from our product candidates could be rare and not frequently observed in our clinical trials. In larger post marketing authorization trials, however, data could show that the infection risk, while small, does exist. If unacceptable side effects arise in the development of our product candidates, we, the FDA, EMA or comparable foreign regulatory authorities, the institutional review boards, or IRBs, at the institutions in which our studies are conducted, or ethics committees, or the data safety monitoring board, or DSMB, could suspend or terminate our clinical trials or the FDA, EMA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be required to conduct post-marketing studies or clinical trials;
- regulatory authorities may require the addition of labeling statements, such as a ‘‘black box’’ warning or a contraindication;
- we may be required to implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

Companies with microbiome products or differing microbial products may produce negative clinical data which will adversely affect public perception of monoclonal microbials, and may negatively impact regulatory approval of, or demand for, our potential products.

Our monoclonal microbial product candidates are pharmaceutical compositions of commensal microbes. While we believe our approach is distinct from microbiome therapies, negative data from clinical trials using microbiome-based therapies (*e.g.*, fecal transplant) and other microbial therapies could negatively impact the perception of the therapeutic use of microbial-based products. This could negatively impact our ability to enroll patients in clinical trials. The clinical and commercial success of our potential products will depend in part on the public and clinical communities’ acceptance of the use of monoclonal microbials. Moreover, our success depends upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing monoclonal microbial technologies, even if not ultimately attributable to our product candidates, and the resulting publicity

could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for our product candidates that are approved, if any, and a decrease in demand for any such products.

Catastrophic loss of our master cell banks could significantly impair our ability to manufacture our product candidates.

Our monoclonal microbial product candidates require that we manufacture from master cell banks, or MCBs, of our microbial strains. There is a possibility of a catastrophic failure or destruction of our MCBs. This could make it impossible for us to continue to manufacture a specific product. Recreating and recertifying our MCBs is possible but not certain and could put at risk the supply of our product candidates for preclinical studies or clinical trials or any products, if approved, to our customers.

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

All of our product candidates are currently in clinical or preclinical development. We dosed the first subject in our first clinical trial of EDP1066 in April 2018 and expect to initiate clinical trials of EDP1815 and EDP1503 in the fourth quarter of 2018. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval, and the risk of failure through the product 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 results of a clinical trial do not necessarily predict final results. For example, in our initial clinical trials, drug products will be delivered in a capsule coated for targeted release in the gut. This formulation has not previously been clinically tested, nor are we able to dose mice with a capsule coated for targeted release in the gut. Our ongoing and planned clinical trials will be the first time this formulation is tested, and we cannot assure you that the results of this formulation will be consistent with the observations from our preclinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, 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 the type and number of clinical trials the FDA will require us to conduct before we may successfully gain approval, referred to as licensure in the United States, to market any of our product candidates. Prior to approving a new therapeutic product, the FDA generally requires that 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. Additionally, the FDA requires that investigation include adequate tests to demonstrate the safety of the new therapeutic product. Additional clinical trials could cause us to incur significant development costs, delay or prevent the commercialization of our products or otherwise adversely affect our business.

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

- regulators, IRBs or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may demonstrate undesirable side effects or produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to, or regulators, IRB or ethics committees may require that we or our investigators, suspend or terminate clinical trials of our product candidates 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 any future collaborators, requiring us to bear more of the burden of developing certain microbial strains;
- 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; or
- have the product removed from the market after obtaining marketing approval.

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, such as the EMA. We are developing our product candidates, EDP1066 and EDP1815, to treat inflammatory diseases, beginning with psoriasis and atopic dermatitis, and EDP1503 to treat multiple types of cancer. There are a limited number of patients from which to draw for clinical studies.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the availability of other treatments for the disease under investigation;
- the existence of competing clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- our payments for conducting clinical trials;
- the patient referral practices of physicians;
- the 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 or volunteers for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in

increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate in any jurisdiction will prevent us from commercializing the product candidate in that jurisdiction, and may affect our plans for commercialization in other jurisdictions as well. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third parties to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy to such regulatory authorities' satisfaction. 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 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 monoclonal microbials. The FDA, EMA or other foreign regulatory authorities may delay, limit, or deny the approval of 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 as 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, EMA 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 are often susceptible to varying interpretations and many companies that have believed that their products performed satisfactorily in clinical trials have nonetheless failed to obtain FDA, EMA or the applicable foreign regulatory agency approval for their products. The FDA, EMA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from nonclinical and clinical studies. Upon the review of data from any pivotal trial, the FDA, EMA or applicable foreign regulatory agency may request that the sponsor conduct additional analyses of the data and, if it believes the data are not satisfactory, could advise the sponsor to delay filing a marketing application.

Even if we eventually complete clinical testing and receive approval of a biologics license application, or BLA, or foreign marketing authorization for one of our product candidates, the FDA, EMA or applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA, EMA or the applicable foreign regulatory agency may also approve our products for a more limited indication and/or a narrower patient population than we originally request, and the FDA, EMA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our products. 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 monoclonal microbials and the gut-body network is an emerging field, and it is possible that the FDA, EMA or other regulatory authorities could issue regulations or new policies in the future affecting our monoclonal microbials that could adversely affect our product candidates.

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

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

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for multiple initial indications that we identify as most likely to succeed, in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and product development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements, in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

We may seek fast track designation for some of our product candidates. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA fast track designation. Fast track designation provides increased opportunities for sponsor meetings with the FDA during 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 a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Fast track designation does not assure ultimate approval by the FDA. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our product development program.

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

We may seek a breakthrough therapy designation for our 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. 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 may also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the designation.

We may seek orphan drug designation for some of our product candidates, but may not be able to obtain it.

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, 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.

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. Market exclusivity based on orphan drug designation is distinct from exclusivity conveyed by other regulations and under issued patents; the periods of exclusivity may run concurrently. 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.

In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA or EMA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We may seek orphan drug designation and exclusivity for some of our product candidates. However, even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if we are unable to assure sufficient quantity of the drug or biologic to meet the needs of patients with the rare disease or condition. We also may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products.

Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety 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 or if the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Risks Related to our Dependence on Third Parties and Manufacturing

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 rely, and expect to continue to rely, on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials and investigator-sponsored trials, including our clinical trial of EDP1066, and anticipated clinical trials for EDP1815 and EDP1503.

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 may be required in certain instances to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases, such as *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 product required by our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We rely on third parties for the manufacture of our product candidates for 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 the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval.

This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates on a timely basis or at all, or that such quantities will be available at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

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

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of manufacturing agreements by the third-party manufacturers;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;
- misappropriation or disclosure of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of agreements by third-party manufacturers at times that are costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current Good Manufacturing Practices, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. The contract manufacturers we rely on to produce our product candidates have never produced a FDA-approved therapeutic. If our contract manufacturers are unable to comply with cGMP regulation or if the FDA does not approve their facility upon a pre-approval inspection, our product 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 product candidates that we may develop may compete with other products for access to manufacturing facilities. Any failure to gain access to these limited manufacturing facilities could severely impact the clinical development, marketing approval and commercialization of our product candidates.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for required raw materials used in the manufacture of our product candidates or for the manufacture of finished product. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts.

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

We 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 a significant number of qualified employees to staff these facilities. We may not be able to develop commercial-scale manufacturing facilities that are adequate to produce materials for additional later-stage clinical trials or commercial use.

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

Risks Related to Commercialization of Our Product Candidates and Other Legal Compliance Matters

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

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current psoriasis treatment involves the use of steroids and biologics that are well established in the medical community, and physicians may continue to rely on these treatments. If our product candidates receive approval but do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our approved product candidates, if any, will depend on a number of factors, including:

- their efficacy, safety and other potential advantages compared to alternative treatments;
- the clinical indications for which our products are approved;

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

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

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of our product candidates. 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 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 an adequate number 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
- the inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.

Outside the United States, we may rely on third parties to sell, market and distribute our product candidates. We may not be successful in entering into arrangements with such third parties or may be 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 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, including AbbVie Inc., Agenus Inc., AstraZeneca plc, Bristol-Myers Squibb, Celgene Corporation, F. Hoffmann-La Roche A.G., Gilead Sciences, Inc., Incyte Corporation, Johnson & Johnson, Merck, Novartis International A.G., Pfizer Inc. and Regeneron Pharmaceuticals, Inc., as well as smaller, early-stage companies, that are pursuing the development of products, including microbial-based therapeutics in some instances, for 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.

Potential competitors also include academic institutions, government agencies and other public and private research organizations.

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 delay us from obtaining FDA approval to market our product candidates and result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a microbial-based therapeutic which will likely share our same regulatory approval requirements. For more information, please see “Risk Factors-Our product candidates for which we intend to seek approval as a biologic products may face competition sooner than anticipated, which may delay us from marketing our product candidates.” 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 could 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 drugs 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 drug 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 or cost-effective for a specific indication, 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 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.

Our current product liability insurance coverage and any product liability insurance coverage that we acquire in the future 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.

Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing 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. The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

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. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. 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 products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In Europe, the European Commission has granted marketing authorizations for 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 product candidates in the European Union 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, EMA or other applicable regulatory 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, EMA or other applicable regulatory approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals for our product candidates from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

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

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

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to specific conditions of approval, including a requirement to implement a risk evaluation and mitigation strategy, which could include requirements for a medication guide, communication plan, or restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

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

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

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

Noncompliance with similar European Union 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. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues. If regulatory sanctions are applied or if regulatory approval is withheld or withdrawn, the value of our company and our operating results will be adversely affected.

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

Our relationships with customers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from governmental healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

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

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program, such as Medicare and Medicaid; a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (described below);
- the false claims and civil monetary penalties laws, including the federal False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim or from knowingly or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members; manufacturers are required to submit subsequent reports to the government by the 90th day of each calendar year;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to our business practices, including but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, pricing information or marketing expenditures; and
- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval for 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, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the Affordable Care Act that are of importance to our potential product candidates are the following:

- establishment of a new pathway for approval of lower-cost biosimilars to compete with biologic products, such as those we are developing;
- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

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

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain.

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

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Individual states in the United States have become increasingly aggressive 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 European Union, the pricing of prescription drugs 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 European Union member states and parallel distribution or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If coverage and reimbursement of our products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

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

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

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

Risks Related to Our Intellectual Property

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

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

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. Prosecution of our patent portfolio is at a very early stage, and we are just beginning to reach the statutory deadlines for deciding whether and where to initiate prosecution in specific foreign jurisdictions by filing national stage applications based on our Patent Cooperation Treaty applications. As those deadlines come due, we will have to decide whether and where to pursue patent protection for the various inventions claimed in our patent portfolio, and we will only have the opportunity to obtain patents in

those jurisdictions where we pursue protection. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as, with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition and operating results.

Pursuant to our current and future license agreements with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Our patent portfolio is in the early stages of prosecution. We currently have seven issued U.S. patents. Although we have numerous patent applications pending, substantive prosecution has begun in only a small number of those applications. We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents or our current patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, we are pursuing claims to compositions of certain bacterial populations. Any claims that are issued may provide coverage for such compositions and/or their use. However, such claims would not prevent a third party from commercializing alternative compositions that do not include 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. These and other factors may provide opportunities for our competitors to design around our patents, should they issue.

Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming similar methods or by claiming subject matter that could dominate our patent position. In addition, given the early stage of prosecution of our portfolio, it may be some time before we understand how patent offices react to our patent claims and whether they identify prior art of relevance that we have not already considered, which could be an impediment to our patents issuing.

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

We may be subject to a third-party pre-issuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. For example, in October 2018, Genome & Co. petitioned the USPTO to initiate a post grant review of a patent issued to the University of Chicago, to which we have an exclusive license from the University of Chicago. Although we believe that the subject patent is valid, there is a possibility that the USPTO could invalidate or require the University of Chicago to narrow the claims contained in the patent. Any limitation on the protection of the subject technology could hinder our ability to develop and commercialize applicable product candidates.

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;
- 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 fail to comply with our obligations in the agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose rights that are important to our business.

We have entered into and may be required to enter into in the future, intellectual property license agreements that are important to our business. These license agreements may impose various diligence, milestone payment, royalty and other obligations on us. For example, we have entered into exclusive license agreements with the University of Chicago and Mayo Clinic pursuant to which we are required to use efforts to engage in various development and commercialization activities with respect to licensed products and are required to satisfy specified milestone and royalty payment obligations. If we fail to comply with any obligations under our agreements with licensors, we may be subject to termination of the license agreement in whole or in part or increased financial obligations to our licensors, in which case our ability to develop or commercialize products covered by the license agreement will be impaired. Further, we may need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our licensors.

In addition, disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; and
- our diligence obligations under the license agreement and what activities satisfy those obligations.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

The intellectual property which we have licensed from the University of Chicago and Mayo Clinic was discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

We have licensed certain intellectual property from the University of Chicago and Mayo Clinic. These agreements indicate that the rights licensed to us are subject to the obligations to and the rights of the U.S. government, including those set forth in the Bayh-Dole Act of 1980, or the Bayh-Dole Act. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future therapeutics based on the licensed intellectual property. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or nonexclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." While the U.S. government has sparingly used, and to our knowledge never successfully exercised, such march-in rights, any exercise of the march-in rights by the U.S. government could harm our competitive position, business, financial condition, results of operations, and prospects. If the U.S. government exercises such march-in rights, we may receive compensation that is deemed reasonable by the U.S. government in its sole discretion, which may be less than what we might be able to obtain in the open market. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources.

In addition, the U.S. government requires that any therapeutics embodying any invention generated through the use of U.S. government funding be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. therapeutic manufacturers for therapeutics covered by such intellectual property.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also seek to enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate, 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 has also developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, in particular the first to file provisions, only became effective on March 16, 2013. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Thus, for our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law.

Moreover, some of the patent applications in our portfolio will be subject to examination under the pre-Leahy-Smith Act law and regulations, while other patents applications in our portfolio will be subject to examination under the law and regulations, as amended by the Leahy-Smith Act. This introduces additional complexities into the prosecution and management of our portfolio.

In addition, the Leahy-Smith Act limits where a patentee may file a patent infringement suit and provides opportunities for third parties to challenge any issued patent in the USPTO. These provisions apply to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a federal court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims because it may be easier for them to do so relative to challenging the patent in a federal court action. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

A number of cases decided by the Supreme Court have involved questions of when claims reciting abstract ideas, laws of nature, natural phenomena and/or natural products are eligible for a patent, regardless of whether the claimed subject matter is otherwise novel and inventive. These cases include *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 12-398 (2013) or *Myriad*; *Alice Corp. v. CLS Bank International*, 573 U.S. 13-298 (2014); and *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, or *Prometheus*, 566 U.S. 10-1150 (2012). In response to these cases, the USPTO has issued guidance to the examining corps.

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

Numerous patents and pending applications are owned by third parties in the fields in which we are developing product candidates, both in the United States and elsewhere. It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products. We are aware of several pending patent applications containing one or more claims that could be construed to cover some of our product candidates or technology, should those claims issue in their original form or in the form presently being pursued. In addition, we are aware of a third-party patent family that includes issued and allowed patents, including in the United States, with claims that, if valid and enforceable, could be construed to cover some of our product candidates or their methods of use.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringe 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 names, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

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

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

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

Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

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

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

Risks Related to Employee Matters and Managing Growth and Other Risks Related to Our Business

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

We are highly dependent on Balkrishan (Simba) Gill, 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 due to the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

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

A variety of risks associated with operating internationally could materially adversely affect our business.

We currently have limited international operations, but our business strategy incorporates potentially expanding internationally if any of our product candidates receive regulatory approval. 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.

The United Kingdom's planned exit from the European Union may adversely impact our business.

In a non-binding referendum on the United Kingdom of Great Britain and Northern Ireland's membership in the European Union in June 2016, a majority of the United Kingdom's electorate voted for the United Kingdom's withdrawal from the European Union ("Brexit"). A process of negotiation will determine the future terms of the United Kingdom's relationship with the European Union and its members. While Article 50 of the Lisbon Treaty was invoked by the United Kingdom on March 29, 2017, substantial uncertainty remains regarding the outcome of the negotiations, as well as the scope and duration of a transitionary period, if any, following the expiration of the Article 50 period on March 29, 2019. This uncertainty was exacerbated by the lack of a decisive majority following the United Kingdom general election in June 2017 and, following months of negotiation, the rejection by United Kingdom's Parliament in January 2019 of a withdrawal agreement and related statement on future relations negotiated by representatives of the United Kingdom and the European Union.

Depending on the terms of Brexit, the United Kingdom could lose its present rights or terms of access to the single EU market and EU customs areas and to the global trade deals negotiated by the European Union on behalf of its members. The uncertainty regarding new or modified arrangements, or initially the absence of such arrangements, between the United Kingdom and other countries following Brexit may have a material adverse effect on the movement of goods between the United Kingdom and members of the European Union and the United States, including the interruption of or delays in imports into the United Kingdom of goods originating within the European Union and exports from the United Kingdom of goods originating there. For example, shipments into the United Kingdom of drug substance manufactured for the Company in the European Union may be interrupted or delayed and thereby prevent or delay the manufacture in the United Kingdom of drug product. Similarly, shipments out of the United Kingdom of drug product to the United States or the European Union may be interrupted or delayed and thereby prevent or delay the delivery of drug product to clinical sites. Such a situation could hinder our ability to conduct current and planned clinical trials and have an adverse effect on our business.

Our business and operations would suffer in the event of information technology and other system failures or security breaches of or unauthorized access to our systems.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, or to attachments to emails and other security breaches or unauthorized access by persons inside our organization or with access to our internal systems. The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusions, including by computer hackers, foreign governments and cyber terrorists, generally has increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our systems safeguard important confidential personal data regarding patients enrolled in our clinical trials. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption to our product development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

We rely on a set of cloud-based software services and access these services via the Internet for the vast majority of our computing, storage, bandwidth, and other services. Any disruption of or interference with our use of our cloud-based services would negatively affect our operations and could seriously harm our business.

We use several distributed computing infrastructure platforms for business operations, or what is commonly referred to as “cloud” computing services and we access these services via the Internet. Any transition of the cloud services currently provided by an existing vendor to another cloud provider would be difficult to implement and will cause us to incur significant time and expense. Given this, any significant disruption of or interference with our use of these cloud computing services would negatively impact our operations and our business would be seriously harmed. If our employees or partners are not able to access our cloud computing services or encounter difficulties in doing so, we may experience business disruption. The level of service provided by our cloud computing vendors, including the ability to secure our confidential information and the confidential information of third parties that is shared with us, may also impact the perception of our company and could seriously harm our business and reputation and create liability for us. If a cloud computing service that we use experiences interruptions in service regularly or for a prolonged basis, or other similar issues, our business could be seriously harmed.

In addition, a cloud computing service may take actions beyond our control that could seriously harm our business, including:

- discontinuing or limiting our access to its platform;
- increasing pricing terms;
- terminating or seeking to terminate our contractual relationship altogether;
- establishing more favorable relationships with one or more of our competitors; or
- modifying or interpreting its terms of service or other policies in a manner that impacts our ability to run our business and operations.

Our cloud computing services have broad discretion to change and interpret its terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing services may also alter how we are able to process data on the platform. If a cloud computing services makes changes or interpretations that are unfavorable to us, our business could be seriously harmed.

Our efforts to protect the information shared with us may be unsuccessful due to the actions of third parties, software bugs, or other technical malfunctions, employee error or malfeasance, or other factors. In addition, third parties may attempt to fraudulently induce employees or users to disclose information to gain access to our data or third-party data entrusted to us. If any of these events occur, our or third-party information could be accessed or disclosed improperly. Some partners or collaborators may store information that we share with them on their own computing system. If these third parties fail to implement adequate data-security practices or fail to comply with our policies, our data may be improperly accessed or disclosed. And even if these third parties take all these steps, their networks may still suffer a breach, which could compromise our data.

Any incidents where our information is accessed without authorization, or is improperly used, or incidents that violate our policies, could damage our reputation and our brand and diminish our competitive position. In addition, affected parties or

government authorities could initiate legal or regulatory action against us over those incidents, which could cause us to incur significant expense and liability or result in orders or consent decrees forcing us to modify our business practices. Concerns over our privacy practices, whether actual or unfounded, could damage our reputation and brand and deter users, advertisers, and partners from using our products and services. Any of these occurrences could seriously harm our business.

We are also subject to many federal, state, and foreign laws and regulations, including those related to privacy, rights of publicity, data protection, content regulation, intellectual property, health and safety, competition, protection of minors, consumer protection, employment, and taxation. These laws and regulations are constantly evolving and may be interpreted, applied, created, or amended in a manner that could seriously harm our business.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, and prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to take action with respect to regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees and statutory, regulatory and policy changes. In addition, government funding of the FDA, the SEC and other government agencies on which our operations may rely 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 regulatory submissions to be reviewed or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, including as recently as December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government 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. Similarly, a prolonged government shutdown could prevent the timely review of our patent applications by the USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Additionally, government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly fund our business.

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 only made one acquisition to date, and our ability to do so successfully is unproven beyond this instance. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

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

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

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

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock, and we could be subject to securities class action litigation as a result.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares of common stock at or above the price at which you purchase the shares. 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;
- adverse actions taken by regulatory agencies with respect to our preclinical studies or clinical trials, manufacturing or sales and marketing activities;
- any adverse changes to our relationship with third party contractors or manufacturers;
- development of new product candidates that may address our markets and may make our existing 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 product development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- press reports or other negative publicity, whether or not true, about our business;
- 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.

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

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.

Based on the number of shares of common stock outstanding as of February 8, 2019, our executive officers, directors and stockholders who own more than 5% of our outstanding common stock and their respective affiliates will, in the aggregate, hold shares representing approximately 75% 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. They may also have interests that differ from yours and may vote in a way with which you disagree, and which may be adverse to your interests. This concentration of ownership control may have the effect of delaying, deferring or preventing a change in

control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and might ultimately affect the market price of our common stock.

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. For example, in November 2018, holders of approximately 28.3 million shares of our common stock formerly subject to a lock-up agreement entered into in connection with our IPO became eligible to resell their shares in the open market (subject to volume limitations as to resales by affiliates of the Company pursuant to Rule 144 of the Securities Act). Moreover, holders of an aggregate of approximately 24.9 million shares of our common stock 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, including entities affiliated with Flagship Pioneering, until such shares can otherwise be sold without restriction under Rule 144 of 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 JOBS Act, and may remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the initial public offering of our common stock, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our outstanding common stock that are held by non-affiliates exceeds $700 million as of the prior June 30, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- 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.

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 elected to take advantage of this extended transition period.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that 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, or our annual revenues are more than $100 million during the most recently completed fiscal year and 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, are exempt from the auditor attestation requirements of Section 404, 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, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations. 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.

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

As a public company, and particularly after we are no longer an emerging growth company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives.

Moreover, these rules and regulations have increased our legal and financial compliance costs and made 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.

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

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

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC.

We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

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

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target preclinical studies or clinical studies and/or 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 could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

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

- 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.

Our restated certificate of incorporation provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

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 any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty owed by any director, officer, employee or stockholder to us or our stockholders, any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or any action asserting a claim governed by the internal affairs doctrine. We believe these provisions benefit 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. The provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes, and may have the effect of discouraging lawsuits, including those 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. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may

incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our results of operations and financial condition.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation and expansion of our business. Therefore, you should not rely on an investment in our common stock as a source for any future dividend income.

Our board of directors has significant discretion as to whether to distribute dividends. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other things, our future results of operations and cash flow, our capital requirements and surplus, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on your investment in our common stock will likely depend entirely on any future capital appreciation, if any, of our common stock. There is no guarantee that our common stock will appreciate in value or even maintain the price at which you purchased our common stock.

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

As of December 31, 2018, we had federal and state net operating loss carryforwards of $98.0 million and $91.2 million, respectively. A portion of the federal net operating losses will begin to expire at various dates through 2037. The state net operating losses will begin to expire at various dates through 2038. As of December 31, 2018, we also had federal research and development tax credit carryforwards of $2.1 million and state research and development tax credit carryforwards of $0.8 million, which begin to expire in 2033. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation’s stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in the future, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017, or the TCJA, may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Furthermore, under the TCJA, although the treatment of NOLs generated before December 31, 2017 has generally not changed, NOLs generated in calendar year 2018 and beyond will not be subject to expiration but will only be able to offset 80% of taxable income. This change may require us to pay federal income taxes even if we have NOL carryforwards that could otherwise offset our taxable income.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

The TCJA has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs”), adopting elements of a territorial tax system, imposing a one-time transition tax, or repatriation tax, on all undistributed earnings and profits of certain U.S.-owned foreign corporations, revising the rules governing net operating losses and the rules governing foreign tax credits, and introducing new anti-base erosion provisions. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities.

While some of the changes made by the TCJA may adversely affect us in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors and auditors 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters is located in Cambridge, Massachusetts, where we currently lease 40,765 square feet of office and laboratory space under a sublease agreement that expires in September 2025. We also lease 6,437 square feet of office and laboratory space in Cambridge, Massachusetts that we sublease to a third party. This lease and sublease both expire in May 2020. We believe that our facilities are sufficient to meet the current needs of the company and that suitable space will be available as and when needed.

Item 3. Legal Proceedings

We are not subject to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

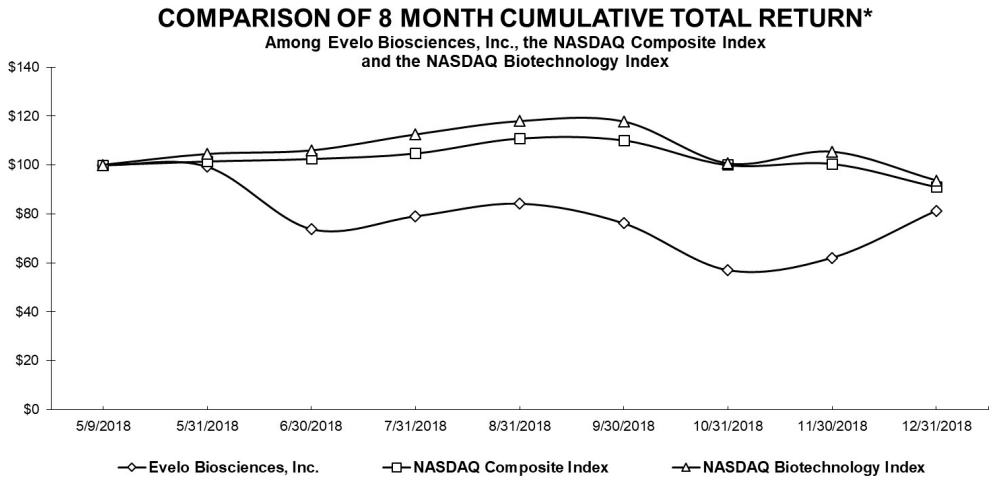
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock began trading on the NASDAQ Global Select Market on May 9, 2018, under the symbol “EVLO” Prior to that time, there was no public market for our common stock.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed “soliciting material” or to be “filed” with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act. The following graph shows a comparison from May 9, 2018 (the date our common stock commenced trading on the NASDAQ Global Select Market) through December 31, 2018, of the cumulative total return for our common stock, the NASDAQ Composite Index, and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on May 9, 2018. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.



* $100 invested on May 9, 2018 in stock or in index, including reinvestment of dividends.

Holders of Record

As of February 8, 2019, we had approximately 54 holders of record of our common stock. Certain shares are held in “street” name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial conditions, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Use of Proceeds

On May 11, 2018, we completed the initial public offering of our common stock, or the IPO, and issued and sold 5,312,500 shares of our common stock at a public offering price of $16.00 per share, for gross proceeds of $85.0 million and $75.8 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us. None of these expenses consisted of payments made by us to directors, officers or persons owning 10% or more of our common stock or to their associates, or to our affiliates.

The offer and sale of all of the shares in the offering was registered under the Securities Act pursuant to a registration on Form S-1 (Reg. No. 333-224278), as amended, which was declared effective by the Securities and Exchange Commission, or the SEC, on May 8, 2018. The managing underwriters for our IPO were Morgan Stanley & Co. LLC and Cowen and Company, LLC.

The net proceeds from our initial public offering have been invested in government backed $1 net asset value money market funds and U.S. treasury securities. There has been no material change in the expected use of the net proceeds from our initial public offering as described in our Prospectus. As of December 31, 2018, we had used $42.6 million of the net proceeds from our IPO.

Item 6. Selected Financial Data

The following table sets forth our selected consolidated financial data. We derived the consolidated statement of operations data for the years ended December 31, 2018, 2017, and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017, from our audited consolidated financial statements, included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated balance sheet as of December 31, 2016 from our audited consolidated financial statements not included in this report. Our historical results are not necessarily indicative of results to be expected for any period in the future. The selected consolidated financial data presented below should be read in conjunction with Part II, Item 7A "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes thereto, included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section is not intended to replace our consolidated financial statements and the related notes thereto.

Statement of Operations Data:

	Year Ended December 31,		
	2018	2017	2016
	(in thousands, except share and per share amounts)		
Statement of Operations Data:			
Operating expenses:			
Research and development	$ 39,885	$ 19,957	$ 9,134
General and administrative	18,218	7,574	3,891
Total operating expenses	58,103	27,531	13,025
Loss from operations	(58,103)	(27,531)	(13,025)
Other (expense) income:			
Interest income (expense), net	1,563	(215)	(287)
Other expenses	(406)	(301)	(20)
Other income (expense), net	1,157	(516)	(307)
Net loss	$ (56,946)	$ (28,047)	$ (13,332)
Convertible preferred stock dividends	(3,937)	(6,085)	(1,645)
Net loss attributable to common stockholders	$ (60,883)	$ (34,132)	$ (14,977)
Net loss per share attributable to common stockholders, basic and diluted(1)	$ (2.78)	$ (9.10)	$ (5.28)
Weighted average number of common shares outstanding, basic and diluted(1)	21,871,029	3,750,790	2,834,733

Balance Sheet Data:

	As of December 31,		
	2018	2017	2016
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents and short-term investments	$ 147,919	$ 38,246	$ 15,536
Working capital(2)	142,387	34,938	13,472
Total assets	159,867	43,788	18,570
Long-term debt	12,305	9,966	9,931
Convertible preferred stock	—	83,702	33,863
Accumulated deficit	(113,381)	(56,411)	(28,341)
Total stockholders' equity (deficit)	136,949	(54,723)	(28,337)

(1) See Note 2 to our audited consolidated financial statements for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

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

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

The following discussion and analysis should be read in conjunction with Part II, Item 6."Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and analysis and other parts of this Annual Report on Form 10-K contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Part I, Item1A"Risk Factors" and elsewhere in this Annual Report on Form 10-K. You should carefully read the "Risk Factors" section of this Annual Report on Form 10-K to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."

Overview

Evelo Biosciences is discovering and developing potential therapies designed to engage immune cells in the small intestine and drive therapeutic effects throughout the body. The action of our therapies is based on the central role of the small intestine of the gut in controlling immune and biological activity throughout the body. We refer to this relationship as the gut-body network. The gut-body network represents the connections of the small intestine to all organs and tissues. We believe that we have the potential to use the unexplored biology of the gut-body network to develop novel therapies that could transform the treatment of many diseases, potentially driving profound benefits to patients and society.

We are developing monoclonal microbials, a potential new modality of oral biologic medicines. Monoclonal microbials are orally-delivered pharmaceutical compositions of naturally-occurring, specific single strains of microbes. Our monoclonal microbials engage immune cells in the small intestine and drive changes in systemic biology without systemic exposure and without colonizing the gut in preclinical models. We have built a proprietary platform designed to develop monoclonal microbials as therapeutics. Our platform integrates tools and capabilities necessary to source, select, develop and manufacture monoclonal microbials as therapies.

Clinical Programs

We are advancing monoclonal microbials to potentially treat a spectrum of immune mediated diseases with an initial focus on inflammatory diseases and oncology. The efficiency of our platform has, in a relatively short period of time, allowed us to advance three product candidates into clinical trials for a range of inflammatory diseases and cancers.

- **EDP1066, a monoclonal microbial candidate for inflammatory diseases:** In April 2018 we initiated our ongoing Phase 1b placebo-controlled dose-escalating safety and tolerability study of EDP1066 in approximately 36 healthy volunteers and up to 96 patients with mild to moderate psoriasis or atopic dermatitis. Exploratory endpoints include the evaluation of a

variety of clinical measures of disease and pharmacodynamic markers, including biomarker signals from paired biopsies of affected skin in patients. We expect initial clinical data from this study in the second quarter of 2019.

- **EDP1815, a monoclonal microbial candidate for inflammatory diseases:** In November 2018 we initiated our ongoing Phase 1b placebo-controlled dose-escalating safety and tolerability study of EDP1815 in approximately 24 healthy volunteers and up to 108 patients with mild to moderate psoriasis or atopic dermatitis. Exploratory endpoints include the evaluation of a variety of clinical measures of disease and pharmacodynamic markers, including biomarker signals from paired biopsies of affected skin in patients. We expect initial clinical data from this study in the second half of 2019.

- **EDP1503, a monoclonal microbial candidate for oncology**. In December 2018 we initiated our ongoing Phase 1/2 open-label study of EDP1503 in combination with KEYTRUDA (pembrolizumab) in three groups of patients: microsatellite stable colorectal cancer; triple-negative breast cancer; and patients across multiple tumor types who have relapsed on prior PD-1/L1 inhibitor treatment. We estimate that we will enroll up to 120 subjects in this study which will assess the safety and tolerability, immune response markers and overall response rates achieved with EDP1503 in combination with KEYTRUDA. We expect initial clinical data from this study in the first half of 2020.

In January 2019, the University of Chicago initiated a Phase 2a investigator-sponsored clinical study of EDP1503 in combination with KEYTRUDA in melanoma patients. The University of Chicago will enroll up to 70 PD-l-naïve and PD-1-relapsed melanoma patients in this study which is assessing the safety, tolerability and overall response rates achieved with EDP1503 in combination with KEYTRUDA. Additionally, we expect to evaluate immune response markers from biopsies taken during the study. We anticipate initial clinical data from this study in the second half of 2020.

In addition to these ongoing clinical trials we expect to initiate future additional clinical trials related to these product candidates and potential new product candidates. For instance, in the first half of 2019, we expect to initiate an additional immuno-pharmacology clinical trial in healthy volunteers with EDP1066. Our intention is to finalize the selection of the next wave of inflammation indications after data from the ongoing EDP1066 and EDP1815 clinical trials have been analyzed. Potential indications include asthma, psoriatic arthritis, rheumatoid arthritis and inflammatory bowel disease.

We were incorporated and commenced operations in 2014. Since our incorporation, we have devoted substantially all of our resources to developing our clinical and preclinical candidates, building our intellectual property portfolio and process development and manufacturing function, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations primarily with proceeds from sales of common and convertible preferred stock to our equity investors and borrowings under a loan and security agreement, as amended, with a financial institution. Through December 31, 2018, we received gross proceeds of $172.0 million from sales of convertible preferred stock and borrowings under our loan and security agreement. On May 11, 2018, we completed our initial public offering, or the IPO, of 5,312,500 shares of our common stock at a public offering price of $16.00 per share. The shares began trading on the Nasdaq Global Select Market on May 9, 2018 under the symbol "EVLO." The gross proceeds from the IPO were $85.0 million and the net proceeds were approximately $75.8 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. Upon the closing of the IPO all of the Company’s outstanding shares of convertible preferred stock automatically converted into 22,386,677 shares of common stock at the applicable conversion rate then in effect.

On April 27, 2018, we effected a 1-for-4.079 reverse stock split of our common stock. Stockholders entitled to fractional shares as a result of the reverse stock split received a cash payment in lieu of receiving fractional shares. These cash payments were not material. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split. The financial statements have also been retroactively adjusted to reflect adjustments to the conversion ratio for each series of convertible preferred stock effected in connection with the reverse stock split.

We are a development stage company and have not generated any revenue. All of our product candidates are in early clinical or preclinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Since our inception, we have incurred significant operating losses and we continue to incur significant research and development and other expenses related to our ongoing operations. For the years ended December 31, 2018, 2017 and 2016, our net loss was $56.9 million, $28.0 million and $13.3 million, respectively. As of December 31, 2018, we had an accumulated deficit of $113.4 million. We do not expect to generate revenue from sales of any products for the foreseeable future, if at all.

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

- continue the ongoing proof of concept trials for EDP1066, EDP1815 and EDP1503;
- potentially initiate additional clinical trials for EDP1066, EDP1815 and EDP1503;
- initiate or advance the clinical development of any additional monoclonal microbial product candidates;
- conduct research and continue preclinical development of potential product candidates;
- make strategic investments in manufacturing capabilities, including potentially planning and building our own manufacturing facility;
- maintain our current intellectual property portfolio and opportunistically acquire complementary intellectual property;
- increase research and development employees and employee-related expenses including salaries, benefits, travel and stock-based compensation expense; and
- seek to obtain regulatory approvals for our product candidates.

In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

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.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2018, our principal source of liquidity is cash, cash equivalents and short-term investments, which totaled approximately $147.9 million. We expect that our existing cash, cash equivalents and short-term investments will enable us to fund our planned operating expenses and capital expenditure requirements into the second half of 2020. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. See “Liquidity and Capital Resources.”

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future if at all. If our development efforts for our current product candidates or additional product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

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 investigative sites, external laboratories and contract research organizations, or CROs, that conduct research, preclinical activities and clinical trials on our behalf
- manufacturing process-development costs as well as technology transfer and other expenses incurred with contract manufacturing organizations, or CMOs, that manufacture drug substance and drug product for use in our preclinical activities and any current or future clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel in our research and development functions;
- expenses to acquire technologies to be used in research and development;
- 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 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 consolidated financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Our primary focus of research and development since inception has been building a platform to enable us to develop medicines based on an understanding of the gut-body network and to show potential clinical utility. Our platform and program expenses consist principally of costs, such as preclinical research, clinical and preclinical manufacturing activity costs, clinical development costs, licensing expense as well as an allocation of certain indirect costs, facility costs and depreciation expense. We do not allocate personnel costs, which include salaries, discretionary bonus and stock-based compensation costs, as such costs are separately classified as research and development personnel costs.

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 continue our ongoing clinical trials for our product candidates, including EDP1066, EDP1815 and EDP1503, initiate additional clinical trials, continue to discover and develop additional product candidates, hire additional research and development personnel, build manufacturing capabilities and expand into additional therapeutic areas.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of our current product candidates and/or any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our product candidates;
- our ability to establish an appropriate safety profile with Investigational New Drug-enabling toxicology studies;
- our ability to establish and maintain agreements with third-party manufacturers and other entities for clinical trial supply and future commercial supply, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of the product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We expect our research and development expenses to increase at least over the next several years as we continue to implement our business strategy, advance our current programs, expand our research and development efforts, seek regulatory approvals for any product candidates that successfully complete clinical trials, identify and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts.

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 administrative consulting services; insurance costs; administrative travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

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

Interest Income (Expense), Net

Interest income (expense), net consisted primarily of interest earned on our cash, cash equivalents and short-term investments balances offset by interest expense at the stated rate on borrowings under our loan and security agreement,

amortization of deferred financing costs and interest expense related to the accretion of debt discount associated with the loan and security agreement.

Other Expenses

Other expenses primarily consist of non-cash changes in the fair value of warrants issued in connection with our loan and security agreement, as well as the change in fair value of a derivative instrument issued in February 2018 in conjunction with the modification of our debt arrangement.

Income Taxes

Since our inception in 2014, 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.

Results of Operations

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 (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2018	2017	
Operating expenses:			
Research and development	$ 39,885	$ 19,957	$ 19,928
General and administrative	18,218	7,574	10,644
Total operating expenses	58,103	27,531	30,572
Loss from operations	(58,103)	(27,531)	(30,572)
Other (expense) income:			
Interest income (expense), net	1,563	(215)	1,778
Other expense	(406)	(301)	(105)
Other income (expense), net	1,157	(516)	1,673
Net loss	$ (56,946)	$ (28,047)	$ (28,899)

Research and Development Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2018	2017	
Gut-body network platform expenses	$ 7,972	$ 3,806	$ 4,166
Inflammation programs	13,852	4,284	9,568
Oncology programs	6,012	3,706	2,306
Other program expenses	—	566	(566)
Research and development personnel costs (including stock-based compensation)	12,049	7,595	4,454
Total research and development expenses	$ 39,885	$ 19,957	$ 19,928

Research and development expenses were $39.9 million for the year ended December 31, 2018, compared to $20.0 million for the year ended December 31, 2017. The increase of $19.9 million was due primarily to increases of $9.6 million in costs for our inflammation programs, driven primarily by external manufacturing costs and clinical trial expenses, an increase of $4.2 million in gut-body network platform expenses in line with our strategy to maximize the potential of our platform, as well as an increase of $2.3 million for our oncology programs primarily related to increased costs associated with external manufacturing and clinical development activities partially offset by decreased preclinical costs. Personnel costs increased $4.5 million due primarily to increases in research and development headcount and an increase of $1.7 million in stock-based compensation expense. We expect that our research and development expenses will continue to increase in the foreseeable future as we continue our clinical trials for our product candidates, including EDP1066, EDP1815 and EDP1503, initiate new clinical trials, continue discovery and development efforts for additional product candidates, hire additional research and development personnel and seek to increase manufacturing capabilities and possibly expand into additional therapeutic areas.

General and Administrative Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2018	2017	
General and administrative personnel costs (including stock-based compensation)	$ 8,816	$ 3,237	$ 5,579
Professional fees	5,377	2,758	2,619
Facility costs, office expense and other	4,025	1,579	2,446
Total general and administrative expenses	$ 18,218	$ 7,574	$ 10,644

General and administrative expenses were $18.2 million for the year ended December 31, 2018, compared to $7.6 million for the year ended December 31, 2017. The increase of $10.6 million primarily reflects costs required to support our growing organization and public company status. Personnel costs increased by $5.6 million due primarily to increases in general and administrative headcount and compensation, including an increase of $2.9 million in stock-based compensation expense. Facility and other costs increased $2.4 million primarily due to the expansion of our leased space to support the growth of the Company. Professional fees increased $2.6 million, reflecting increase in legal, patent and other professional consulting fees. We expect general and administrative expenses to continue to increase due to higher personnel and related costs, professional fees and consulting expenses in support of the continued growth of the Company.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2018 was income of $1.2 million compared to an expense of $0.5 million for the year ended December 31, 2017. This increase was primarily driven by a $2.2 million increase in interest earned on higher average cash and investments balances in 2018 partially offset by an increase of $0.4 million in interest expense related to higher average 2018 borrowings under our loan and security agreement.

Comparison of Years Ended December 31, 2017 and 2016

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

	Year Ended December 31,		Increase/ (Decrease)
	2017	2016	
Operating expenses:			
Research and development	$ 19,957	$ 9,134	$ 10,823
General and administrative	7,574	3,891	3,683
Total operating expenses	27,531	13,025	14,506
Loss from operations	(27,531)	(13,025)	(14,506)
Other (expense) income:			
Interest expense, net	(215)	(287)	72
Other expense	(301)	(20)	(281)
Other (expense) income, net	(516)	(307)	(209)
Net loss	$ (28,047)	$ (13,332)	$ (14,715)

Research and Development Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2017	2016	
Gut-body network platform expenses	$ 3,806	$ 2,064	$ 1,742
Inflammation programs	4,284	—	4,284
Oncology programs	3,706	2,581	1,125
Other program expenses	566	393	173
Research and development personnel costs (including stock-based compensation)	7,595	4,096	3,499
Total research and development expenses	$ 19,957	$ 9,134	$ 10,823

Research and development expenses were $20.0 million for the year ended December 31, 2017, compared to $9.1 million for the year ended December 31, 2016. The increase of $10.8 million was due primarily to an increase of $4.3 million in costs for our inflammation programs, including the external preclinical research, preclinical manufacturing activity costs and licensing expense, an increase of $1.7 million in platform expense due to the overall growth of the research and development departments in-line with our growth, an increase of $1.1 million in costs for the oncology programs, primarily due to increases in external preclinical research and preclinical manufacturing activity in 2017, and an increase of $3.5 million in personnel costs, including increases in salaries and bonus of $2.4 million and increases in other headcount expenses to support research and development activity.

General and Administrative Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2017	2016	
General and administrative personnel costs (including stock-based compensation)	$ 3,237	$ 2,035	$ 1,202
Professional fees	2,758	826	1,932
Facility costs, office expense and other	1,579	1,030	549
Total general and administrative expenses	$ 7,574	$ 3,891	$ 3,683

General and administrative expenses were $7.6 million for the year ended December 31, 2017, compared to $3.9 million for the year ended December 31, 2016. The increase of $3.7 million was primarily due to an increase of $1.9 million in professional fees, including legal, patent and other professional consulting fees related to business development and an increase of $1.2 million in personnel costs, including an increase of $0.5 million in stock-based compensation expense and $0.4 million in salaries and bonus. The remaining increase was related to recruiting, benefits and other various expenses.

Other Income (Expense), Net

Other income (expense), net for the year ended December 31, 2017 was an expense of $0.5 million, compared to an expense of $0.3 million for the year ended December 31, 2016. This overall increase was driven by a $0.3 million increase in other expense as a result of an increase in the fair value of the warrants as well as an increase in interest expense on our debt, which payments began during August 2016. This was partially offset by an increase in interest income of $0.1 million from the larger cash balance in 2017.

Liquidity and Capital Resources

To date, we have financed our operations primarily with the proceeds from the initial public offering of our common stock combined with proceeds from previous sales of our convertible preferred stock to our equity investors and borrowings under the loan and security agreement. From our inception through December 31, 2018, we have received gross proceeds of $257.0 million from such transactions, including $15.0 million borrowed under the loan and security agreement. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $147.9 million and an accumulated deficit of $113.4 million. We expect that our existing cash, cash equivalents and short-term investments will enable us to fund our planned operating expenses and capital expenditure requirements into the second half of 2020.

Debt financing

On June 16, 2016, the Company acquired Epiva, a privately held research company, focused on microbes for inflammatory diseases in order to create synergies and expand the depth of the Company's research platform. In connection with the acquisition, we assumed Epiva's credit facility (the "Credit Facility") and the related $3.0 million of outstanding debt. Subsequent to the acquisition, we amended the Credit Facility to allow us to borrow up to $15.0 million, including the $3.0 million that was outstanding on the modification date and extending the maturity to August 15, 2020. During 2016, we borrowed an additional $7.0 million, bringing the total amounts outstanding as of December 31, 2016 and 2017 to $10.0 million. In February 2018, we drew the additional $5.0 million available under the Credit Facility. This resulted in an increase to the interest rate to the higher of (i) prime plus 0.25% or (ii) 4.50% per annum. In conjunction with this drawdown, the interest only payment period was extended through to August 15, 2019. Upon the expiration of the interest only period, amounts borrowed will be repaid over 24 equal monthly payments of principal plus interest accrued through August 15, 2021. As such, $2.5 million and $12.3 million of the debt obligation have been included as current and long-term, respectively, on our consolidated balance sheet. We have the ability to prepay the outstanding loan at our option with a prepayment fee of 0.5% if the prepayment is made between August 15, 2018 and August 15, 2019 and with no prepayment fee thereafter.

We have incurred losses and generated negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. We incurred net losses of approximately $57.0 million, $28.0 million and $13.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. Until such time, if ever, as we can generate revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaborations, license and development agreements. To the extent that we raise additional capital through future equity offerings or debt financings, the ownership interest of common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of the common stockholders. Debt and equity financings, 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. There can be no assurance that such financings will be obtained on terms acceptable to us, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us we may have to significantly delay, scale back or discontinue our research and development programs or future commercialization efforts. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties for one or more of our current or future drug candidates, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or to grant licenses on terms that may not be favorable to us. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

Cash Flows

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

	Year Ended December 31,		
	2018	**2017**	**2016**
Cash used in operating activities	$ (47,279)	$ (23,265)	$ (12,314)
Cash (used in)/provided by investing activities	(60,128)	(1,742)	9,263
Cash provided by financing activities	162,012	48,967	15,742
Net increase in cash, cash equivalents and restricted cash	$ 54,605	$ 23,960	$ 12,691

Operating Activities

Net cash used in operating activities for the year ended December 31, 2018, was $47.3 million, primarily due to our net loss of $56.9 million. This was partially offset by non-cash charges, including stock-based compensation expense of $6.1 million, depreciation expense of $1.9 million, change in fair value of warrant liability of $0.4 million and reduction in working capital of $1.2 million.

Net cash used in operating activities for the year ended December 31, 2017, was $23.3 million primarily due to our net loss of $28.0 million. This was partially offset by non-cash charges, including stock-based compensation expense of $1.5 million, depreciation expense of $0.8 million, change in fair value of warrant liability of $0.3 million and change in working capital of $2.2 million.

Net cash used in operating activities for the year ended December 31, 2016, was $12.3 million, primarily due to our net loss of $13.3 million. This was partially offset by non-cash charges, including stock-based compensation expense of $0.4 million, depreciation of $0.5 million and change in working capital of $0.1 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2018, was $60.1 million, primarily consisting of the purchase of investments totaling $136.1 million, partially offset by maturities of investments totaling $81.3 million. Additionally, the purchase of capital equipment totaled $5.5 million during the period, slightly offset by $0.2 million of cash received for the sale of certain equipment.

Net cash used in investing activities for the year ended December 31, 2017, was $1.7 million, primarily due to the purchase of capital equipment during the period.

Net cash provided by investing activities for the year ended December 31, 2016, was $9.2 million, which consisted of $10.5 million of cash received in the acquisition of Epiva, slightly offset by the purchase of capital equipment of $1.3 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2018 was $162.0 million, primarily consisting of net proceeds of $75.8 million from our IPO, net proceeds of $81.3 million from the issuance of our Series C Preferred Stock as well as net proceeds of approximately $5.0 million from the issuance of long-term debt. This is partially offset by a payment made for the settlement of a derivative liability of $0.3 million.

Net cash provided by financing activities for the year ended December 31, 2017 was $49.0 million, primarily consisting of net proceeds of $48.9 million from the issuance of our Series B Preferred Stock.

Net cash provided by financing activities for the year ended December 31, 2016, was $15.7 million, primarily consisted of net proceeds of $7.5 million from the issuance of Series A Preferred Stock and Series A-2 Preferred Stock, gross proceeds of $11.0 million from the issuance of long-term debt, $1.0 million received as shareholders' payable for Series B Preferred Stock issued in 2017 and $0.2 million from the exercise of stock options. These were offset by repayment of long-term debt of $4.0 million.

Funding Requirements

We have incurred losses and cumulative negative cash flows from operations since our inception. As of December 31, 2018, we had an accumulated deficit of $113.4 million. We anticipate that we will continue to incur significant losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase. As a result, we will need additional capital to fund our operations, which we may raise through a combination of the sale of equity, debt financings, or other sources, including potential collaborations.

We expect our expenses to increase substantially in connection with our ongoing development activities related to the initiation of clinical studies and preclinical work on additional monoclonal microbial product candidates, which are still in development, and our follow-on therapeutics and other programs. In addition, we expect to incur additional costs associated with increased personnel and operating as a public company. We anticipate that our expenses will increase substantially if and as we:

- continue our proof of concept clinical trials of EDP1066, EDP1815 and EDP1503;
- advance the clinical development of any additional monoclonal microbial product candidates;
- conduct research and continue preclinical development of potential product candidates;
- make strategic investments in manufacturing capabilities, including potentially planning and building a small-scale commercial manufacturing facility;
- maintain our current intellectual property portfolio and opportunistically acquire complementary intellectual property;
- seek to obtain regulatory approvals for our product candidates;
- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our transition to a public company; and
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

We expect that our cash, cash equivalents and short-term investments as of December 31, 2018, will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2020. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. Our forecast is based on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of EDP1066, EDP1815 and EDP1503, any additional monoclonal microbial product candidates or any follow-on programs and because the extent to which we may enter into collaborations with third parties for development of these product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements for our technology platform or our other programs will depend on many factors, including:

- the progress and results of our proof of concept clinical studies of EDP1066, EDP1815 and EDP1503;
- the cost of manufacturing clinical supplies of our product candidates;
- the scope, progress, results and costs of preclinical development, laboratory testing for any other potential product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;

- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such acquisitions or investments in businesses.

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. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Additional debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interest of existing stockholders. The terms of our existing loan and security agreement with Pacific Western Bank preclude us from paying dividends on our equity securities without Pacific Western Bank's consent. If we lack sufficient capital to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations would be materially adversely affected.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, 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 or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates to third parties that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2018 and the effect such obligations are expected to have on our liquidity and cash flows in future periods (in thousands):

	Payments Due by Period				
	Total	Less Than 1 Year	1 – 3 Years	4 – 5 Years	More Than 5 Years
Operating lease commitments(1)	$ 20,620	$ 2,803	$ 5,860	$ 6,217	$ 5,740
Debt obligations(2)	16,471	3,342	13,129	—	—
Obligations for research, development, manufacturing and other(3)	3,875	2,422	1,453	—	—
Total	$ 40,966	$ 8,567	$ 20,442	$ 6,217	$ 5,740

(1) Amounts in the table reflect payments due for our laboratory and office space in Cambridge, Massachusetts under two operating lease agreements that are scheduled to expire in 2020 and 2025, net of future minimum sublease payments.

(2) Reflects the contractually required principal and interest payments payable pursuant to our loan and security agreement, which was amended in February 2018.

(3) Amounts represent the minimum cash amounts due on contractually obligated research, development and manufacturing contracts. Amounts exclude royalties and future milestones under current license agreements as we cannot estimate if they will occur.

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.

Product Licenses

In addition to the amount set forth in the table above, we have certain obligations under licensing agreements with third parties that are contingent upon achieving various development, regulatory and commercial milestones. Pursuant to our license agreement with the Mayo Foundation for Medical Education and Research, an affiliate of Mayo Clinic, or Mayo Clinic, for the development and commercialization of certain microbes including our candidate EDP1815, we are required to make milestone payments to Mayo Clinic of up to an aggregate of approximately $1.0 million upon achievement of specific development milestones and approximately $56 million upon achievement of specific regulatory and commercial milestones. Through December 31, 2018, we have paid milestones totaling $0.2 million to the Mayo Clinic, all of which were incurred during 2018. Pursuant to our license agreement with the University of Chicago for the development and commercialization of certain microbes for the treatment of cancer, including our candidate EDP1503, we are required to make payments to the University of Chicago of up to an aggregate of approximately $60.9 million upon achievement of specific development milestones, the vast majority of which are associated with specific regulatory and commercial milestone. Through December 31, 2018, we have incurred milestones totaling $0.4 million under the license agreement with the University of Chicago, all of which were incurred during 2018. Finally, pursuant to the terms of each of these license agreements, when and if commercial sales of a product commence, we will pay royalties to our licensors on net sales of the respective products.

Off-Balance Sheet Arrangements

As of December 31, 2018, we did not have, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations are based on our consolidated financial statements which are prepared in accordance with generally accepted accounting principles, or GAAP, in the United States of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis using historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions and conditions.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated 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 including, but not limited to, clinical trials and preclinical studies;
- investigative sites and other providers in connection with clinical trials and preclinical studies;
- other research and development service providers such as academic institutions and laboratory services providers in connection with discovery, preclinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials and preclinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs, investigative sites, laboratories and other providers that conduct and manage those studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. 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 milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees and directors based on the fair value on the date of grant and recognize the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue stock options and restricted stock awards with only service-based vesting conditions and record the expense for these awards using the straight-line method, adjusting for pre-vesting forfeitures in the period in which the forfeitures occur. We measure stock-based awards granted to consultants and non-employees based on the fair value of the award on the date at which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Use of this model requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options, and our expected dividend yield. Prior to May 2018, we were a privately-held company with limited operating history and no company-specific historical and implied volatility information and accordingly, we estimate our expected volatility based on the historical volatility of a group of publicly traded peer companies. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. We use the simplified method prescribed by SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of options granted to employees and directors. We base the expected term of options granted to consultants and non-employees on the contractual term of the options. We determine the risk-free interest rate by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

Determination of the Fair Value of Common Stock

Due to the absence of an active market for our common stock prior to the commencement of trading of our common stock on the NASDAQ Global Select Market on May 9, 2018 in connection with our IPO, our board of directors estimated the fair value of our common stock at various dates, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Our determination of the fair value of our common stock was performed using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Following our IPO, it is no longer necessary for us to estimate the fair value of our common stock in connection with our accounting for stock options or other equity awards, as the fair value of our common stock can be determined by reference to its closing price on The NASDAQ Global Select Market on the date of the applicable grant.

For financial statement purposes and prior to the consummation of our IPO, we performed common stock valuations, with the assistance of a third-party specialist, at various dates, which resulted in valuations of our common stock of $2.49 per share as of January 15, 2017, $3.06 per share as of March 31, 2017, $4.53 per share as of June 30, 2017, $6.32 per share as of September 30, 2017 and $8.12 per share as of December 31, 2017. In addition to these valuations, we considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the preferential rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies for our product candidates;
- our stage of development and our business strategy;
- external market conditions affecting the biotechnology and pharmaceutical industries;

- trends within the biotechnology and pharmaceutical industries;
- our financial position, including cash and cash equivalents on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering ("IPO"), or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biotechnology and pharmaceutical industries.

There are significant judgments and estimates inherent in these valuations. These judgments and estimates include assumptions regarding our future operating performance, the stage of development of our product candidates, the timing of a potential IPO or other liquidity event and the determination of the appropriate valuation methodology at each valuation date. If we had made different assumptions, our stock-based compensation expense, net loss attributable to common stockholders and net loss per share attributable to common stockholders could have been significantly different.

Valuation Methodologies

Our common stock valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock

Our common stock valuation of January 15, 2017 was prepared using the back-solve method to calculate the total equity value and the option-pricing method, or OPM, to allocate the total equity value. The back-solve method derives the implied equity value for one type of equity security from a contemporaneous transaction involving another type of security. We used the back-solve method to calculate the total equity value of our company in the January 15, 2017 valuation as we had recently completed convertible preferred stock financings that should be considered in estimating the fair value of our equity per the Practice Aid. Our remaining common stock valuations were performed using the OPM, or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM, which we refer to as the hybrid method. The method selected was based on the availability and the quality of information to develop the assumptions for the methodology.

OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock.

The OPM uses the Black-Scholes option-pricing model to price the call options. This model defines the fair values of securities as functions of the current fair value of a company and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

PWERM. Under the PWERM methodology, the fair value of common stock is estimated based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock.

Hybrid Method. The hybrid method is a PWERM where the equity value in one of the scenarios is calculated using an OPM. In the hybrid method used by us, two types of future-event scenarios were considered: an IPO and a M&A scenario. The enterprise value for the IPO scenario was determined using a market approach. The enterprise value for the remaining private scenario was determined using the M&A back-solve approach for the March 2017, February 7, 2018 and March 30, 2018 valuations as we had recently completed a round of financing in our equity securities. The June 30, 2017, September 30, 2017 and December 31, 2017 valuations utilized the guideline IPO method for the IPO scenario and the guideline transactions method under the merger and acquisition, or M&A, scenario to determine the value of the Company. In the IPO scenario, we allocated the value to the various share classes using the direct waterfall approach and under the M&A scenario, we utilized the OPM to allocate the value to the respective share classes. The relative probability of each type of future-event scenario was determined by our board of directors based on an analysis of market conditions at the time, including then-current IPO valuations of similarly situated companies, and expectations as to the timing and likely prospects of the future-event scenarios.

Valuation of Warrants to Purchase Convertible Preferred Stock

We have classified warrants to purchase shares of our Series A, Series A-1, and Series A-3 and Series B convertible preferred stock as a liability on our balance sheets as these warrants were free-standing financial instruments exercisable into contingently redeemable shares. The warrants were initially recorded at fair value on the date of grant, and were subsequently remeasured to fair value at each balance sheet date while the instrument was outstanding. Changes in fair value of these warrants were recognized as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss.

We used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the preferred stock warrants. We assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement included the fair value per share of the underlying convertible preferred stock, the remaining contractual term of the warrant, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determined the fair value per share of the underlying preferred stock by taking into consideration our most recent sales of our convertible preferred stock, results obtained from third-party valuations and additional factors that we deem relevant. During the period that these instruments were outstanding, we had historically been a private company and lacked company-specific historical and implied volatility information of our stock. Therefore, we estimated expected stock volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrants. We estimated a 0% dividend yield based on the expected dividend yield and the fact that we have never paid or declared dividends. Significant changes to the fair value of the underlying stock would have resulted in a significant change in the fair value measurements.

Upon closing of the Company's IPO on May 11, 2018, the warrants converted to common stock warrants. On that date, the Company performed the final remeasurement of the warrants using the fair value of the underlying common shares of $16.00 per share on May 11, 2018, recorded the change in fair value in other income (expense), net in the consolidated statement of operations and comprehensive loss and reclassified the carrying value to additional paid in capital. All outstanding warrants were exercised in full in the second quarter of 2018.

Item 7A. Quantitative and Qualitative Disclosure about Market Risk

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2018, our cash and cash equivalents consisted of cash and money market accounts. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, an immediate 10% change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

As of December 31, 2018, we had $15.0 million of borrowings outstanding under term loans pursuant to our loan and security agreement with Pacific Western Bank. These term loans bear interest at a variable annual rate equal to the greater of (a) 0.25% above the Prime Rate or (b) 4.50%, thereby exposing us to interest rate risk. Based on the $15.0 million of principal outstanding as of December 31, 2018, an immediate 10% change in the Prime Rate would not have a material impact on our debt-related obligations, financial position or results of operation.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2018 and 2017.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear in this Annual Report on Form 10-K beginning on page F-1 and are incorporated by reference into this Item 8.

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

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of December 31, 2018, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our auditors will not be required to formally opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act.

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 was no change in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, that occurred during our most recent fiscal quarter that has materially affected, or is 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

The information required by this Item will be set forth in the sections entitled “Proposal No. 1 Election of Directors,” “Corporate Governance” and “Stock Ownership” of our proxy statement for our 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018, and is incorporated into this Annual Report on Form 10-K by reference.

Item 11. Executive Compensation

The information required by this Item will be set forth in the sections entitled “Executive Compensation” and “Director Compensation” of our proxy statement for our 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018, and is incorporated into this Annual Report on Form 10-K by reference.

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

Other than the information set forth below, the information required by this Item will be set forth in the section entitled “Stock Ownership” of our Proxy Statement for our 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018, and is incorporated into this Annual Report on Form 10-K by reference

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides information as of December 31, 2018, regarding our common stock that may be issued under: (1) the Evelo Biosciences, Inc. 2015 Stock Incentive Plan, or the 2015 Plan; (2) Evelo Biosciences, Inc. 2018 Stock Incentive Plan, or the 2018 Plan; and (3) the Evelo Biosciences, Inc. 2018 Employee Stock Purchase Plan (the “2018 ESPP”).

Plan category:	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants, and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants, and Rights (b)	Number of Securities Available for Future Issuance Under Equity Compensation Plans (excludes securities reflected in column (a)) (c)
Equity compensation plans approved by stockholders			
2015 Plan (1)	4,213,835	$ 4.33	—
2018 Plan (2)	703,976	$ 13.49	844,853
2018 ESPP	—	$ —	336,356
Equity compensation plans not approved by stockholders	—	$ —	—
Total	4,917,811	$ 5.64	1,181,209

(1) In connection with our IPO, we adopted the 2018 Plan and will not make future grants or awards under the 2015 Plan. As such, the 113,006 securities previously reserved under the 2015 Plan have been excluded from the table above.

(2) Pursuant to the terms of the 2018 Plan, the number of shares of common stock available for issuance under the 2018 Plan automatically increases on each January 1, until and including January 1, 2028, by an amount equal to the lesser of (A) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares of common stock as is determined by the board of directors.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item will be set forth in the sections entitled "Corporate Governance" and "Certain Transactions with Related Persons" of our proxy statement for our 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018, and is incorporated into this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item will be set forth in the section entitled "Proposal No. 2 Ratification of Appointment of Independent Registered Public Accounting Firm" of our proxy statement for our 2019 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2018, and is incorporated into this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements.

The response to this portion of Item 15 is set forth under Item 8 hereof.

(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.

(a)(3) Exhibits.

		Incorporated by Reference				
Exhibit Number	**Description of Exhibit**	**Form**	**File No.**	**Exhibit**	**Filing date**	**Filed Herewith**
3.1	Restated Certificate of Incorporation of Evelo Biosciences, Inc.	8-K	001-38473	3.1	5/11/18	
3.2	Amended and Restated Bylaws of Evelo Biosciences, Inc.	8-K	001-38473	3.2	5/11/18	
4.1	Fourth Amended and Restated Investors' Rights Agreement, dated February 9, 2018, by and among Evelo Biosciences, Inc. and the investors named therein	S-1/A	333-224278	4.1	4/30/18	
4.2	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-224278	4.2	4/30/18	
10.1#	2015 Stock Incentive Plan, as amended, and U.K. sub-plan and forms of agreements thereunder	S-1/A	333-224278	10.1	4/30/18	
10.2#	2018 Incentive Award Plan, and U.K. sub-plan and forms of awards thereunder	S-1/A	333-224278	10.2	4/30/18	
10.3#	2018 Employee Stock Purchase Plan	S-1/A	333-224278	10.3	4/30/18	
10.4#	Non-Employee Director Compensation Program	S-1/A	333-224278	10.4	4/30/18	
10.5#	Executive Severance Plan	S-1/A	333-224278	10.5	4/30/18	
10.6#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-224278	10.6	4/30/18	
10.7	Lease between Evelo Biosciences, Inc. and 620 Memorial Leasehold LLC, dated July 14, 2015, as amended on January 24, 2018	S-1/A	333-224278	10.7	4/30/18	
10.8	Sublease Agreement between Evelo Biosciences, Inc. and Bio-Rad Laboratories, Inc., dated December 27, 2017	S-1/A	333-224278	10.8	4/30/18	
10.9#	Terms and Conditions of Employment between Evelo Biosciences, Inc. and Duncan McHale, M.D., Ph.D., effective as of May 11, 2018	S-1/A	333-224278	10.9	4/30/18	
10.10#	Offer Letter between Evelo Biosciences, Inc. and Balkrishan (Simba) Gill, Ph.D., dated June 25, 2015, as amended on April 26, 2018	S-1/A	333-224278	10.11	4/30/18	

10.11#	Offer Letter between Evelo Biosciences, Inc. and Mark Bodmer, Ph.D., dated October 6, 2015	S-1/A	333-224278	10.10	4/30/18	
10.12	Master Services Agreement, dated September 1, 2018, between Evelo Biosciences, Inc. and Weatherden Ltd					*
10.13†	Patent License Agreement between Mayo Foundation for Medical Education and Research and Evelo Biosciences, Inc., dated August 6, 2017	S-1/A	333-224278	10.14	4/30/18	
10.14†	Exclusive License Agreement between The University of Chicago for an Immuno-oncology Technology and Evelo Biosciences, Inc, dated March 10, 2016	S-1/A	333-224278	10.15	4/30/18	
10.15†	Exclusivity and Commitment Agreement between Biose and Evelo Biosciences, Inc., dated February 15, 2018	S-1/A	333-224278	10.16	4/30/18	
10.16	Loan and Security Agreement between Pacific Western Bank and Evelo Biosciences, Inc., dated August 15, 2016, as amended on June 14, 2017, August 18, 2017 and February 7, 2018	S-1/A	333-224278	10.17	4/30/18	
21.1	Subsidiaries of Evelo Biosciences, Inc.	S-1	333-224278	21.1	4/13/18	
23.1	Consent of Ernst & Young LLP					*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					**
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*

* Filed herewith

** Furnished herewith

# Indicates management contract or compensatory plan.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment.

Certain agreements filed as exhibits to this Annual Report on Form 10-K contain representations and warranties that the parties thereto made to each other. These representations and warranties have been made solely for the benefit of the other parties to such agreements and may have been qualified by certain information that has been disclosed to the other parties to such agreements and that may not be reflected in such agreements. In addition, these representations and warranties may be intended as a way of allocating risks among parties if the statements contained therein prove to be incorrect, rather than as actual statements of fact. Accordingly, there can be no reliance on any such representations and warranties as characterizations of the actual state of facts. Moreover, information concerning the subject matter of any such representations and warranties may have changed since the date of such agreements.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the audited consolidated financial statements or notes thereto.

Item 16. Form 10-K Summary

Not applicable.

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.

EVELO BIOSCIENCES, INC.

Date: February 15, 2019

By: /s/ Balkrishan (Simba) Gill, Ph.D.
Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Balkrishan (Simba) Gill Balkrishan (Simba) Gill, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	February 15, 2019
/s/ Jonathan Poole Jonathan Poole	Chief Financial Officer (principal financial and accounting officer)	February 15, 2019
/s/ Noubar B. Afeyan Noubar B. Afeyan, Ph.D.	Chairman of the Board of Directors	February 15, 2019
/s/ Ara Darzi Lord Ara Darzi	Director	February 15, 2019
/s/ David R. Epstein David R. Epstein	Director	February 15, 2019
/s/ Theodose Melas-Kyriazi Theodose Melas-Kyriazi	Director	February 15, 2019
/s/ David P. Perry David P. Perry	Director	February 15, 2019
/s/ Nancy A. Simonian Nancy A. Simonian, M.D.	Director	February 15, 2019

EVELO BIOSCIENCES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Evelo Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Evelo Biosciences, Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and 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 at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the 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 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Boston, MA
February 15, 2019

Evelo Biosciences, Inc.
Consolidated Balance Sheets
(In thousands, except per share and share amounts)

	December 31,	
	2018	**2017**
Assets		
Current assets:		
Cash and cash equivalents	$ 93,101	$ 38,246
Short-term investments	54,818	—
Prepaid expenses and other current assets	3,703	531
Total current assets	151,622	38,777
Property and equipment, net	6,925	3,496
Other assets	1,320	1,515
Total assets	$ 159,867	$ 43,788
Liabilities, convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,519	$ 1,411
Accrued expenses	4,965	2,199
Other current liabilities	2,751	229
Total current liabilities	9,235	3,839
Noncurrent liabilities:		
Long-term debt, net of current portion	12,305	9,966
Deferred rent, net of current portion	1,071	478
Other noncurrent liabilities	307	526
Total liabilities	22,918	14,809
Commitments and contingencies		
Convertible preferred stock:		
Convertible preferred stock, $0.001 par value; none and 66,311,563 shares authorized at December 31, 2018 and 2017, respectively; none and 65,833,096 shares issued and outstanding at December 31, 2018 and 2017, respectively; aggregate liquidation preference of $0 and $89,975 at December 31, 2018 and 2017, respectively	—	83,702
Stockholder's equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 and no shares authorized at December 31, 2018 and 2017, respectively; no shares issued and outstanding at December 31, 2018 and 2017, respectively	—	—
Common stock, $0.001 par value; 200,000,000 and 23,780,338 shares authorized at December 31, 2018 and 2017, respectively; 31,951,540 and 4,138,483 shares issued and 31,825,769 and 3,880,607 shares outstanding at December 31, 2018 and 2017, respectively	32	4
Additional paid-in capital	250,316	1,684
Accumulated other comprehensive loss	(18)	—
Accumulated deficit	(113,381)	(56,411)
Total stockholders' equity (deficit)	136,949	(54,723)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 159,867	$ 43,788

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

Evelo Biosciences, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2018	**2017**	**2016**
Operating expenses:			
Research and development	$ 39,885	$ 19,957	$ 9,134
General and administrative	18,218	7,574	3,891
Total operating expenses	58,103	27,531	13,025
Loss from operations	(58,103)	(27,531)	(13,025)
Other income (expense):			
Interest income (expense), net	1,563	(215)	(287)
Other expenses	(406)	(301)	(20)
Other income (expense), net	1,157	(516)	(307)
Net loss	$ (56,946)	$ (28,047)	$ (13,332)
Convertible preferred stock dividends	(3,937)	(6,085)	(1,645)
Net loss attributable to common stockholders	$ (60,883)	$ (34,132)	$ (14,977)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.78)	$ (9.10)	$ (5.28)
Weighted-average number of common shares outstanding, basic and diluted	21,871,029	3,750,790	2,834,733
Comprehensive loss:			
Net loss	$ (56,946)	$ (28,047)	$ (13,332)
Other comprehensive loss:			
Unrealized loss on investments, net of tax of $0	(18)	—	—
Comprehensive loss	$ (56,964)	$ (28,047)	$ (13,332)

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

Evelo Biosciences, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount				
Balance-January 1, 2016	12,536,945	$ 7,773	1,961,265	$ 2	$ —	$ —	$ (4,473)	$ (4,471)
Issuance of Series A-1 and A-3 Preferred Stocks and Common Stock as part of the acquisition of Epiva	18,851,705	16,950	1,389,939	2	—	—	(9,409)	(9,407)
Issuance of Series A and A-2 Preferred Stocks for cash, net of issuance costs	6,666,668	7,495	—	—	—	—	—	—
Vesting of restricted common stock	—	—	216,146	—	67	—	—	67
Exercise of stock options	—	—	51,193	—	32	—	—	32
Stock-based compensation expense	—	—	—	—	419	—	—	419
Accretion of preferred stock to redemption value	—	1,645	—	—	(518)	—	(1,127)	(1,645)
Net loss	—	—	—	—	—	—	(13,332)	(13,332)
Balance-December 31, 2016	38,055,318	$ 33,863	3,618,543	$ 4	$ —	$ —	$ (28,341)	$ (28,337)
Issuance of Series B Preferred Stock for cash, net of issuance costs	27,777,778	49,807	—	—	—	—	—	—
Vesting of restricted common stock	—	—	154,920	—	57	—	—	57
Exercise of stock options	—	—	106,654	—	79	—	—	79
Other issuances of common stock	—	—	490	—	15	—	—	15
Accretion of preferred stock to redemption value	—	32	—	—	(9)	—	(23)	(32)
Stock-based compensation expense	—	—	—	—	1,542	—	—	1,542
Net loss	—	—	—	—	—	—	(28,047)	(28,047)
Balance-December 31, 2017	65,833,096	$ 83,702	3,880,607	$ 4	$ 1,684	$ —	$ (56,411)	$ (54,723)
Issuance of Series B and Series C Preferred Stock, net of issuance costs	25,482,199	82,076	—	—	—	—	—	—
Proceeds from Initial Public Offering, net of underwriting costs and commissions	—	—	5,312,500	5	75,809	—	—	75,814
Conversion of preferred stock into common stock	(91,315,295)	(165,778)	22,386,677	22	165,756	—	—	165,778
Reclassification of warrant liability	—	—	—	—	819	—	—	819
Vesting of restricted common stock	—	—	113,641	—	36	—	—	36
Exercise of stock options and warrants	—	—	132,344	1	129	—	—	130
Stock-based compensation expense	—	—	—	—	6,059	—	—	6,059
Unrealized loss on investments	—	—	—	—	—	(18)	—	(18)
Retroactive adjustment to beginning accumulated deficit and additional paid-in capital resulting from adoption of ASU 2016-09	—	—	—	—	24	—	(24)	—
Net loss	—	—	—	—	—	—	(56,946)	(56,946)
Balance-December 31, 2018	—	$ —	31,825,769	$ 32	$ 250,316	$ (18)	$ (113,381)	$ 136,949

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

Evelo Biosciences, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2018	**2017**	**2016**
Operating activities			
Net loss	$ (56,946)	$ (28,047)	$ (13,332)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	6,059	1,542	419
Depreciation expense	1,935	834	495
Change in fair value of warrant and debt derivative liability	406	301	20
Non-cash interest expense	103	35	28
Changes in assets and liabilities excluding effect of assets and liabilities assumed in 2016 acquisition of Epiva (Note 7):			
Prepaid expenses and other current assets	(3,052)	(347)	(3)
Accounts payable	(221)	774	(43)
Accrued expenses and other current liabilities	3,594	1,733	273
Other liabilities	843	(90)	(171)
Net cash used in operating activities	(47,279)	(23,265)	(12,314)
Investing activities			
Purchase of investments	(136,087)	—	—
Proceeds from sales and maturities of investments	81,250	—	—
Cash acquired in the 2016 acquisition of Epiva	—	—	10,486
Purchases of property and equipment	(5,462)	(1,742)	(1,250)
Proceeds from the sale of fixed assets	171	—	27
Net cash used in investing activities	(60,128)	(1,742)	9,263
Financing activities			
Net proceeds from the issuance of common stock upon completion of initial public offering	75,829	—	—
Deferred issuance costs	—	(15)	—
Net proceeds from the issuance of convertible preferred stock	81,336	48,903	7,495
Net proceeds from the issuance of long-term debt	4,975	—	11,000
Settlement of derivative liability	(250)	—	—
Proceeds from the exercise of stock options, restricted common stock and warrants	122	79	247
Repayment of long-term debt	—	—	(4,000)
Change in stockholders' payable	—	—	1,000
Net cash provided by financing activities	162,012	48,967	15,742
Net increase in cash, cash equivalents and restricted cash	54,605	23,960	12,691
Cash, cash equivalents and restricted cash – beginning of year	39,746	15,786	3,095
Cash, cash equivalents and restricted cash – end of year	$ 94,351	$ 39,746	$ 15,786
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 742	$ 437	$ 204
Noncash investing and financing activities			
Conversion of convertible preferred stock into common stock upon closing of initial public offering	$ 165,778	$ —	$ —
Conversion of convertible preferred stock warrants into common stock warrants	$ 819	$ —	$ —
Property and equipment additions in accounts payable and accrued expenses	$ 348	$ 84	$ —
Issuance of debt derivative liability in connection with long-term debt facility	$ 150	$ —	$ —
Issuance of warrants in connection with long-term debt facility	$ 89	$ —	$ 76
Accretion of convertible preferred stock to redemption value	$ —	$ 32	$ 1,645
Long-term debt assumed in acquisition of Epiva, net of discount	$ —	$ —	$ 2,923
Net non-cash assets acquired in acquisition of Epiva	$ —	$ —	$ 57

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

Evelo Biosciences, Inc.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Evelo Biosciences, Inc. ("Evelo" or the "Company") is a biotechnology company which was incorporated in Delaware on May 6, 2014. The Company focuses on the development of monoclonal microbials, which are designed to act on the gut-body network for the treatment of many diseases, beginning with inflammatory diseases and cancer. The Company is headquartered in Cambridge, Massachusetts.

The Company is devoting substantially all of its efforts to research and development and raising capital. The Company has not generated any revenue related to its primary business purpose to date. The Company is subject to a number of risks similar to those of other development stage companies, including dependence on key individuals, the need to develop commercially viable products, competition from other companies, many of whom are larger and better capitalized, and the need to obtain adequate additional financing to fund the development of its products.

On April 27, 2018, the Company filed an amended and restated certificate of incorporation with the Secretary of State of the State of Delaware, to effect a 1-for-4.079 reverse stock split of the Company's common stock. All share and per share data shown in the accompanying consolidated financial statements and related notes have been retroactively revised to reflect the reverse stock split.

On May 11, 2018, the Company completed an initial public offering (the "IPO") of 5,312,500 shares of its common stock for aggregate gross proceeds of $85.0 million. The Company received $75.8 million in net proceeds after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. Upon closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 22,386,677 shares of common stock at the applicable conversion ratio then in effect.

The Company has incurred operating losses since inception and expects such losses and negative operating cash flows to continue for the foreseeable future. Through December 31, 2018, the Company has raised gross proceeds of approximately $257.3 million from the sale of common stock, the sale of convertible preferred stock, and from the issuance of debt. At December 31, 2018, the Company had cash, cash equivalents and short-term investments of $147.9 million. The Company recorded net losses of $56.9 million, $28.0 million and $13.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, the Company had an accumulated deficit of $113.4 million.

The transition to profitability is dependent upon the successful development, approval, and commercialization of its products and product candidates and the achievement of a level of revenues adequate to support its cost structure. Based on the Company's current operating plan, the Company believes that its cash, cash equivalents and short-term investments at December 31, 2018 will be sufficient to fund operations and capital expenditures for at least the twelve months following the filing of this Annual Report on Form 10-K. Management's belief with respect to its ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional funding sooner than would otherwise be expected. There can be no assurance that the Company will be able to obtain additional funding on acceptable terms, if at all.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standard Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Significant Accounting Policies

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of stock-based awards. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned, controlled subsidiary, Evelo Biosciences Security Corporation. All intercompany transactions and balances of the subsidiary have been eliminated in consolidation.

Subsequent Event Considerations

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the consolidated financial statements to provide additional evidence for certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required. The Company has evaluated all subsequent events and determined that there are no material recognized or unrecognized subsequent events requiring disclosure, other than those disclosed in this Annual Report on Form 10-K.

Emerging Growth Company Status

Evelo is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and it may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Evelo may take advantage of these exemptions until it is no longer an emerging growth company. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. Evelo has elected to use the extended transition period for complying with new or revised accounting standards; and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. Evelo may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of this offering or such earlier time that it is no longer an emerging growth company. Evelo would cease to be an emerging growth company if it has more than $1.07 billion in annual revenue; or has more than $700.0 million in market value of its stock held by non-affiliates (and it has been a public company for at least 12 months and has filed one annual report on Form 10-K); or it issues more than $1.0 billion of non-convertible debt securities over a three-year period.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash, cash equivalents and short-term investments. The Company places its cash, cash equivalents and short-term investments in primarily two custodian accounts at accredited financial institutions. The Company's available-for-sale investments primarily consist of U.S. Treasury securities. The Company has not experienced any realized losses on any of its accounts and management believes such funds are subject to minimal credit risk. Such deposits have and will continue to exceed federally insured limits.

As of December 31, 2018 and 2017, the Company has no off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

The Company is subject to a number of risks similar to other early-stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical testing or clinical trials, its reliance on third parties to conduct its clinical trials, the need to obtain regulatory and marketing approvals for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's product candidates, its right to develop and commercialize its product candidates pursuant to the terms and conditions of the licenses granted to the Company, protection of proprietary technology, the ability to make milestone, royalty or other payments due under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate product revenue or achieve profitability.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity (deficit) that are excluded from net loss. The Company's only element of other comprehensive income (loss) is unrealized gains and losses on available-for-sale investments. Comprehensive loss totaled $57.0 million for the year ended December 31, 2018 and was not significantly different than net loss. For the years ended December 31, 2017 and 2016 comprehensive loss was equal to net loss.

Cash, Cash Equivalents and Restricted Cash

Cash equivalents are comprised of highly liquid investments that are readily convertible into cash with original maturities of three months or less. Cash and cash equivalents include cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates market value. The Company's restricted cash consists of restricted cash in connection with building leases for the Company's office and laboratory premises. Restricted cash as of December 31, 2018 and 2017 was $1.3 million and $1.5 million, respectively, and is classified within other assets on the accompanying consolidated balance sheet. The following reconciles cash, cash equivalents and restricted cash as of December 31, 2018 and 2017, as presented on our statements of cash flows to their related balance sheet accounts (in thousands):

	December 31,	
	2018	2017
Cash and cash equivalents:		
Cash	$ 1,300	$ 13,204
Money Market Funds	91,801	25,042
Total cash and cash equivalents	93,101	38,246
Restricted cash	1,250	1,500
Cash, cash equivalents and restricted cash	$ 94,351	$ 39,746

Investments

The Company accounts for and classifies its investments as either "available-for-sale," "trading," or "held-to-maturity," in accordance with the accounting guidance related to the accounting and classification of certain investments in debt and equity securities. The determination of the appropriate classification is based primarily on management's intent to sell the investment at the time of purchase. As of December 31, 2018, all of the Company's investments were classified as available-for-sale securities.

Available-for-sale securities are those securities which the Company views as available for use in current operations, if needed. The Company generally classifies its available-for-sale securities as short-term investments, even though the stated maturity date may be one year or more beyond the current balance sheet date. Available-for-sale investments are stated at fair value with their unrealized gains and losses included in accumulated other comprehensive loss within stockholders' (deficit) equity, until such gains and losses are realized in other income (expense) within the consolidated statements of operations and comprehensive loss or until an unrealized loss is considered other-than-temporary.

The Company recognizes other-than-temporary impairments of its investments in debt securities when there is a decline in fair value below the amortized cost basis and if (a) it has the intent to sell the security or (b) it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. If either of these conditions is met, the Company recognizes the difference between the amortized cost of the security and its fair value at the impairment measurement date in the consolidated statements of operations and comprehensive loss. If neither of these conditions is met, the Company must perform additional analyses to evaluate whether the unrealized loss is associated with the creditworthiness of the issuer of the security rather than other factors, such as interest rates or market factors. If the Company determines from this analysis that it does not expect to receive cash flows sufficient to recover the entire amortized cost of the security, a credit loss exists, the impairment is considered other-than-temporary and is recognized in its consolidated statements of operations and comprehensive loss.

Fair Value of Financial Instruments

ASC 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities;
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and
- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The Company did not elect to measure any additional financial instruments or other items at fair value.

Warrants to Purchase Convertible Preferred Stock

The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as equity. These warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a component of other income/(expense), until the earlier of their exercise or expiration or the completion of a liquidation event, at which time the warrant liability may be reclassified to stockholders' equity if the criteria for recording the warrant as an equity instrument are met. Per the terms of the warrants, upon completion of a qualified public offering, any unexercised warrants are converted into warrants to purchase common shares.

Property and Equipment

Property and equipment consists of computer hardware and software, furniture and fixtures, office equipment, research and lab equipment, and leasehold improvement recorded at cost. Lab equipment used in research and development activities is only capitalized when it has an alternative future use. These amounts are depreciated using the straight-line method over the estimated useful lives of the assets. Purchased assets that are not yet in service are recorded to construction-in-process and no depreciation expense is recorded. Once they are placed in service they are reclassified to the appropriate asset class.

A summary of the estimated useful lives is as follows:

Classification	Estimated Useful Life
Computer hardware	3 - 5 Years
Computer software	3 years
Furniture and fixtures	7 years
Research and lab equipment (new/used)	5 years / 3 years
Leasehold improvements	Lesser of asset life or remaining life of lease

Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company periodically evaluates property and equipment for impairment whenever events or changes in circumstances indicate that a potential impairment may have occurred. If such events or changes in circumstances arise, the Company compares the carrying amount of the long-lived assets to the estimated future undiscounted cash flows expected to be generated by the long-lived assets. If the estimated aggregate undiscounted cash flows are less than the carrying amount of the long-lived assets, an impairment charge, calculated as the amount by which the carrying amount of the assets exceeds the fair value of the assets, is recorded. The fair value of the long-lived assets is determined based on the estimated discounted cash flows expected to be generated from the long-lived assets. The Company has not recorded any such impairment charges during the years presented.

Deferred Rent

Certain of the Company's operating lease agreements include scheduled rent escalations over the lease term, as well as lease incentives. Rent expense is charged ratably over the life of the lease. Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the buildings the Company occupies. Lease incentives are recorded as a deferred rent liability and are amortized on a straight-line basis over the term of the lease as a reduction to rent expense.

Research and Development Costs

Research and development costs are expensed in the period incurred. Research and development expenses consist of both internal and external costs such as payroll, consulting, and manufacturing costs associated with the development of the Company's product candidates. Costs for certain development activities, such as clinical trials and manufacturing development activities, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided to the Company by its vendors on their actual costs incurred or level of effort expended. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid or accrued research and development expenses.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The Company has and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects. Any milestone payments made for Intellectual Property after regulatory approval, or that have alternative future use, are capitalized and amortized.

Income Taxes

The Company records deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is provided to reduce the net deferred tax assets to the amount that will more likely than not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Stock-Based Compensation

The Company records stock-based compensation for options granted to employees and directors based on the grant date fair value of awards issued. The expense is recorded over the requisite service period, which is the vesting period, on a straight-line basis. The Company uses the Black-Scholes option-pricing model to determine the fair value of stock options. The determination of the fair value of stock options on the date of grant using an option-pricing model is affected by the Company's common stock price, as well as a number of other assumptions. The Company records forfeitures as they occur.

The Company accounts for stock-based compensation arrangements with non-employees based upon the fair value of the consideration received or the equity instruments issued, whichever is more reliably measurable. The measurement date for non-employee awards is generally the date performance of services required from the non-employee is complete. Stock-based compensation costs for non-employee awards are recognized as services are provided, which is generally the vesting period, on a straight-line basis. The unvested portion of the stock options is subject to re-measurement over the vesting period and forfeitures are recorded as they occur.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Net loss applicable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. Diluted net loss per share applicable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the dilutive net loss per share applicable to common stockholders calculation, convertible preferred stock, warrants, stock options, and unvested restricted stock are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

Recently Adopted Accounting Pronouncements

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. Some of the areas of simplification apply only to non-public companies. This guidance was effective on December 31, 2016 for public entities. For entities other than public business entities, the amendments are effective for annual periods beginning after December 15, 2017, and interim periods within annual periods beginning after December 15, 2018. Early adoption is permitted for an entity in any interim or annual period for which financial statements have not been issued or made available for issuance. An entity that elects early adoption must adopt all amendments in the same period. The Company adopted ASU 2016-09 effective January 1, 2018 and the adoption of this guidance did not have a material impact on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash* ("ASU 2016-18"). The amendments of ASU 2016-18 were issued to address the diversity in classification and presentation of changes in restricted cash and restricted cash equivalents on the statement of cash flows which is currently not addressed under Topic 230. ASU 2016-18 would require an entity to include amounts generally described as restricted cash and restricted cash equivalents with cash and cash equivalents when reconciling the beginning of period and end of period total amounts on the statement of cash flows. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non-public entities. Early adoption is permitted and the standard must be applied retrospectively. The Company adopted this standard as of January 1, 2017 retrospectively for all periods presented.

In January 2017, the FASB issued ASU 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU 2017-01"). This new standard clarifies the definition of a business and provides a screen to determine when an integrated set of assets and activities is not a business. The screen requires that when substantially all of the fair value of the gross assets acquired (or disposed of) is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. Early adoption is permitted. The Company adopted the requirements of ASU 2017-01 as of January 1, 2016 and applied the screen when evaluating the nature of the assets received in connection with the acquisition of Epiva in 2016. As a result of applying this screen the Company concluded that Epiva was not a business.

In May 2017, the FASB issued ASU 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for both public entities and non-public entities. Early adoption is permitted. The Company adopted ASU 2016-09 during 2018 and the adoption of this guidance did not have a material impact on the Company's consolidated financial statements.

Accounting Pronouncements Issued and Not Adopted as of December 31, 2018

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606) ("ASU 2014-09"), and further updated through ASU 2016-12 ("ASU 2016-12"), which amends the existing accounting standards for revenue recognition. ASU 2014-09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non-public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. The Company will adopt ASU 2014-09 on January 1, 2019 and has concluded the adoption will not have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which supersedes the guidance in former ASC 840, *Leases*. The new 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. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2018, for public entities and no later than for annual reporting periods beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020 for non-public entities. Early adoption is permitted for all entities. ASU 2016-02 is expected to impact the Company's consolidated financial statements as the Company has certain operating lease arrangements for which the Company is the lessee. Management is currently evaluating the impact the adoption of ASU 2016-02 will have on its consolidated financial statements and related disclosures.

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"). The amendments in ASU 2018-18 make targeted improvements to generally accepted accounting principles (GAAP) for collaborative arrangements by clarifying that certain transactions between collaborative arrangement participants should be accounted for as revenue under Topic 606 when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in Topic 606 should be applied, including recognition, measurement, presentation, and disclosure requirements. In addition, unit-of-account guidance in Topic 808 was aligned with the guidance in Topic 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of Topic 606. ASU 2018-18 is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period. The amendments in this Update should be applied retrospectively to the date of initial application of Topic 606. The Company will adopt ASU 2018-18 on January 1, 2019 and has concluded the adoption will not have a material impact on its consolidated financial statements as the Company does not have any collaborative agreements under which any participant is considered a customer of the Company.

3. Investments

As of December 31, 2018 and 2017, the Company had short-term investments, consisting entirely of U.S. treasury securities, of $54.8 million and none, respectively.

The following table summarizes the Company's investments held at December 31, 2018, which are all classified as available-for-sale (in thousands):

Description	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
December 31, 2018:				
U.S. treasury securities	$ 54,836	$ —	$ (18)	$ 54,818
Total	$ 54,836	$ —	$ (18)	$ 54,818

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2018 the balance in the Company's accumulated other comprehensive loss was comprised of activity related to the Company's available-for-sale investments. There were no material realized gains or losses recognized on the sale or maturity of available-for-sale securities during the years ended December 31, 2018 or 2017, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same periods.

As of December 31, 2018, the aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months was $54.8 million and none of these securities had remaining maturities of greater than one year. The Company has the intent and ability to hold such securities until recovery. The Company determined that there has been no material change in the credit risk of the above investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of December 31, 2018 or 2017.

4. Fair Value Measurements

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value as of December 31, 2018 and 2017(in thousands):

Description	December 31, 2018	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 91,801	$ 91,801	$ —	$ —
U.S. treasury securities included within short-term investments	$ 54,818	$ —	$ 54,818	$ —
Total	$ 146,619	$ 91,801	$ 54,818	$ —

Description	December 31, 2017	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 25,042	$ 25,042	$ —	$ —
Total	$ 25,042	$ 25,042	$ —	$ —
Liabilities:				
Preferred Stock Warrant Liability	$ 424	$ —	$ —	$ 424
Total	$ 424	$ —	$ —	$ 424

As of December 31, 2018 and 2017, the Company's cash equivalents and short-term investments have been initially valued at the transaction price and subsequently valued utilizing a third party pricing service. The Company validates the prices provided by its third-party pricing service by understanding the models used and obtaining market values from other pricing sources.

Preferred Stock Warrant Liabilities (the Warrants) relate to warrants to purchase convertible preferred stock issued by the Company in connection with entering into debt facility transactions from 2015 through 2018 as well as assuming warrants to purchase convertible preferred stock in connection with the acquisition of Epiva, a privately held research company. These Warrants are considered a Level 3 liability since their fair value measurements are based, in part, on significant inputs not observed in the market and reflect the Company's assumptions as to the fair value of the underlying convertible preferred stock and the expected volatility of the Company's convertible preferred stock, as well as estimates regarding the number of shares for which the Warrants were exercisable.

The estimated fair value of the Warrants was determined using the Black-Scholes option-pricing model. In periods that the instruments were outstanding, a significant input to the fair value of the Warrants was the fair value of the Series A Preferred Stock, Series A-1 Preferred Stock, Series A-3 Preferred Stock and Series B Preferred Stock. The fair value of the Warrants was remeasured at each reporting date using then-current assumptions with changes in fair value charged to other expense on the statements of operations and comprehensive loss.

As of December 31, 2017, the Warrants were valued at $0.4 million and included in other non-current liabilities on the consolidated balance sheets. The assumptions used represent the Company's best estimates at the time of valuation. The following assumptions were used in valuing the material Warrants:

	December 31, 2017
Risk-free interest rate	2.3 - 2.4 %
Expected dividend yield	0.00%
Expected term (in years)	7.9 - 8.6
Expected volatility	81 - 82 %
Fair value of preferred stock	$2.41 - 2.56

Based on the terms and conditions of the Company's Warrants, upon closing of the Company's IPO on May 11, 2018, the Warrants converted to common stock warrants. On that date, the Company performed the final remeasurement of the Warrants using the fair value of the underlying common shares of $16.00 per share on May 11, 2018, recorded the change in fair value in other income (expense), net in the consolidated statement of operations and comprehensive loss and reclassified the carrying value to additional paid-in capital. All outstanding warrants were exercised in full in the second quarter of 2018.

The following assumptions were used to measure the fair market value of the Warrants at conversion on May 11, 2018.

Risk-free interest rate	2.3 - 2.4 %
Expected dividend yield	0.00%
Expected term (in years)	7.5 - 9.8
Expected volatility	81 - 82 %
Fair value of common stock	$ 16.00

In May 2018, all of the outstanding warrants, totaling 56,008, were exercised for common stock at exercise prices ranging from $2.45 to $7.34 per share, of which, 8,599 shares were repurchased by the Company in a cashless transaction. The Company received net proceeds of $0.1 million in connection with the exercise of warrants settled in cash.

As part of the February 2018 debt drawdown, the Company's loan and security agreement was amended to include the payment of a $0.3 million success fee to the financial institution in the event of a liquidation event, including an initial public offering. The success fee represents an embedded derivative which the Company has bifurcated from the debt arrangement and carried at fair value. The debt derivative was initially considered a Level 3 liability, since the fair value measurements were based, in part, on significant inputs not observed in the market and reflected the Company's best estimate of the probability of an IPO. As a result of the completion of the IPO in May, the Company remeasured the fair value of the success fee to the full payment amount.

The following table provides a roll-forward of the fair value of the warrant and debt derivative liabilities measured at fair value on a recurring basis using Level 3 significant unobservable inputs (in thousands):

	Warrant Liability	Debt Derivative Liability
Balance at December 31, 2017	$ 424	$ —
Issuance of embedded derivative instrument	—	150
Change in fair value of derivative instrument included in other income (expense), net	—	100
Settlement of derivative instrument	—	(250)
Issuance of warrants to purchase convertible preferred stock	89	—
Balance at Change in fair value of warrant liability, included in other income (expense), net	306	—
Exercise of warrants	(819)	—
Balance at December 31, 2018	$ —	$ —

The estimated fair value of long-term debt approximates its carrying value as the effective interest rate approximates market rates. The fair value of long-term debt, which may differ from its carrying value, is determined by market interest rates from debt arrangements which are observed in market trading which are similar to the Company's arrangement and are considered a Level 2 input.

5. Property and Equipment, Net

Property and equipment consists of the following (in thousands):

	December 31,	
	2018	2017
Property and equipment:		
Lab equipment	$ 5,393	$ 3,189
Leasehold improvements	1,824	1,334
Furniture and fixtures	525	217
Computers and software	115	77
Office equipment	9	9
Construction-in-process	1,011	99
Property and equipment	8,877	4,925
Less: accumulated depreciation	(1,952)	(1,429)
Property and equipment, net	$ 6,925	$ 3,496

The Company recognized $1.9 million, $0.8 million and $0.5 million of depreciation expense for the years ended December 31, 2018, 2017 and 2016, respectively.

6. Accrued Expenses

Accrued expenses consists of the following (in thousands):

	December 31,	
	2018	2017
Accrued external research and development expenses	$ 1,587	$ 715
Accrued payroll and related expenses	2,198	256
Accrued professional fees	1,010	1,081
Accrued other	170	147
Total accrued expenses	$ 4,965	$ 2,199

7. Acquisition with Epiva Biosciences, Inc. (Epiva)

On June 16, 2016, the Company acquired Epiva, a privately held research company, focused on microbes for inflammatory diseases in order to create synergies and expand the depth of the Company's research platform. Epiva held intellectual property rights related to microbes affecting the inflammatory diseases. The acquisition resulted in the exchange of all shares of Epiva stock for shares of the Company's stock at an exchange rate of 1-for-0.8333. The holders of Epiva common stock and common stock options received shares of the Company's common stock or options. The holders of Epiva Series A and A-2 Preferred Stock received shares of the Company's Series A-1 and A-3 Preferred Stock, respectively.

Both the Company and Epiva received funding from various investment funds that are managed by the same entity. The Company assessed the ownership structure of the two companies as well as the investment funds and determined, based on the ownership structure and other rights provided through other relevant arrangements, such as voting rights agreements, limited partnership agreements and general partnership agreements, that the ultimate controlling parent of each of the Company and Epiva was the same entity both immediately before and immediately after the acquisition. As a result, the Company and Epiva were considered to be under common control and the transaction was considered to be a related party transaction.

The net assets received by the Company as a result of the acquisition were determined to represent an asset and not a business. This conclusion was primarily based on the fact that substantially all of the fair value of the gross assets received, excluding cash acquired, related to Epiva's intellectual property rights. This conclusion considered the nature of Epiva's operations immediately prior to the acquisition as well as Epiva's limited operating history.

As the acquisition was considered to represent an asset acquisition under common control, the assets and liabilities received were initially recorded by the Company at Epiva's carrying value on the date of acquisition. The operations associated with the assets received from Epiva are presented within the statements of operations on a prospective basis from the date of the acquisition.

Assets and liabilities received from Epiva as of June 16, 2016 (at the historical carrying value of Epiva) are as follows (in thousands):

Assets:		
Cash and cash equivalents	$	10,411
Prepaid expenses and other current assets		156
Property and equipment, net		406
Other assets		71
Total assets	$	11,044
Liabilities:		
Accounts payable	$	438
Accrued expenses		74
Long-term debt, net of debt discount		2,923
Other noncurrent liabilities		64
Total liabilities	$	3,499

8. Loan and Security Agreement

In November 2015, the Company entered into a loan and security agreement with a financial institution. The arrangement allowed the Company to borrow up to $4.0 million and, if certain criteria were met, to borrow up to an additional $1.5 million. The Company drew $4.0 million under the facility in the first half of 2016 and repaid these amounts in 2016. In connection with this arrangement, the Company issued a warrant that was originally exercisable into 100,000 shares of Series A Preferred Stock. The warrant was initially recorded at fair value and subsequently marked-to-market through the statements of operations. The issuance costs were expensed in 2016 upon the repayment of the loan.

In connection with the 2016 acquisition of Epiva, the Company assumed Epiva's credit facility (the "Credit Facility") and the related $3.0 million of outstanding debt. Subsequent to the acquisition, the Company amended the Credit Facility to allow the Company to borrow up to $15.0 million, including the $3.0 million that was outstanding on the modification date and extending the maturity to August 15, 2020. During 2016, the Company borrowed an additional $7.0 million, bringing the total amounts outstanding as of December 31, 2016 and 2017 to $10.0 million. Under the terms of the Credit Facility the Company is required to make interest only payments through August 15, 2018. Upon the expiration of the interest only period, amounts borrowed will be repaid over 24 equal monthly payments of principal plus interest accrued through August 15, 2020. The amounts outstanding under the facility have an interest rate of the higher of (i) prime plus 0.25% or (ii) 3.75% per annum. The loan is secured by a lien on all Company assets, excluding intellectual property.

In February 2018, the Company drew the additional $5.0 million available under the Credit Facility. This resulted in an increase to the interest rate to the higher of (i) prime plus 0.25% or (ii) 4.50% per annum. The interest only payment period was extended to August 15, 2019. Upon the expiration of the interest only period, amounts borrowed will be repaid over 24 equal monthly payments of principal plus interest accrued through August 15, 2021. As such, $2.5 million and $12.3 million of the debt obligation, net of debt discount, have been included as current and long-term, respectively, on the Company's consolidated balance sheet. The Company was provided the ability to prepay the outstanding loan at its option with a prepayment fee of 2% of principal amount if prepayment was made before August 15, 2018 or 0.5% if the prepayment is made between August 15, 2018 and August 15, 2019.

In conjunction with the February 2018 drawdown, the Company issued a warrant to purchase up to 34,722 shares of the Company's Series B preferred stock at an exercise price of $1.80 per share. As part of the February 2018 drawdown, the loan and security agreement was amended to include the payment of a $0.3 million success fee to the financial institution in the event of a liquidation event, including an initial public offering. The success fee represented an embedded derivative which the Company bifurcated from the debt arrangement and carried at fair value. In May of 2018, the Company completed its IPO and paid the success fee of $0.3 million. In addition, the warrant issued in February of 2018 was exercised in May 2018.

The Company has the following minimum aggregate future loan payments at December 31, 2018 (in thousands):

2019	$	3,342
2020		8,021
2021		5,108
Total minimum payments	$	16,471
Less amounts representing interest and discount		(1,666)
Less current portion		(2,500)
Long-term debt, net of current portion	$	12,305

The Credit Facility contains negative covenants restricting the Company's activities, including limitations on cash deposits, dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and certain other business transactions. There are no financial covenants associated with the agreement. The obligations under the agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company's business, operations or financial or other condition. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and non-current liabilities based on scheduled principal payments.

Interest expense related to the Company's Credit Facility for the years ended December 31, 2018, 2017 and 2016 was $0.9 million, $0.5 million and $0.3 million, respectively.

9. In-License Agreements

Mayo Foundation for Medical Education and Research

On June 10, 2016, the Company entered into a Research and License Agreement, (the "2016 Mayo License Agreement") with Mayo Foundation for Medical Education and Research ("Mayo"). Under the 2016 Mayo License Agreement, Mayo was entitled to certain participation rights in connection with the issuance and sale of Series B Preferred Stock. The 2016 Mayo License Agreement allowed Mayo to purchase shares at the same price paid as other investors and is considered to be a fair value contract. In 2017, Mayo purchased 1,666,667 shares of Series B Preferred Stock at $1.80 per share. Also pursuant to the 2016 Mayo License Agreement, Mayo received 490 shares of common stock upon the completion of certain project milestones as well as warrants to purchase common stock (the "Mayo Warrants") exercisable for 18 shares and 116 shares of common stock upon the completion of certain additional project milestones. The Mayo Warrants were fully vested and expensed in 2016. On April 9, 2018, Mayo Foundation exercised its warrant and was issued 134 shares of common stock.

On August 6, 2017, the Company and Mayo entered into a license agreement ("2017 Mayo License Agreement"). Under the 2017 Mayo License Agreement, Mayo granted the Company (i) an exclusive, worldwide, sublicensable license under Mayo's rights to certain intellectual property and microbial strains (ii) a non-exclusive, worldwide, sublicensable license to certain related know-how, in each case, to develop and commercialize certain microbial strains and licensed products incorporating any such strains. As consideration, the Company paid a nonrefundable upfront fee of $0.2 million and annual license maintenance fees. Nonrefundable upfront fees were expensed in full to research and development expense in 2017. Annual maintenance fees will be expensed as incurred over the term of the agreement. The Company may owe Mayo milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $56.0 million in the aggregate, as well as royalties on net sales of licensed products in low single-digit percentages. As of December 31, 2018, the Company has incurred milestone payments to date totaling approximately $0.2 million under the agreement of which no amounts are currently due.

University of Chicago

On March 10, 2016, the Company and the University of Chicago entered into a patent license agreement ("2016 University of Chicago Agreement"). Under the 2016 University of Chicago Agreement, the University of Chicago granted the Company (i) an exclusive, royalty-bearing and sublicensable license under the Licensed Patents and (ii) a non-exclusive, royalty-bearing, sublicensable license to access the technical information to diligently develop and commercialize Licensed Products. As consideration, the Company paid a nonrefundable upfront fee of less than $0.5 million and will pay annual license maintenance fees. Nonrefundable upfront fees were expensed in full to research and development expense in 2016. Annual maintenance fees will be expensed as incurred over the term of the agreement. The Company may owe the University of Chicago milestone payments, totaling an aggregate of approximately $60.9 million, upon the achievement of certain development, regulatory, and commercial milestones, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages. In addition, the Company also agreed to pay the University of Chicago a share of sublicense revenue. As of December 31, 2018, the Company has incurred milestone payments to date totaling approximately $0.4 million under the agreement of which approximately $0.1 million is currently due.

10. Commitments and Contingencies

Lease Obligations

In January 2018, the Company entered into an operating sublease arrangement to lease approximately 40,765 square feet for its office and research development space at 620 Memorial Drive, Cambridge, MA 02139 from February 2018 to September 2025. The Company maintains an additional separate operating lease for office and laboratory space that is scheduled to expire in 2020. The leases require security deposits, which the Company has primarily met with letters of credit from a financial institution that are secured with cash on deposit.

In June 2018, the Company entered into a sublease arrangement with a third party to lease space subject to an operating lease that is scheduled to expire in 2020. The future minimum rental payments to be received under this agreement total $0.7 million and are equivalent to the minimum payments due from the Company to the landlord.

The Company recorded $3.2 million, $1.0 million and $0.5 million of rent expense for the years ended December 31, 2018, 2017 and 2016, respectively, which are net of sublease rental income of $0.2 million, none and none, respectively.

The minimum aggregate future lease commitments at December 31, 2018, are as follows (in thousands):

2019	$	3,280
2020		3,088
2021		2,973
2022		3,062
2023		3,154
Thereafter		5,740
	$	21,297

Biose Industrie

On February 15, 2018, the Company entered into an Exclusivity and Commitment Agreement with Biose Industrie (“Biose”), a French corporation, in which Biose has agreed to exclusively manufacture certain microbial biotherapeutic products for the Company and reserve agreed upon manufacturing resources to conduct manufacturing runs for such products. Under the terms of this agreement, the Company agreed to annual fees in the mid-six digits in consideration of both exclusivity for the manufacture of monoclonal microbials and for a set minimum number of manufacturing runs per year. Exclusivity fees paid and any minimum commitments are expensed as incurred. At December 31, 2018, aggregate minimum payments over the remaining contract life total approximately $2.0 million.

The Company may periodically become subject to legal proceedings and claims arising in connection with on-going business activities, including claims or disputes related to patents that have been issued or that are pending in the field of research on which the Company is focused. The Company is not a party to any material litigation and does not have contingency reserves established for any litigation liabilities.

11. Stockholders’ Equity (Deficit) and Convertible Preferred Stock

Common Stock

On April 27, 2018, the Company filed an amendment to its certificate of incorporation with the Secretary of State of the State of Delaware, to effect a 1-for-4.079 reverse stock split of the Company’s common stock. All share and per share data shown in the consolidated financial statements and related notes have been retroactively revised to reflect the reverse stock split.

On May 11, 2018, the Company completed an IPO of 5,312,500 shares of its common stock for aggregate gross proceeds of $85.0 million. The Company received approximately $75.8 million in net proceeds after deducting underwriting discounts and commissions and other estimated offering expenses payable by the Company. Upon closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 22,386,677 shares of common stock at the applicable conversion ratio then in effect

On May 11, 2018, the Company filed a restated certificate of incorporation with the Secretary of the State of Delaware, which became effective in connection with the closing of the IPO. Pursuant to the restated certificate of incorporation, the Company is authorized to issue 200,000,000 shares of common stock and 10,000,000 shares of preferred stock.

Convertible Preferred Stock

Upon closing of the IPO in May 2018, all 91,315,295 outstanding shares of the Series A, Series A-1, Series A-2, Series A-3, Series B and Series C Preferred Stock automatically converted into 22,386,677 shares of the Company’s common stock at

the applicable conversion ratio of 1-for-4.079. Prior to conversion, all shares of Preferred Stock accrued a cumulative dividend of 8% per annum. Dividends for the applicable periods are included in net loss attributable to common shareholders on the condensed consolidated statement of operations through the conversion date. All accrued dividends earned on Preferred Stock were forfeited as of the conversion.

In February and March 2018, the Company issued a total of 25,232,199 shares of Series C Preferred Stock at purchase price of $3.23 for gross proceeds $81.5 million under the same terms as the Series B Preferred Stock.

In 2017, the Company issued a total of 27,777,778 shares of Series B Preferred Stock at purchase price of $1.80 for gross proceeds $50.0 million in four separate closings in the first half of 2017. The terms of the Series B Preferred Stock modified certain terms of the existing Series A, A-1, A-2, and A-3 Preferred Stock. The amendments include removing certain redemption rights and allowing the Series B Preferred Stock to vote as part of the class of preferred stockholders. The amendments representing a modification of the Series A, Series A-1, Series A-2, and Series A-3 Preferred Stock. The Company concluded the modification did not result in incremental value to the shareholders and as such no incremental expense was recorded. Based on the removal of the redemption rights, the Company concluded that it was no longer probable that the Series A, Series A-1, Series A-2 and Series A-3 shares would become redeemable. As such, the Company ceased accreting these amounts to their redemption value each reporting period.

12. Stock-Based Compensation

2018 Incentive Award Plan

The Company’s board of directors adopted on April 18, 2018, and the Company’s stockholders approved, the 2018 Incentive Award Plan (the “2018 Plan”), which became effective May 8, 2018 and under which the Company may grant cash and equity-based incentive awards to the Company’s employees, officers, directors, consultants and advisors. Following the effectiveness of the 2018 Plan, the Company ceased making grants under the 2015 Stock Incentive Plan (as amended the “2015 Plan"). The 2018 Plan allows the Company to grant awards for up to 1,344,692 shares of common stock plus that number of shares of common stock subject to awards outstanding under the 2015 Plan, that are forfeited, lapse unexercised or are settled in cash. Each year starting with 2019, the number of shares available for grants of awards under the 2018 Plan will be increased automatically on January 1 by a number of shares of common stock equal to the lesser of 4% of the shares of common stock outstanding on the final day of the preceding calendar year or the number of shares determined by the Company’s board of directors. Accordingly, effective January 1, 2019, the number of shares authorized for issuance under the 2018 Incentive Plan was increased by 1,273,031 shares. The 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it.

The exercise price of stock options granted under the 2018 Plan is equal to not less than the fair market value of a share of the Company’s common stock on the grant date. Other terms of awards, including vesting requirements, are determined by the board of directors and are subject to the provisions of the 2018 Plan. Stock options granted to employees generally vest over a four-year period but may be granted with different vesting terms. Certain options provide for accelerated vesting in the event of a change in control. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. Stock options granted under the 2018 Plan expire no more than 10 years from the date of grant. As of December 31, 2018, equity-based incentive awards for the purchase up to 703,976 shares of the Company’s common stock have been issued under the 2018 Plan, of which none have been canceled or exercised. As of December 31, 2018, 844,853 shares of common stock are available for future grant under the 2018 Plan, which includes 204,137 shares subject to awards that were originally granted, and have since the effective date of the 2018 Plan been canceled or repurchased, under the 2015 Plan.

2015 Stock Incentive Plan

Prior to the approval of the 2018 Plan, the Company granted equity awards under the 2015 Plan, which originally provided for grant of incentive stock options, non-qualified stock options, restricted stock awards, or RSAs, and other stock-based awards to the Company’s employees, officers, directors, consultants and advisors.

The terms of stock awards agreements, including vesting requirements, are determined by the board of directors and are subject to the provisions of the 2015 Plan. Stock options granted to employees generally vest over a four-year period but may be granted with different vesting terms. A limited number of awards contain performance-based vesting criteria and for such awards that are deemed probable of vesting, the Company records expense in the period in which such determination is made through any estimated remaining vesting period. Certain options provide for accelerated vesting in the event of a change in control. Awards granted to non-employee consultants generally vest monthly over a period of one to four years. Stock options issued under the 2015 Plan expire no more than 10 years from the date of grant. As of the adoption of the 2018 Plan, the Company ceased making awards under the 2015 Plan.

Under the 2015 Plan, the Company was authorized to grant equity awards up to an aggregate of 5,417,044 shares of common stock. As of December 31, 2018, an aggregate of 5,758,518 options and other equity awards had been granted under the 2015 Plan, of which 904,550 have been exercised, 640,151 have been canceled and 18,468 have been repurchased as of

December 31, 2018. A total of 113,006 shares previously reserved under the 2015 Plan that had not been exercised or were otherwise subject to outstanding exercise awards were no longer authorized as of May 8, 2018.

Stock-based compensation expense included in the Company's statements of operations is as follows (in thousands):

Stock-Based Compensation Expense

Stock-based compensation expense included in the Company's statements of operations is as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development	$ 2,508	$ 849	$ 205
General and administrative	3,551	693	214
Total stock-based compensation expense	$ 6,059	$ 1,542	$ 419

Stock Options

A summary of the Company's stock option activity and related information is as follows:

	Shares	Weighted Average - Exercise Price	Weighted Average - Remaining Contractual Life	Aggregate Intrinsic Value(1) (in thousands)
Options outstanding at December 31, 2017	3,179,536	$ 1.88	9.05	$ 19,803
Granted	2,013,157	$ 11.27		
Exercised	(84,801)	$ 0.83		
Canceled	(190,081)	$ 4.56		
Options outstanding at December 31, 2018	4,917,811	$ 5.64	8.52	$ 37,395
Exercisable at December 31, 2018	1,465,230	$ 1.57	7.63	$ 16,775
Vested and expected to vest as of December 31, 2018 (2)	4,917,811	$ 5.64	8.52	$ 37,395

(1) The aggregate intrinsic value of 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 common stock as of the end of the period.

(2) This reflects the Company's adoption and election under ASU 2016-9 to recognize forfeitures as they occur.

The Company had 3,452,581 unvested stock options outstanding as of December 31, 2018. The weighted-average fair value of options granted during the years ended December 31, 2018, 2017 and 2016 was $8.00, $4.89 and $1.06, respectively. The aggregate intrinsic value of options exercised during the years ended December 31, 2018, 2017 and 2016 was $1.0 million, $0.8 million and $0.8 million, respectively.

When utilizing the Black-Scholes option-pricing model to determine the grant date fair value of stock options granted to employees as well as the vesting or re-measurement date fair value for awards granted to non-employees, the Company used the following weighted average, or ranges of, assumptions for options granted to employees and options granted to non-employees:

Employee option grants

	Year Ended December 31,		
	2018	2017	2016
Risk-free interest rate	2.74%	2.03%	1.33%
Expected life (in years)	6.17	6.18	5.66
Volatility	77.0%	79.5%	87.2%
Expected dividend rate	0.00%	0.00%	0.00%

Expected Term: The expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The expected life is applied to the stock option grant group as a whole as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population.

Expected Volatility: The Company used an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that were deemed to be representative of future stock price trends as the Company does not have any trading history for its common stock.

Risk-Free Interest Rate: The Company based the risk-free interest rate over the expected term of the options based on the constant maturity rate of U.S. Treasury securities with similar maturities as of the date of the grant.

Expected Dividend: The Company has not paid and does not anticipate paying any dividends in the near future. Therefore, the expected dividend yield was zero.

Fair Value of Underlying Common Stock: Prior to the commencement of trading of the Company's common stock on the NASDAQ Global Select Market, or NASDAQ, on May 9, 2018 in connection with the Company's IPO, the Company determined the fair value of the underlying common stock based on input from management and approved by the Board of Directors, which utilized the valuation of the Company's enterprise value determined utilizing various methods including the back-solve method, the option-pricing method, or OPM, or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM. The total enterprise value was then allocated to the various outstanding equity instruments, including the underlying common stock, utilizing the option-pricing model. Following the Company's IPO, the fair value of the underlying common stock has been determined by referencing the closing price on the NASDAQ on the date of each award.

Non-employee option grants

	Year Ended December 31,		
	2018	**2017**	**2016**
Risk-free interest rate	2.71%	2.30%	2.35%
Expected life (in years)	8.29	9.43	9.51
Volatility	75.6%	78.9%	89.0%
Expected dividend rate	0.00%	0.00%	0.00%

The Company estimates the expected life of options granted based on the remaining contractual term of the option for options granted to non-employees.

On January 30, 2018, the Company issued 250,000 shares of Series B Preferred Stock to a non-employee consultant as part of the consideration for the service performed and completed in 2017. The Company recognized $0.7 million as general and administrative expense in the consolidated statement of operations of which $0.1 million was recorded in 2018.

As of December 31, 2018, total unrecognized stock-based compensation expense relating to unvested stock options was $18.7 million. This amount is subject to change as the unvested portion of the stock options granted to non-employees is subject to re-measurement over the vesting period. This amount is expected to be recognized over a weighted average period of 3.10 years.

Restricted Stock

The Company permitted the early exercise of certain stock options prior to vesting by certain directors and officers. This practice ceased in 2017. Any shares issued pursuant to unvested options are restricted and subject to repurchase by the Company until the conditions for vesting are met. Accordingly, the Company has recorded the proceeds from the issuance of restricted stock as a liability in the consolidated balance sheets included as a component of other current and noncurrent liabilities based on the scheduled vesting dates. The amounts paid for shares purchased under an early exercise of stock options and subject to repurchase by the Company are reported in stockholders' equity (deficit) once those shares vest. Upon termination of employment of an option holder, the Company has the right to repurchase, at the original purchase price, any unvested restricted shares.

In 2016, there were 640,268 options exercised prior to vesting for total proceeds of $0.2 million to the Company. These exercises are not considered substantive for accounting purposes, and as such the related shares are treated as restricted share liabilities given the implicit repurchase feature. As of December 31, 2018, the Company has recognized restricted stock liability of $0.1 million as other noncurrent liabilities.

The Company reclassified $0.1 million to stockholders' equity (deficit) upon vesting of restricted shares during each of the years ended December 31, 2018, 2017 and 2016, respectively. The remaining proceeds related to the unvested options of $0.1 million as of December 31, 2018 will be reclassified to stockholders' equity (deficit) as the shares vest over a remaining weighted average vesting period of 1.18 years.

A summary of restricted stock activity is as follows:

	Shares	Weighted-Average Price
Outstanding at December 31, 2017	257,876	$ 0.40
Vested	(113,627)	$ 0.32
Repurchased	(18,468)	$ 0.49
Outstanding at December 31, 2018	125,781	$ 0.45

As of December 31, 2018, the Company had $0.3 million of unrecognized stock-based compensation expense related to its employee unvested restricted stock awards which is expected to be recognized over a remaining weighted average vesting period of 1.64 years.

2018 Employee Stock Purchase Plan

The Company's board of directors adopted on April 18, 2018, and the Company's stockholders approved, the 2018 Employee Stock Purchase Plan (the "ESPP"), which became effective on May 8, 2018. A total of 336,356 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock that may be issued under the ESPP will automatically increase on the first day of each calendar year, beginning in 2020 and ending in 2028, by an amount equal to the lesser of (i) 1% of the number of shares of the Company's common stock outstanding on the last day of the applicable preceding calendar year and (ii) an amount determined by the Company's board of directors. Offering periods under the ESPP will commence when determined by the plan administrator. The Company has not begun any offering periods under the ESPP.

13. Income Taxes

The Company has not recorded a tax provision for the periods presented due to the losses incurred and the need for a full valuation allowance on net deferred tax assets. The difference between the income tax expense at the U.S. federal statutory rate and the recorded provision is primarily due to the valuation allowance provided on all deferred tax assets. The Company's loss before income tax for the periods presented was generated entirely in the United States:

	December 31,	
	2018	2017
U.S. federal tax statutory rate	21.0 %	34.0 %
State taxes, net of federal benefit	6.5 %	5.6 %
Non-deductible stock compensation	(1.0)%	(1.0)%
Other non-deductible expenses	(0.6)%	(0.5)%
Credits	2.3 %	0.8 %
Change in federal tax rate due to tax reform	— %	(22.5)%
Change in valuation allowance	(28.2)%	(16.5)%
Other	— %	0.1 %
	— %	— %

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 26,339	$ 13,183
Research and development credits	2,721	1,175
Capitalized research and development, patent and start-up costs	360	241
Accrued expenses	918	267
Stock based compensation	1,017	217
Depreciation	(281)	(66)
Deferred tax assets before valuation allowance	31,074	15,017
Valuation allowance	(31,074)	(15,017)
Net deferred tax assets	$ —	$ —

On December 22, 2017, the Tax Cuts and Jobs Act (the Act) was enacted in the United States. The Act incorporates significant changes to U.S. corporate income tax laws including, among other things, a reduction in the statutory federal corporate income tax rate from 35% to 21%, an exemption for dividends received from certain foreign subsidiaries, a one-time repatriation tax on deemed repatriated earnings from foreign subsidiaries, eliminating the alternative minimum tax (AMT), immediate expensing of certain depreciable tangible assets, changing rules related to net operating loss carryforwards, and limitations on the deduction for net interest expense and certain executive compensation. In December 2017, the SEC issued SAB 118, which directs taxpayers to consider the impact of the U.S. legislation as "provisional" when it does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law. The Company did not have any material changes to amounts previously recorded in 2017 as provisional under SAB 118.

As of December 31, 2017, as a result of the Act, we remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The Company has no foreign earnings and therefore is not subject to transition tax. The amount recorded related to the remeasurement of our deferred tax balance was a $6.3 million provision that was offset by a valuation allowance.

As of December 31, 2018, the Company had approximately $98.0 million and $91.2 million in federal and state Net Operating Losses ("NOLs"), respectively. The Federal NOLs include $49.9 million which expire at various dates through 2037 and $48.0 million which carryforward indefinitely. The state NOLs expire at various dates through 2038. As of December 31, 2018, the Company had federal and state research credits of $2.1 million and $0.8 million, respectively, which expire at various dates through 2033.

Realization of future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the Internal Revenue Code provisions, certain substantial changes in the Company's ownership, including the sale of the Company or significant changes in ownership due to sales of equity, have limited and may limit in the future, the amount of net operating loss carryforwards which could be used annually to offset future taxable income. The Company has not yet completed an analysis of ownership changes. The Company may also experience ownership changes in the future as a result of subsequent shifts in stock ownership, some of which may be outside the Company's control. As a result, the Company's ability to use pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to the Company. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. All NOLs generated post tax reform will have an indefinite life, are not subject to carryback provisions and are limited to 80% of income in any year.

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 net deferred tax assets as of December 31, 2018 and 2017, respectively. The valuation allowance increased by $16.1 million in 2018, primarily due to increases in net operating losses and research and development credits. Management reevaluates the positive and negative evidence at each reporting period.

As of December 31, 2018 and 2017, the Company had no unrecognized tax benefits, respectively. 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 twelve months.

14. Net Loss Per Share

Basic and diluted net loss per common share is determined by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding during the period. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock, restricted common stock, convertible preferred stock and warrants to purchase convertible preferred stock, outstanding during the period determined using the if-converted and treasury stock methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and therefore basic and diluted net loss per share have been equivalent.

The following table presents securities that have been excluded from the computations of diluted weighted-average shares outstanding as they would be anti-dilutive:

	Year Ended December 31,		
	2018	2017	2016
Convertible preferred shares (as converted to common stock)	—	16,139,518	9,329,570
Warrant to purchase convertible preferred shares (as converted to common stock) and common shares	—	47,628	47,628
Unvested common stock from early exercise of options	125,781	257,876	412,796
Stock options to purchase common stock	4,917,811	3,179,536	2,127,261
Total	5,043,592	19,624,558	11,917,255

15. Related Party Transactions

The Company entered into an employment agreement with Duncan McHale, an executive officer of Weatherden Ltd ("Weatherden"), a United Kingdom based clinical development consulting firm, as of December 15, 2017. Pursuant to the terms of the agreement, the Company has agreed to pay Mr. McHale £0.3 million per year to serve as the Company's Chief Medical Officer. The Company receives clinical advisory services from Weatherden through a supply of service agreement that was entered into during 2017 and, subsequently, a master services agreement in 2018. Duncan McHale, the Company's Chief Medical Officer is a part owner of Weatherden. During the years ended December 31, 2018, 2017 and 2016, the Company paid Weatherden $0.7 million, $0.3 million and $0.0 million, respectively. As of December 31, 2018 and 2017, the amounts due to Weatherden were $0.2 million and $0.2 million, respectively.

In June 2018, the Company entered into a subleasing arrangement with VL46, an affiliate of one of its stockholders, Flagship Venture Funds. Under the terms of the sublease, the Company will invoice VL46 for an aggregate $0.9 million in rent payments which are due during the period from July 1, 2018 through April 30, 2020 plus any related taxes and lease operating costs. As of December 31, 2018, $0.2 million related to this sublease agreement has been recorded as an offset to rent expense within the consolidated statements of operations and comprehensive loss.

In May 2014, the Company entered into a services agreement with Flagship Ventures Management, Inc., an affiliate of one of its stockholders, Flagship Venture Funds, to provide general and administrative services to the Company, including the employer portions of employee health and dental benefit plans for Evelo Biosciences employees and consulting services. The Company made payments under the agreement of $0.0 million, $0.0 million and $0.2 million during the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, no amounts were due to Flagship Ventures Management, Inc. related to the services agreement.

16. Selected Quarterly Financial Information

The following table contains quarterly financial information for 2018 and 2017. 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.

	Three Months Ended			
	2018			
(in thousands except per share data)	March 31	June 30	September 30	December 31
Total operating expenses	$ 10,425	$ 15,228	$ 16,457	$ 15,993
Total other expense (income), net	75	(82)	(600)	(550)
Net loss	$ (10,500)	$ (15,146)	$ (15,857)	$ (15,443)
Convertible preferred stock dividends	(2,417)	(1,520)	—	—
Net loss attributable to common stockholders	$ (12,917)	$ (16,666)	$ (15,857)	$ (15,443)
Net loss per share applicable to common stockholders, basic and diluted	$ (3.29)	$ (0.85)	$ (0.50)	$ (0.49)

(in thousands except per share data)	Three Months Ended 2017 March 31	June 30	September 30	December 31
Total operating expenses	$ 5,208	$ 6,218	$ 8,038	$ 8,067
Total other expense, net	162	143	135	76
Net loss	$ (5,370)	$ (6,361)	$ (8,173)	$ (8,143)
Convertible preferred stock dividends	(1,225)	(1,422)	(1,708)	(1,730)
Net loss attributable to common stockholders	$ (6,595)	$ (7,783)	$ (9,881)	$ (9,873)
Net loss per share applicable to common stockholders, basic and diluted	$ (1.81)	$ (2.09)	$ (2.61)	$ (2.57)

Exhibit 10.2

Master Services Agreement

This Master Consultancy Services Agreement ("Agreement") dated September 1, 2018 is made between:

A **WEATHERDEN LTD** a company incorporated in England & Wales (registration number 09241011) whose registered office is Units 4 & 5, Swinford Farm, Eynsham, Oxford, OX29 4BL ('the Consultancy' or 'Weatherden'), and

B **EVELO BIOSCIENCES, INC** a company incorporated in Delaware whose registered office is 620 Memorial Drive, Suite 200 West, Cambridge, Ma, Massachusetts, 02139 ('the Client' or 'Evelo').

The Consultancy agrees to supply, and the Client agrees to engage the Consultancy's Services on the following terms:

1. **Nature of this Agreement**

1.1 This is a Master Agreement and defines the terms under which the Consultancy will undertake such Services for the Client as may be agreed between the parties from time to time. No changes will apply unless in writing and signed by both parties.

1.2 Entering this Agreement does not of itself oblige the Client to offer any work to the Consultancy nor for the Consultancy to provide or the Client to accept or pay for any particular consultancy services. Neither party wishes to create or imply any mutuality of obligation between themselves either in the course of or between any performance of the services or during any notice period.

1.3 Where it is agreed between the parties that any Services are to be provided, a schedule in the form annexed to this Agreement setting out the nature of the Services, the charging basis, and any other material terms (a 'Schedule') will be produced by the Consultancy and provided to the Client.

1.4 On receipt of a Schedule

1.4.1 if the Client accepts its terms, the Client will promptly sign and return one copy to the Consultancy

1.4.2 if the Client does not accept its terms, the Client will promptly advise the Consultancy.

1.5 Upon a Schedule being signed by both parties, it will become a contract binding on the parties.

1.6 A contract formed on the basis of a Schedule referencing these terms is governed only by the terms of this Agreement, and by no others, except where both parties expressly agree in writing. In particular, it is agreed that any purchase order or other such document from the Client or Consultancy is intended for the Client's own administrative purposes only, and that notwithstanding its wording, neither a Purchase Order nor its content will have any legal effect. Save to the extent expressly provided, all conditions, warranties or other terms implied by statute or common law are hereby excluded to the fullest extent permitted by law.

1.7 Either party may request change to the nature or scope of Services covered by a Schedule. Any such request shall be sufficiently detailed to enable the other party to assess the impact of the proposed change. No such change will become effective until agreed in writing between the parties and shall become a change order as discussed in Section 5.

1.8 This Agreement is not exclusive; the Client acknowledges that the Consultancy enters this Agreement in the course of its business of providing services to its customers, and the Consultancy is and remains at liberty to also provide services to third parties; it is the Consultancy's responsibility to ensure it does not enter any third-party engagement which might cause a conflict of interest to arise or violate any of the terms herein. The Client is and remains at liberty to engage services (including similar services) from third parties. The Consultancy reserves the right to decline to provide any advice and assistance outside the scope of the Services as specified in Schedules agreed between the parties, even if the Consultancy may previously have provided such additional advice and assistance.

2. **Services**

2.1 The Consultancy will provide Services as agreed from time to time in Schedules, so far as is reasonably practicable within any agreed timescale, in compliance with applicable laws and regulations, written instructions from Client, and with all proper skill and care.

2.2 As an independent agency,

2.2.1 the Consultancy will not require or be subject to supervision direction or control as to its daily activities or the manner of performance thereof, and itself accepts the responsibility for the proper provision of Services

2.2.2 for the avoidance of doubt, the Client shall not (and does not have the right to) exercise supervision, direction or control as to the manner of performance of the Services

2.2.3 it is the Consultancy's responsibility to (and the Consultancy shall) maintain Professional Indemnity, Employer's Liability (where legally required), and Public Liability insurance reasonably sufficient to cover such liabilities and obligations of the Consultancy as may arise in connection with the provision of the Services (in each on such terms and in such amount as a reasonably prudent person would consider to be adequate).

2.3 The Consultancy is responsible for providing personnel who have sufficient qualifications and training to perform the Services herein and for maintaining reasonable continuity in personnel providing Services on its behalf,

2.3.1 but reserves the right to make changes to those personnel providing the Services from time to time upon written approval from Client;

2.3.2 no additional charge will be made for any handover period, and

2.3.3 the Consultancy remains responsible

2.3.3.1 for any supervision and direction of its personnel in the provision of the Services, and

2.3.3.2 in any event for all Services performed on its behalf.

2.4 Where the Consultancy's charges are on a time and materials basis, or where any individual who will provide Services is named in a Schedule (or the Client has a reasonable expectation that the Services will primarily be provided by a specific individual), it is the Consultancy's responsibility to ensure

2.4.1 that the relevant skills and experience of any replacement personnel remain commensurate with the fee rates charged, and

2.4.2 that any replacement personnel have the necessary skills to perform the Services without the need for additional training by the Client.

2.5 It is the Client's responsibility

2.5.1 to afford the Consultancy with such reasonable access, information and staff cooperation as the Consultancy may reasonably require for the proper performance of any Services, and

2.5.2 where the Consultancy provides the Services at the premises of the Client, to ensure that all relevant Health and Safety policies, risks, information and relevant statutory compliance measures are disclosed to the Consultancy to the extent required by applicable law.

2.6 Consultancy will not use a subcontractor to perform the Services or otherwise subcontract its obligations hereunder without the prior written consent of Client, other than team members operating through companies as individuals as listed in the Schedules, for the agreed upon amounts as listed in the Schedules. Any permitted subcontractor will be obligated to perform in accordance with this Agreement and Consultancy will be responsible for the actions and omissions of such subcontractor as if Consultancy had made such actions or omissions itself.

3. **Confidentiality**

3.1 Unless the parties have signed a separate agreement containing more specific provisions in relation to confidentiality (in which case the provisions of such agreement will continue to apply in lieu of this clause), each party

3.1.1 will keep any confidential information disclosed by the other secret, and

3.1.2 on termination (or sooner if required) will at the option of the owner thereof return or destroy such confidential information of the owner, however that the party may retain one (1) copy in its confidential files solely for purposes of exercising the party's rights hereunder, satisfying its obligations hereunder or complying with any legal proceeding or requirement with respect thereto and further, provided, that the party shall not be required to erase electronic files created in the ordinary course of business during automatic system back-up procedures pursuant to its electronic record retention and destruction practices that apply to its own general electronic files. Such retained copies of confidential information shall remain subject to the confidentiality and non-use obligations herein.

3.1.3 shall only share confidential information with its employees and agents who are bound by confidentiality agreements with terms at least as restrictive as those herein and provided that the disclosing partner shall be responsible for any breach of this section by its employees and agents.

3.1.4 Neither anything contained in this Agreement, nor any delivery of any confidential information to the other Party will be deemed to grant to the Receiving Party any rights or licenses under any intellectual property rights (including, without limitation, patent applications, patents, extensions, trade secrets, trademarks, copyrights and/or rights in non-public information) of the disclosing party, except as necessary for Consultancy to perform the Services or for Client to make use of the Services, Data, Deliverables and/or any intellectual property rights.

3.1.5 For clarity, Client's confidential information will further include the Data, and Materials, both as further defined herein.

3.2 Neither party may use or take advantage of any such confidential information of the other party without the discloser's consent, even after the end of this Agreement.

3.3 This obligation does not apply to

3.3.1 information known to the party subject to the obligation of confidentiality before disclosure by the other party, and free of any obligation of confidentiality, or

3.3.2 information independently developed or acquired by the party subject to the obligation of confidentiality, without reference or access to the other party's confidential information, and free of any obligation of confidentiality, or

3.3.3 information which becomes public knowledge without fault on the part of the party subject to the obligation of confidentiality.

3.4 The provisions of clause 3.1 shall not prevent a party disclosing confidential information of the other party if and to the extent such disclosure is required pursuant to any legal or regulatory requirement applicable provided advance written notice is provided to the other party where reasonably possible to allow the other party to seek a protective order or otherwise attempt to limit.

4. **Copyright and Intellectual Property Rights**

4.1 'Deliverable' means a work produced by the Consultancy in the course of Services for delivery to the Client.

4.1.1 Where Consultancy's pre-existing works are with the knowledge and written consent of the Client incorporated in any Deliverable, Consultancy hereby grants to Client a non-exclusive, irrevocable, world-wide, royalty free licence to use, modify and distribute such pre-existing works, but only as part of the Deliverable; all other rights in the pre-existing works are reserved.

4.1.2 Subject thereto, all rights in any Deliverable pass to the Client upon payment of all fees not in dispute due to the Consultancy which relate to that Deliverable, and the Consultancy hereby assigns and such rights, and if necessary, will execute a formal assignment thereof on request by the Client.

4.1.3 Further, Consultancy agrees that, as between Consultancy and Client, Client owns all rights, title, and interest in any data generated from the Services ("Data"), Deliverables, and/or rights (including, without limitation, intellectual property rights such as patent applications, patents, extensions, trade secrets, trademarks, copyrights and/or rights in non-public information) related to the (a) Material or its uses, (b) Data, (c) Deliverables and/or (d) improvements, developments, discoveries, and designs which are conceived, recorded, and/or reduced to practice by Consultancy, alone or jointly with others, (1) in connection with the Services or (2) which are related to the Material or its uses or (3) are developed using the Material or the Confidential Information (collectively with the rights in 4.1.2, "Inventions"). Consultancy hereby assigns to Client all of Consultancy's rights to and interest in any Inventions. If any of Client's ownership rights contemplated under this section is not perfected, fails to arise, reverts or terminates by operation of law, then Consultancy hereby grants to Client an exclusive (even to Consultancy), irrevocable, perpetual, fully paid-up, royalty-free, transferable, sub-licensable (through multiple layers of sub-licensees), worldwide license to all rights, title and interest in the Inventions. Consultancy will act as necessary to perfect, maintain, and/or enforce (to "Protect") Client's rights in the Inventions, including, without limitation, reviewing, executing and delivering all requested supporting documents. Client will reimburse Consultancy's reasonable out-of-pocket costs for such assistance.

4.2 The Consultancy will indemnify the Client against infringement of third party rights by a Deliverable, provided that the Client notifies the Consultancy of any relevant third-party rights promptly on such rights becoming known to or reasonably suspected by the Client.

4.3 Nothing shall prevent the Consultancy from using techniques, ideas, and other know-how gained during the performance of Services under this Agreement in the furtherance of its own business, provide that such techniques, ideas and other know-how do not contain or rely upon any Client Confidential Information and only to the extent that such does not result in disclosure or abuse of confidential information in breach hereof, or any infringement of any Intellectual Property Rights of the Client.

4.4 Consultancy acknowledges that, as between Consultancy and Client, Client owns any reagents, compounds, biological material, devices or other technology provided to Consultancy in connection with the Services, and any modifications, improvements, fragments, analogs or homologs thereof and/or derivatives of the foregoing ("Materials"). Consultancy will not provide or offer to provide any Material to any third-party or person not performing Services hereunder, without the prior written consent of Client. The Materials are to be used by Consultancy solely for completing the Services. Furthermore, upon Client's request or completion of Services, any unused Material will be, at Client's discretion and instruction, either destroyed or returned to Client.

5. **Charges and Payment**

5.1 All sums due shall be invoiced and paid as specified in the applicable Schedule.

5.2 The Client will pay the Consultancy's invoices within 30 days of receipt of invoice, plus VAT where applicable.

5.3 Unless otherwise specified, where payment is on a time and materials basis, the Consultancy may invoice monthly.

5.4 If any of the Consultancy's invoices becomes overdue and are not in dispute and Consultant has notified Client in writing,

5.4.1 the Consultancy may suspend provision of Services, and any agreed timescale will be automatically extended;

5.4.2 the Consultancy may also terminate this Agreement and any current Schedule for material breach whilst any payment is more than 14 business days overdue.

5.5 Unless noted otherwise in the Schedule, all invoices will be in GB Pounds Sterling and must contain an itemized breakdown of all fees and expenses (and be accompanied by relevant supporting documentation), All invoices must reference a valid Client Purchase Order Number in order for payment to be processed. All other payment terms will be included in the Schedule but under no circumstances will the total payments prior to the initiation of service exceed 20% of the total payments provided in the Schedule.

5.6 Prior to the first payment, Consultancy will submit a completed W-8 or W-9 to Client. Invoices should be sent to Client as specified in the corresponding Schedule. If the Schedule does not specify where invoices should be sent to Client, invoices should be sent to:

Evelo Biosciences, Inc.
620 Memorial Drive
Cambridge, MA 02139
United States of America
Attention: Accounts Payable

and to the email address: finance@evelobio.com

Client will pay a sum equal to the full GBP invoiced value. Both parties are responsible for their own wire transfer charges by electronic transfer to the following account:

IBAN - [XXXXXXXXXXXXXXXXXXXXXX]

BIC - [XXXXXXXXXXX]

Account Number - [XXXXXXXX]

Sort code - [XXXXXX]

5.7 If Client requests any changes in the nature, scope, or cost of the Services or if pricing herein is dependent on incorrect information provided by the Client, or if any specified dependencies / facilities are not available on time not due to any fault of Consultancy, or if any equipment required to be provided by the Client fails to operate correctly (save where the engagement itself is for the repair thereof), the parties will agree on a change order. Consultancy will first notify Client in writing of the cost of such changes and will not proceed without Client's prior written consent. Any such approved changes to Services will be considered an amendment to the applicable Schedule and governed by this Agreement and must be accompanied by a separate PO number and referenced when billing.

5.8 If while performing Services Consultancy will compensate any health care providers for their support of the Services, Consultancy will follow Client's requirements for determining the fair market value for such health care provider support and will reasonably report such compensation and other transfers of value to health care providers to Client in a format and frequency to enable Client to comply with applicable laws and regulations.

6. **Liability**

6.1 Neither party excludes liability for death, personal injury, fraud, or otherwise where it is not lawful to do so. Subject thereto, and except for any breach of the confidentiality section or intellectual property sections herein,

6.1.1 **each party expressly excludes liability for economic, consequential or indirect loss or damage of any kind, or for loss of profit, business, revenue, goodwill or anticipated savings.**

6.1.2 **Except for the indemnity or for claims due to its gross negligence, neither party shall be liable for any loss or damage in excess of three times the total sums payable under a Schedule, except where it may not lawfully exclude or limit liability**

6.2 Consultancy shall indemnify, defend and hold harmless Client, and its respective officers, directors, employees and agents (collectively, the "Client Indemnitees") against any third party claims, to the extent arising out of or relating to: (i) Consultancy or any of its employees or agents' negligence or wilful misconduct in performing obligations under this Agreement; or (iii) Consultancy's breach of this Agreement.

7. **Termination**

7.1 Either party may terminate this Agreement at any time when there is no current Schedule, by immediate written notice.

7.2 Client may terminate any Schedule upon thirty days' written notice with or without cause.

7.3 Either party may terminate this Agreement and any current Schedule at any time if the other is in material breach or if the other becomes insolvent, by immediate written notice.

7.4 Any provision of this agreement which expressly or by implication is intended to come into or continue in force on or after termination of this agreement shall remain in full force and effect.

8. **Force Majeure**

If either party is obstructed in performing any of its obligations under a Schedule by an event outside its reasonable control, then performance to the extent obstructed is suspended for so long as the obstruction continues. Whilst performance is suspended and has been so for more than 7 days, either party may terminate that Schedule by immediate written notice.

9. **Staff obligations and third-party rights**

9.1 The Client is a client of a business undertaking carried on by the Consultancy, and it is not the intention of either to create or allow to arise any employee/employer relationship between the Client and any individual providing Services on behalf of the Consultancy.

9.2 Each party solely retains all the responsibilities and rights of an employer towards and in relation to its own employees. Neither party seconds its employees or any of them to the other. No person providing Services is expected or required to integrate into the Client's business organisation or employed workforce.

9.3 With the exception of agreed subcontractors where it is mutually agreed that Company shall pay the subcontractor directly, the Consultancy will ensure that all remuneration it pays any personnel engaged on the Services is paid and taxed as employment income, within the meaning of the Income Tax (Earnings and Pensions) Act 2003 as amended. Consultancy shall be responsible for the payment of all taxes, for all employment, insurance and other similar taxes with respect to any compensation provided by the Client to Consultancy. Consultant will indemnify Client against any claims brought by or in relation to its own employees, whether such claims relate to employment, tax, national insurance, or otherwise

9.4 Where applicable, the Consultancy is solely responsible for complying with the requirements of the Working Time Regulations 1998 (as amended) and any other legislation relating to workers, in relation to any individual providing Services on its behalf.

9.5 Other than by general advertisement for such position or in response to an initiative by an employee responding to such general advertisement, neither party will employ, engage, or otherwise solicit any person who during the previous 6 months was an officer, employee or sub-contractor of the other and with whom such party had material contact in connection with Services performed under any Schedule, until 6 months after that Schedule has terminated.

9.6 Other than by general advertisement for such position or in response to an initiative by an employee responding to such general advertisement neither party will solicit any person who during the previous 6 months was a client of the other and with whom such party had material contact in connection with Services performed under any Schedule, until 6 months after that Schedule has terminated, unless a fee is mutually agreed by the Consultancy and the Client, typically to be equal 33% of the remuneration of the person hired

9.7 No third-party rights are intended to be conferred or created by this Agreement or any Schedule.

9.8 In this term, ‘employees’ includes, so far as the context permits:

9.8.1 in the case of an LLP or partnership, its partners and employees

9.8.2 in the case of a company, its officers and employees.

10. **Data Protection**

10.1 The parties mutually acknowledge their respective responsibilities (a) to comply with the applicable provisions of the Data Protection Act 1998, General Data Protection Regulation 2016/679/EC and any applicable data protection laws ("(“Data Protection Laws”) with respect to Personal Data, as defined in the Data Protection Laws, and (b) to use Personal Data provided by the other so far as necessary for the proper performance of this Agreement or any Schedule hereto, but not further or otherwise.

10.2 Consultancy shall assist and cooperate as is reasonably necessary or reasonably requested by Client to ensure Client complies with the Data Protection Laws. For Personal Data disclosed to Consultancy in connection with this Agreement (and whether disclosed by Client, data subjects or otherwise), Consultancy will only process such Personal Data as permitted by the Data Protections Laws and for purposes requested by Client and for which Consultancy has appropriate measures (including, without limitation, communicating appropriate policies to employees, managing ongoing compliance, and implementing effective information security) for the Personal Data to prevent (1) unauthorised or unlawful processing of the Personal Data and (2) accidental loss or destruction of, or damage to, the Personal Data.

10.3 Consultancy will not disclose to any third-party or provide to Client any personal data unless the individual to whom such personal data pertains has granted his or her informed written consent to such disclosure. This includes unambiguous and explicit written consent to the potential transfer of personal data outside such person’s country of residence to another jurisdiction, including, without limitation, the United States of America where different data protection rules apply. Consultancy will take all steps required and communicated in writing to Consultancy by Client that Client reasonably considers are necessary to comply with Client’s own obligations under Data Protection Laws.

10.4 Consultancy will ensure that all employees, independent contractors or agents involved in providing Services under this Agreement have granted their written consent to the processing of their personal data by Client for the purposes of this Agreement and to the possible transfer of this data outside their country of residence to another jurisdiction, including, without limitation, the United States of America where different data protection rules apply.

10.5 If either party becomes aware of any unauthorised, unlawful or dishonest conduct or activities, or any breach of the terms of this Agreement relating to Personal Data, such Party will promptly notify the other Party in writing thereof and the Parties will take such action as such party may deem reasonably necessary to prevent any further unauthorised, unlawful or dishonest conduct or activities or breach of the terms of this Agreement relating to Personal Data.

10.6 Appendix 1 shall apply if Consultancy is processing Personal Data on behalf of Client. The Schedules shall include any Personal Data being processed.

11. **Bribery and Corruption**

11.1 The parties shall each comply with all applicable legal requirements relating to bribery and corruption.

11.2 The Consultancy shall comply with any Client policies relating to bribery and corruption that may be disclosed to the Consultancy, as though such policies applied to and had been adopted by the Consultancy.

12. **Notices**

Any notice to be given by either party to the other shall be in writing and may be sent by recorded delivery to the address of the other and shall be deemed to be served 2 days following the date of posting. If to Client, a courtesy copy shall be provided to the email address: legal@evelobio.com

13. **Electronic signatures**

13.1 This Agreement and any Schedule may be signed by electronic signature (whatever the form the electronic signature takes), and that such method of signature shall be equally conclusive of the intention of each party to be bound by its terms and conditions as if signed with manuscript signatures.

13.2 Notwithstanding that this Agreement and/or a Schedule may have been signed by a form of electronic signature, no addition, amendment to, or modification or discharge of, this Agreement and/or a Schedule shall be effective otherwise than in writing on paper and signed with the manuscript signature of each party.

14. **Representations and Warranties**

14.1 Consultancy represents and warrants that:

(a) it is authorized to enter into this Agreement and will make every effort to supply the Services with reasonable care and skill and in compliance with all applicable laws and regulations, including but not limited to any anti-bribery laws such as the U.K. Bribery Act of 2010, as amended, and the US Foreign Corrupt Practices Act of 1977, as amended.

(b) conduct and provision of Services will not knowingly violate any patent, trade secret or other proprietary or intellectual property right of a third party.

(c)Consultancy is under no contractual or other obligation or restriction which is inconsistent with Consultancy's obligations under this Agreement, during the term of this Agreement, Consultancy will not enter into any agreement, either written or oral, in conflict with Consultancy's obligations under this Agreement or under any Schedule;

(a) neither it, nor any of its management or any other employees or independent contractors or agents who will have any involvement in the Services supplied under this Agreement, have (i) been excluded, debarred, suspended or otherwise made ineligible to exercise their profession and activities; or (ii) engaged in any act that would be grounds for such exclusion, debarment or suspension. Upon learning or acquiring knowledge of any facts or circumstances that may lead to actions relating to the representations above (including, without limitation, criminal actions), Consultancy will immediately disclose such facts or circumstances to Client; and Client may immediate terminate the Agreement.

15. **Records, Reports and Audits.**

15.1 Records and Reports. Consultancy will maintain complete and accurate written records of Consultancy's performance of the Services for the longer of (a) three (3) years or (b) as required by applicable laws. As provided in a Schedule or at Client's request, Consultancy will report to Client in a written format acceptable to Client on the progress and results of the Services. Upon completion or termination of the Services, Consultancy will deliver to Client all Data and a final report on the Services.

15.2 Audits. Client may, during regular business hours and upon reasonable prior notice, conduct quality assurance audits and inspections of testing, quality control, documentation, record keeping, and standard and general operating procedures used by Consultancy about Services to monitor Consultancy's compliance with its obligations hereunder. Consultancy will cooperate fully in any inspections and audits conducted by Client under this Section. Consultancy agrees to take any reasonable actions requested by Client to cure any deficiencies noted during any such audit or inspection.

15.3 Government Inspections. Consultancy will notify Client (and when possible in advance) of any inspection of Consultancy's facilities by any regulatory authority which inspection or facilities may relate to the Services, the Material or Data and will allow Client to attend the inspection. Consultancy will promptly share with Client the inspection results and/or reports. Client will have the right to review and comment upon any draft correspondence by Consultancy to the regulatory authority generated because of such inspection prior to submission by Consultancy. If a regulatory authority inspects Client relating to the Services, Client will notify Consultancy and Consultancy will reasonably cooperate with Client in responding to requests from such regulatory authorities and making records available within one (1) business day of Client's request.

16. **Publicity/Publication.**

Neither Party will disclose the existence or substance of this Agreement, except as required by applicable laws or regulations. Neither Party will use the name of the other Party or of any of its employees without such Party's prior written consent. Consultancy will not publish information (including, without limitation, by any written, oral, or electronic communication, manuscript, abstract, poster, presentation, or other publication) relating to the Services, Confidential Information, Material, Data or Inventions, in whole or in part, without the prior written consent of Client. Notwithstanding anything to the contrary in this Agreement, this Agreement may be filed by Client with the Securities

and Exchange Commission, and Client may include in any such filing descriptions of the existence and terms thereof. Client shall reasonably consider Consultancy's timely proposed redactions before such filing.

17. **Law.**

These terms and any non-contractual disputes or claims between the parties are governed by the laws of the defending party, whose courts shall have sole jurisdiction in relation to all matters arising.

18. **Entire Agreement.** This Agreement, together with any Schedule, constitutes the entire agreement between the Parties and supersedes and supplants all prior and contemporaneous representations, agreements, and understandings, whether oral, written or otherwise, between the Parties.

----Signature Page to Follow----

Signed by the parties' authorised representatives as follows:

On behalf of **the Consultancy** by **Houman Ashrafian**
(Authorised Signature)

/s/Houman Ashrafian
Title: Chairman
Date: 14 September 2018

On behalf of **the Client** by **Jennifer Glennon**
(Authorised Signature)

/s/Jennifer Glennon
Title: VP, Finance and Operations
Date: 14 September 2018

Appendix 1

Processing of Personal Data

1. Capitalized words used in this section that are defined in the GDPR shall have the meanings as defined in the GDPR. The Parties agree to further amend the Agreement if and as necessary to comply with the Data Protection Laws, as may be amended over time.

2. As part of the Services, Consultancy processes Personal Data on behalf of the Client as a Data Processor. Any Schedules which includes the Processing of Personal Data shall include a Description of subject-matter and duration of the processing, the nature and purpose of the processing, the type of Personal Data and categories of Data Subjects. As the Data Processor, Consultancy represents and warrants that it shall:

(i) Implement and maintain appropriate technical and organisational measures to comply with the Data Protection Laws to ensure the protection of the rights of Data Subjects.

(ii) Implement and maintain appropriate measures to ensure the security of Data Processing and implement appropriate technical and organisational measures to ensure a level of security appropriate to the risk (including but not limited to, appropriate policies, management and review of ongoing compliance and effective security measures) to prevent any unauthorized or unlawful Processing of Personal Data and to guard against accidental loss or destruction of, or damage to or breach of Personal Data as required by Art. 32 (1) GDPR. These measures will include:

(a) the pseudonymization and encryption of the Personal Data;

(b) the ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and Research Project;

(c) the ability to restore the availability and access to Personal Data in a timely manner in the event of a physical or technical incident;

(d) a process for regularly testing, assessing and evaluating the effectiveness of technical and organizational measures for ensuring the security of the processing.

(iii) Not engage another Data Processor without prior written authorization of Client, and if approved by Client, Consultancy shall ensure that the same data protection obligations as between the Client and Consultancy are imposed on that other Processor by way of a contract, in particular providing sufficient guarantees to implement appropriate technical and organisational measures in such a manner that the processing will meet the requirements of the Data Protection Laws. Under each Schedule, Consultancy will provide Client with a written list of subcontractors providing Processing Services.

(iv) Process the Personal Data only on documented instructions from Client, including with regard to transfers of Personal Data to a third country or an international organization; unless required to do so by law; in such a case, Consultancy shall inform the Client of such legal requirement before processing. If Consultancy is required to use the Personal Data for another purpose by EU or Member State law to which the Consultancy is subject, Consultancy will, unless prohibited by applicable law, promptly (and in no event more than twenty-four (24) hours after receipt of such information) notify Client in writing of that legal requirement before Processing such Personal Data; and to the extent permitted by applicable EU or Member State law, Consultancy will comply with the written directions of Client, limit the nature and scope of the requested disclosure, and disclose the minimum Personal Data necessary;

(v) Ensure that all persons authorized to process the Personal Data have committed themselves to confidentiality or are under an appropriate statutory obligation of confidentiality.

(vi) Assist Client with complying with the obligations in Article 32-36 of the GDPR specifically, including responding to requests from Data Subjects to access their data or exercising any of their rights in a timely manner as required by the GDPR, as well as responding to and notifying Data Subjects of any Personal Data Breach and conducting a data protection impact assessment.

(vii) Notify Client within 24 hours of any Personal Data Breach and as part of such notification describe the nature of the incident and, where possible, the categories and approximate number of Data Subjects concerned and the categories and approximate number of Personal Data records concerned, and provide information regarding the possible effects of such Personal Data Breach upon Client and the applicable Data Subjects. In no case will Consultancy delay notification because of insufficient information but instead, Consultancy will provide and supplement notifications as information becomes available;

(viii) In cooperation with Client and with the written consent and approval of Client, use diligent efforts to promptly investigate (1) any Personal Data Breach and take all necessary and appropriate corrective action (as approved by Client in writing) to remediate such breach and prevent a recurrence of such breach; (2) any request for information from or complaint by a data protection authority/Supervisory Authority in relation to Personal Data that Consultancy Processes for the purpose of providing the Services.

(ix) Retain Personal Data for the longer of the time period necessary to perform the Processing Services or as required by applicable law. Consultancy will, consistent with Client's written instructions, upon expiration or termination of the applicable Schedule, return or safely destroy all Personal Data that Consultancy obtained in connection with performing the Services, including all originals and copies of such Personal Data in any medium, and any materials derived from or incorporating such Personal Data. Consultancy will promptly notify Client in writing once all such information has been returned or destroyed (as applicable in accordance with Client's written instructions). Where continued storage is required by EU or Member State law, Consultancy will inform Client of those requirements.

(x) Assist Client in meeting its GDPR obligations in relation to the security of Processing and conducting any data protection impact assessments.

(xi) Provide Client with the necessary information to assist Client in meeting its obligations under the Data Protection Laws.

(xii) Inform Client immediately if an instruction infringes the Data Protection Laws.

(xiii) Cooperate with any supervisory authorities as required by the Data Protection Laws.

(xiv) Maintain records of its processing activities as required by the Data Protection Laws.

(xv) Employ a Data Protection Officer if required by the Data Protection Laws.

(xvi) Make available to the Client or its agents upon request any information necessary for Consultancy or Client to demonstrate compliance with the Data Protection Laws and allow for and contribute to audits, including inspections, conducted by the Client or its agents.

(xvii) ensure that transfers of Personal Data outside of the European Economic Area are made only (i) to a jurisdiction deemed by the European Commission to have an adequate level of protection; (ii) subject to contractual provisions approved by the European Commission; or (c) pursuant to a framework deemed adequate and approved by the European Commission.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-224841) pertaining to the 2015 Stock Incentive Plan, 2018 Incentive Award Plan and 2018 Employee Stock Purchase Plan, of Evelo Biosciences, Inc. of our report dated February 15, 2019, with respect to the consolidated financial statements of Evelo Biosciences, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2018.

/s/ Ernst & Young LLP
Boston, MA
February 15, 2019

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Balkrishan (Simba) Gill, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2018 of Evelo Biosciences, 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)) 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) [intentionally omitted];
   (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: February 15, 2019

By: /s/ Balkrishan (Simba) Gill, Ph.D.
Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jonathan Poole, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2018 of Evelo Biosciences, 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(s) 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)) 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) [intentionally omitted];
   (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(s) 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: February 15, 2019

By: /s/ Jonathan Poole

Jonathan Poole

Chief Financial Officer

(Principal Financial and Accounting 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, Balkrishan (Simba) Gill, Ph.D., President and Chief Executive Officer of Evelo Biosciences, 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 Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (the "Report") fully complies with the requirements of Sections 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.

Date: February 15, 2019

By: /s/ Balkrishan (Simba) Gill, Ph.D.
Balkrishan (Simba) Gill, Ph.D.
President and Chief Executive Officer
(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, Jonathan Poole, Chief Financial Officer of Evelo Biosciences, 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 Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (the "Report") fully complies with the requirements of Sections 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.

Date: February 15, 2019

By: /s/ Jonathan Poole
Jonathan Poole
Chief Financial Officer
(Principal Financial and Accounting Officer)