Evelo Biosciences, Inc.

2020 Annual Report

April 26, 2021

Dear Stockholders,

Since we launched Evelo in 2015, our mission has always been to develop a new type of medicine – one that:

- is effective across a broad range of diseases,
- is safe and well tolerated,
- can be stored at room temperature, and
- is affordable.

Achieving this would bring about two fundamental shifts in healthcare: the provision of high-quality and innovative treatments to the billions of people in the majority world who have no access to advanced medicines; and the ability to treat all stages of disease.

We have now generated data from five separate clinical cohorts of patients who were dosed with EDP1815, our lead anti-inflammatory drug. Those cohorts spanned patients with psoriasis, atopic dermatitis, and participants in a human experimental model of inflammation. In each of these five cohorts we have seen positive clinical data that is concordant with what we have seen in preclinical studies. In addition, our research activities have given us an improved understanding of EDP1815's mechanism of action.

The preclinical and clinical data we have generated increases our confidence that we will realize our vision.

A step towards delivering medicines to patients

In Q3 of this year, we will see data from our Phase 2 clinical trial of EDP1815 that may put us on the path towards Phase 3 trials, and a step towards delivering medicines to patients with inflammatory diseases. This would be a huge landmark in Evelo's history.

In addition, because we know EDP1815 acts on all three types of T cell-driven inflammation given our preclinical and clinical data, we will be able to begin Phase 2 trials exploring its use in many different inflammatory disease conditions, potentially including asthma, arthritis, and inflammatory bowel disease.

Data from our existing clinical trials have also given us the confidence that we are harnessing a core feature of the human body: the ability of the biology of the small intestinal axis, SINTAX™, to drive a clinical signal. What remains is determining how we optimize that signal, which, like all medicines, is essentially about delivering the right amount of a drug substance, to the right location, in the right form, for the right period of time. We are continuing to discover innovations that do this even better than we have achieved already, opening up the possibilities of using drugs delivered in this way to treat a wide range of diseases, including cancer.

Towards an effective and affordable treatment for COVID-19

The COVID-19 pandemic has confirmed the validity of our goal of bringing affordable and effective medicine to the whole of the world's population. But we also have shown that EDP1815 has a unique profile that could enable it to be used to prevent serious progression of COVID-19 itself, in ways that are not addressable by other drugs.

We know that reducing inflammation is crucial to the treatment of patients with COVID-19. Unlike existing anti-inflammatory drugs, however, which dampen natural antiviral immune responses and are often toxic, EDP1815 has the

potential to treat all stages of COVID-19 infection in a safe and targeted way, reducing abnormal immune response while retaining the immune system's ability to fight the SARS-CoV-2 virus. To examine this further, we are participating in the United Kingdom's TACTIC-E Phase 2/3 clinical trial which is investigating anti-inflammatory treatments for COVID-19.

As the effects of EDP1815 are not limited to a specific viral infection, positive results in this trial could open the way to providing affordable and easy-to-deliver treatments not only for COVID-19 patients across the world, but also for patients affected by future strains of SAR-CoV-2 and by other viruses that are certain to arise.

The COVID-19 pandemic has been a difficult and challenging time for everybody. Unlike many biotech organizations, however, we have been able to keep our clinical trials going, continue our manufacturing operations, and complete two follow-on financings. The fact that we were in a very good position as we entered 2021 is a testament to our teams' resilience and capabilities and we thank them sincerely.

Other ways of exploiting the small intestine axis

We will continue to invest in the platform we have developed to deliver safe, effective, convenient, and affordable medicines via SINTAX, the sensing system in the gut that governs inflammation and immunity throughout the body.

One of the most exciting of these advances is the use of microbial extracellular vesicles (EVs) to treat cancer and inflammatory disease. It has long been known that immunotherapies hold the key to effective cancer treatment, but work done with checkpoint inhibitors has not delivered the results the world had hoped for. EVs offer the potential to broaden the base of cancer immunotherapy and augment current standard-of-care therapies. Thís year we will continue what has been very productive early research into their use.

A deep faith in humans' ability to solve problems

Two key ideas drive the way we work at Evelo:

- **poiesis**: the ability to create things from nothing, to constantly invent and innovate, and
- **entelechy**: the continual drive towards realization of an individual's potential.

We have done a remarkable job embedding these ideas in everything we do and, as a result, we have created an organization that is amazing to work for, helps all of our employees grow, and delivers innovative solutions.

Making a difference to healthcare worldwide

This year we will continue to harness SINTAX to develop better and earlier treatments for hundreds of millions of people worldwide. As always, we conclude by thanking the patients who work with us and thanking you, our stockholders, for your support and your belief in our vision, in us and in our science and potential products.

Simba Gill
Chief Executive Officer and
President

Mark Bodmer
Chief Scientific Officer and
President of Research and Development

This letter contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this letter that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our objectives and anticipated clinical milestones for 2021 and 2022, the promise and potential impact of any of our product candidates or preclinical or clinical trial data.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our limited operating history; our unproven approach to therapeutic intervention; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in regulatory approval; our reliance on third parties and collaborators to expand our microbial library, conduct our clinical trials, manufacture our product candidates, and develop and commercialize our product candidates, if approved; our lack of experience in manufacturing, selling, marketing, and distributing our product candidates; failure to compete successfully against other drug companies; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; our patents being found invalid or unenforceable; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; our management and principal stockholders have the ability to control or significantly influence our business; costs and resources of operating as a public company; unfavorable or no analyst research or reports; and securities class action litigation against us.

These and other important factors discussed under the caption "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2020 and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this letter. Any such forward-looking statements represent management's estimates as of the date of this letter. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this letter.

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES**

For the Fiscal Year Ended December 31, 2020
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	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	EVLO	Nasdaq Global Select Market

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

The aggregate market value of the registrant's the voting and non-voting common stock held by non-affiliates was approximately $112.8 million based on the closing price of the registrant's common stock on June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter. 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 March 5, 2021, there were 53,334,947 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2021 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, 2020, 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 (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (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, progress and receipt of data from our ongoing and planned clinical trials 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 the U.S. Food and Drug Administration (the "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 “Summary Risk Factors” and Part I, Item 1A. “Risk Factors,” below and 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.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. "Risk Factors" in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- 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. Moreover, our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

- 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.

- Our product candidates are based on targeting SINTAX™, the small intestinal axis, which is an unproven approach to therapeutic intervention

- We are dependent on the success of our product candidates. If the product candidates do not successfully complete clinical development or receive regulatory approval, our business may be harmed.

- The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements of the United States and internationally. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.

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

- We do not have our own manufacturing capabilities and will rely on third parties to produce additional clinical supplies, if needed, and commercial supplies of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

- If we are unable to establish our own sales, marketing and distribution capabilities, or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved, and we may not be able to generate any revenue.

- The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

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

- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue clinical trials, limit the commercial

profile of an approved label, or result in significant negative consequences following marketing approval, if any.

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

- The COVID-19 pandemic has adversely impacted and may continue to adversely impact, our business, including our preclinical studies and clinical trials, results of operations and financial condition.

PART I

Item 1. Business

Overview

Evelo Biosciences is discovering and developing a new class of orally delivered investigational medicines that are intended to act on cells in the small intestine to produce therapeutic effects throughout the body. The target cells in the small intestine play a central role in governing human immune, metabolic and neurologic systems. We refer to this biology as the small intestinal axis, or SINTAX™. We have built a platform to discover and develop novel oral medicines which target the small intestinal axis. By harnessing the small intestinal axis, we have the potential to transform healthcare via medicines that have the potential to be effective, safe, convenient and affordable and to thereby treat patients at all stages of diseases and to treat patients globally.

Our first product candidates are orally delivered pharmaceutical preparations of naturally occurring, specific single strains of microbes. In preclinical models, our product candidates engaged immune cells in the small intestine and drove changes in systemic biology without any observed systemic exposure. We have observed in early clinical trials and preclinical studies that our approach led to modulated immune responses throughout the body by acting on the small intestinal axis. Our most advanced product candidate, EDP1815 is being developed for the treatment of inflammatory diseases and the hyperinflammatory response associated with COVID-19. Additional product candidates include EDP1867 and EDP2939 for the treatment of inflammatory disease and EDP1908 for the treatment of cancer.

Orally delivered SINTAX medicines have the potential to address patient needs at all stages of disease due to their potentially superior characteristics over current therapies:

- In preclinical models, our product candidates have acted through multiple clinically relevant and validated biological pathways. By acting on multiple pathways simultaneously, we believe our product candidates could impact disease in ways that are not possible with current single-target or dual-target therapies.

- Our data suggest that our product candidates for inflammatory diseases have the potential to resolve disease causing inflammation whilst preserving immunity, a significant potential benefit. Anti-inflammatory therapies often cause significant immune suppression.

- We believe our product candidates are likely to be well-tolerated as they are derived from naturally occurring, specific single commensal strains of human bacteria, have not shown systemic exposure in clinical trials, and have been cleared from the body with no colonization of the gut.

- Our products candidates are formulated as oral medicines, which many patients prefer over injectable biologics and burdensome application of topical drugs.

- We have developed robust manufacturing processes for our product candidates, allowing for large-scale production and the potential for global, room-temperature stable distribution of our product candidates at affordable prices.

- We believe our discovery and development of oral SINTAX medicines has the potential to be more efficient than other product classes such as cell therapy, monoclonal antibodies and small molecules. We believe that our product candidates will not require the lengthy target validation and compound discovery requirements of conventional drug discovery.

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 targeting SINTAX.

Key elements of our strategy:

- ***Explore the full potential of SINTAX to create an expansive and diversified product portfolio.*** We believe targeting SINTAX has applicability across a broad range of disease areas and we are committed to pursuing opportunities in which our platform has the potential to transform their treatment. Our initial focus is on inflammatory diseases and oncology. 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 explore the potential of SINTAX medicines across the full spectrum of disease severity, including in patients with mild and moderate forms of disease. We intend to pursue what we believe to be the inherent advantages of SINTAX medicines to enable use in all stages of disease.

- ***Advance and scale our SINTAX medicine 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 microbial library and enhance our proprietary *in vitro* and *in vivo* assays to optimize selection of our future product candidates. Our manufacturing processes are designed to ensure the quality and scalability of our product candidates. We plan to continue to invest in novel methods for process development, manufacturing and formulation for our SINTAX medicine. In the future, we intend to invest in commercial scale manufacturing. We plan to leverage the efficiency of our integrated capabilities to accelerate the clinical development of product candidates.

- ***Strengthen and expand our intellectual property to protect our platform and product candidates.*** We have exclusive rights to our technologies including issued composition of matter and method of use patents in the United States for some of our product candidates. We intend to 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 SINTAX medicines.*** 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, atopic dermatitis, asthma, inflammatory bowel disease and multiple sclerosis can result. Conversely, an inadequate immune system response may allow various types of cancer and infections 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-TNFα antibodies are widely used to treat moderate to severe stages of many inflammatory diseases. In 2019, three of the fifteen top selling drugs worldwide were anti-TNFα antibodies, with HUMIRA alone generating worldwide annual net sales of $19.7 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 Broad New Opportunity 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.

SINTAX is Central to Human Biology and Immunology

The small intestine is the largest part of the 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 SINTAX provides an opportunity for immunomodulation throughout the body after oral delivery of products that remain physically restricted to the lumen and lymphoid tissues of the gut. Immunomodulation via SINTAX may represent an underappreciated opportunity to drive therapeutically relevant immune responses throughout the body.

SINTAX and Microbes

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

Multiple mechanisms for direct interactions between microbes and immune cells in the small intestine have been demonstrated. We believe that dendritic cells and macrophages in the lymphoid tissues of the small intestine are key target cells of immunomodulatory microbes. The small intestine has a large surface area and thin and diffuse mucus layer, which allows for close contact between microbes and immune cells. Dendritic cells are a specialized type of immune cell that survey the body's tissues, detecting and presenting 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 small intestine 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 within the mesenteric lymph node and push them towards an inflammatory or immunoregulatory phenotype depending on the specific strain of the 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.

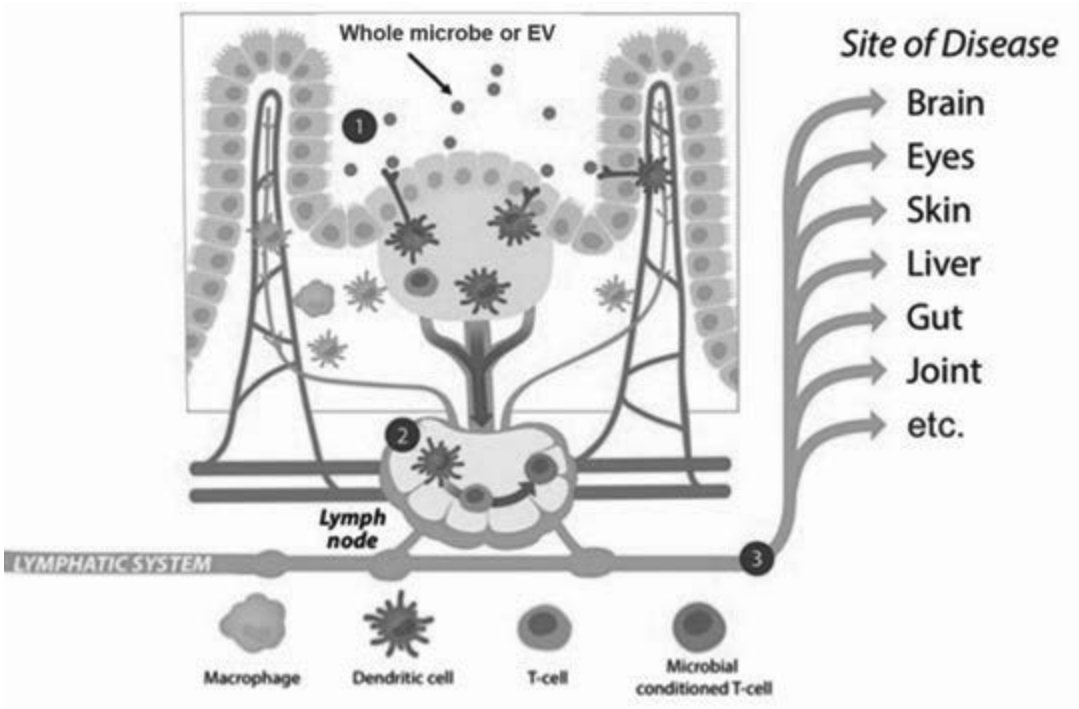


Figure 1: The small intestine and microbes. The small intestine is connected to many other parts of the body via the lymphatic system in green. The cross-section of the small intestine depicts (1) sampling of microbes in the small intestine by dendritic cells and macrophages, (2) conditioning of T-cells 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 SINTAX to suppress or activate immune responses throughout the body. Our Phase 1b clinical data to date also support this theory.

SINTAX medicines as a Potential New Class of Oral Biologic Medicines

Our company was founded to discover and develop therapies that act on SINTAX. 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 SINTAX.

We have developed the tools to isolate, select, and develop specific microbes that have historically been difficult to identify, isolate and culture. This extends from microbial isolation to manufacturing. We have developed proprietary insights and tools that enhance our ability to produce pharmaceutical compositions of microbes at scale. This allows us to deliver potentially therapeutic doses of appropriately formulated strains.

We are developing SINTAX medicines- whole, inactivated microbes and bacterial extracellular vesicles ("EVs") to engage cells in the small intestine and drive changes in systemic biology by either downregulating or upregulating immune responses for the treatment of disease. SINTAX medicines are orally delivered pharmaceutical compositions of specific strains of microbes or EVs from specific strains of microbes.

We believe key features and advantages of our SINTAX medicine candidates are:

- ***Single strain.*** Our product candidates are pharmaceutical compositions of single strains of microbes or EVs produced by single strains of microbes that we have selected for their specific immunomodulatory properties. We extensively characterize the ability of our product candidates to elicit a desired immunomodulatory effect.

- ***Orally administered formulation.*** We intend to deliver our initial product candidates orally in formulations designed for targeted release to specific regions within 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 SINTAX medicines, if approved.

- ***Limited systemic exposure.*** In preclinical studies, we observed that our product candidates 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 SINTAX medicines may have limited systemic off-target side-effects. Our Phase 1b clinical data to date support this potential.

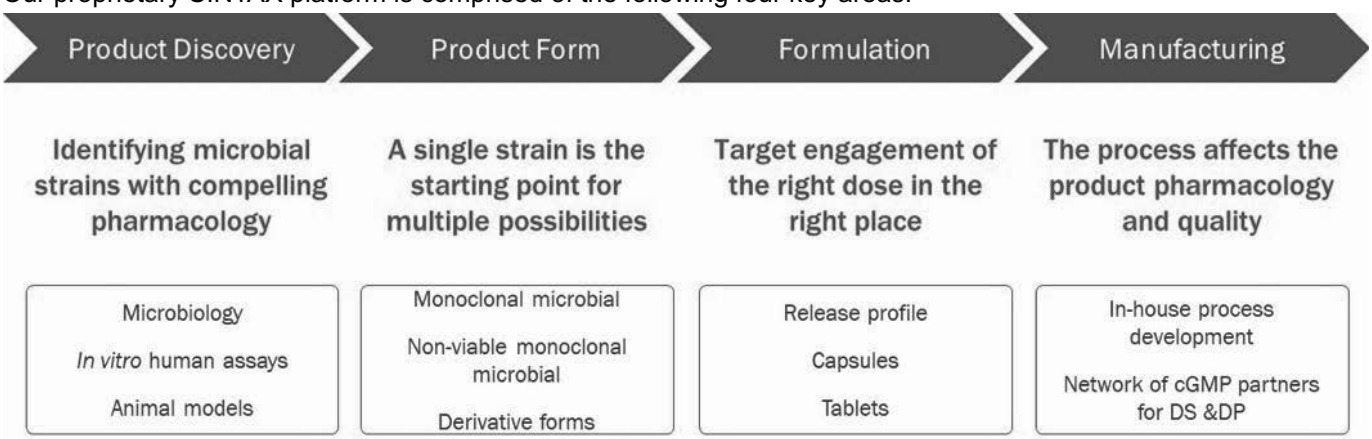
- ***Action on multiple clinically relevant and validated pathways.*** Our preclinical data have shown that SINTAX medicines may act simultaneously on multiple clinically relevant and validated biological pathways. The diseases we intend to treat are multifactorial, and we believe that our potential therapies will be advantageous over single-target treatments. Additionally, our data suggest that SINTAX medicines resolve inflammation whilst preserving immunity, a significant potential benefit compared to other anti-inflammatory therapies that often cause significant immune suppression.

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

SINTAX Medicine Platform

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

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



Candidate discovery. We have assembled a proprietary library of diverse strains of microbes. The continuing accrual of strains in our library is from human mucosal and small intestinal sources in order to benefit from the co-evolution of microbes and the human immune system. We also add to our library through selective licensing agreements and collaborations with academic partners. The proprietary tools within our platform are designed to identify and characterize selected microbes using *in vitro, in vivo* and *ex vivo* assays. Proprietary *in vitro* assays simulate the interactions between microbes and human immune cells, allowing us to evaluate the immunological activity of each microbial strain in relevant experimental systems. Our *in vitro* assays can screen hundreds of microbes, 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 candidates for testing in relevant animal models.

Product form. The activity of our SINTAX medicines 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 SINTAX medicines passed through the gut and did not

distribute around the body or engraft in the gut. Furthermore, this preclinical activity was observed to be independent of the ability of our SINTAX medicines to replicate. From this observation, we believe that activity of SINTAX medicines is likely driven by recognition of structural motifs on the surface of microbes or EVs by immune cells in the small intestine. Our candidate selection process may include an additional manufacturing step for our whole-microbe candidates to develop them as non-replicating product candidates, such as EDP1867. We are also developing reduced forms of our whole-microbe product candidates, or EVs, to target SINTAX. Preclinical studies suggest that this approach may further improve potency and activity and we anticipate the initiation of clinical development of EDP2939 and EDP1908, our initial EV product candidates, in 2022.

Formulation. In our first clinical trials, product candidates were formulated as capsules containing lyophilized powder for targeted release in the small intestine. We have continued to explore potency and dose as it relates to formulation and have developed manufacturing processes that increase the concentration of EDP1815. Additionally, we have developed a tablet formulation with the higher concentration of EDP1815, also for targeted release in the small intestine. We have tested capsules with the higher concentration in a human experimental model of inflammation and we intend to test capsules and tablets with the higher concentration of EDP1815 in patients in our on-going Phase 1b clinical trial during 2021. We are committed to continuously investing in formulation development to improve the potency and delivery of our product candidates and enhance their ability to target and act on SINTAX.

Process development and manufacturing. Process development and manufacturing are critical for the translation of SINTAX medicines into therapies. Our expertise and investments in laboratory and pilot scale development have allowed us to mitigate challenges inherent to manufacturing of SINTAX medicines at clinical scale.

Process development is integrated into our research activities, combining discovery and downstream development. We believe we have achieved control of quality, identity, purity, and potency throughout the process of strain selection, fermentation, EV purification, formulation, and pharmacology, with high yield. Importantly, we believe 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 production in accordance with cGMP regulations. For each of our clinical product candidates, we have observed therapeutic activity in lyophilized powder form and in compressed tablet form in relevant preclinical mouse models and, in the case of EDP1815, in clinical studies using lyophilized powder in capsules.

We have been able to manufacture SINTAX medicines 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 SINTAX medicines.

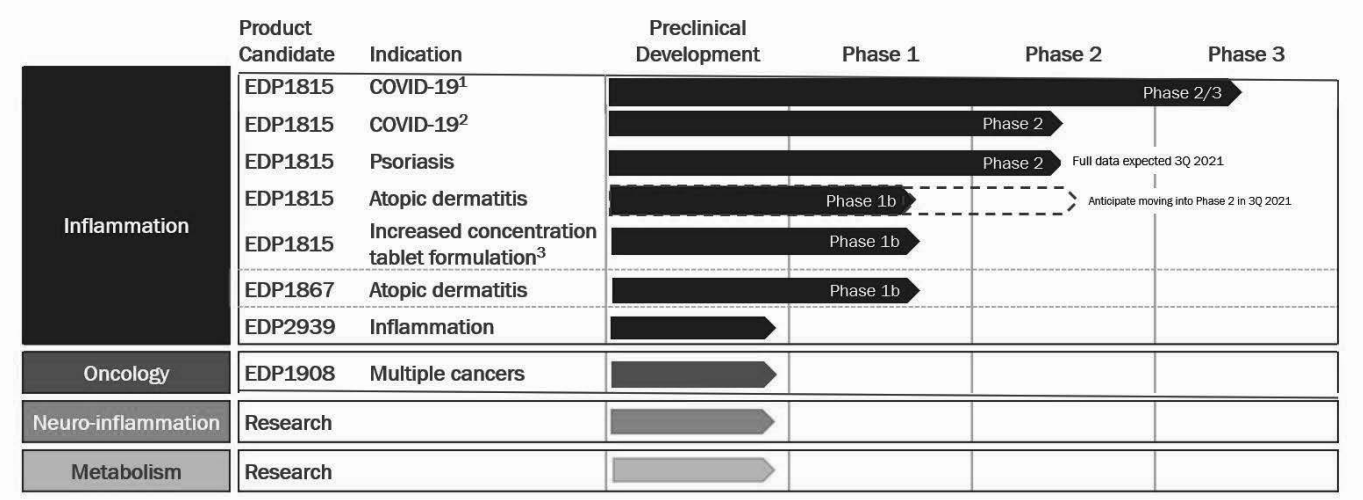
Product Development Strategy and Portfolio

We are advancing SINTAX medicines 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, pharmacodynamic responses 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, including in neuroinflammation and metabolism, 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.

In addition to product candidates based on whole, inactivated microbes, which include EDP1815 and EDP1867, we continue to advance the development of orally delivered EVs. EVs are lipoprotein nanoparticles naturally produced by some bacteria. EVs have the potential to enable increased target engagement driven by their small size as they are approximately 1/1,000th the volume of whole microbes. We have nominated two EV clinical candidates, EDP2939 and EDP1908 for the treatment of inflammatory diseases and cancer respectively and anticipate first-in-human studies of this new product form in 2022.

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



Notes:
[1] The Phase 2/3 TACTIC-E study is an investigator-sponsored study being conducted by Cambridge University Hospitals NHS Foundation Trust
[2] The Phase 2 trial is in collaboration with Rutgers University and Robert Wood Johnson University Hospital
[3] Evelo is conducting Phase 1b studies on increased concentration and tablet formulations of EDP1815

Inflammatory Diseases Portfolio

We have three candidates in development for inflammatory diseases. EDP1815 is a whole-microbe product candidate currently in a Phase 2 trial for the treatment of psoriasis, with plans underway for an additional Phase 2 trial in atopic dermatitis, following positive Phase 1b data announced in December 2020 and January 2021. Additionally, we advanced EDP1867, an inactivated, whole-microbe product candidate, into a Phase 1b study in February 2021 in patients with atopic dermatitis. EDP2939 is our first product candidate based on EVs, and we anticipate initiation of clinical development of this product candidate in 2022.

EDP1815

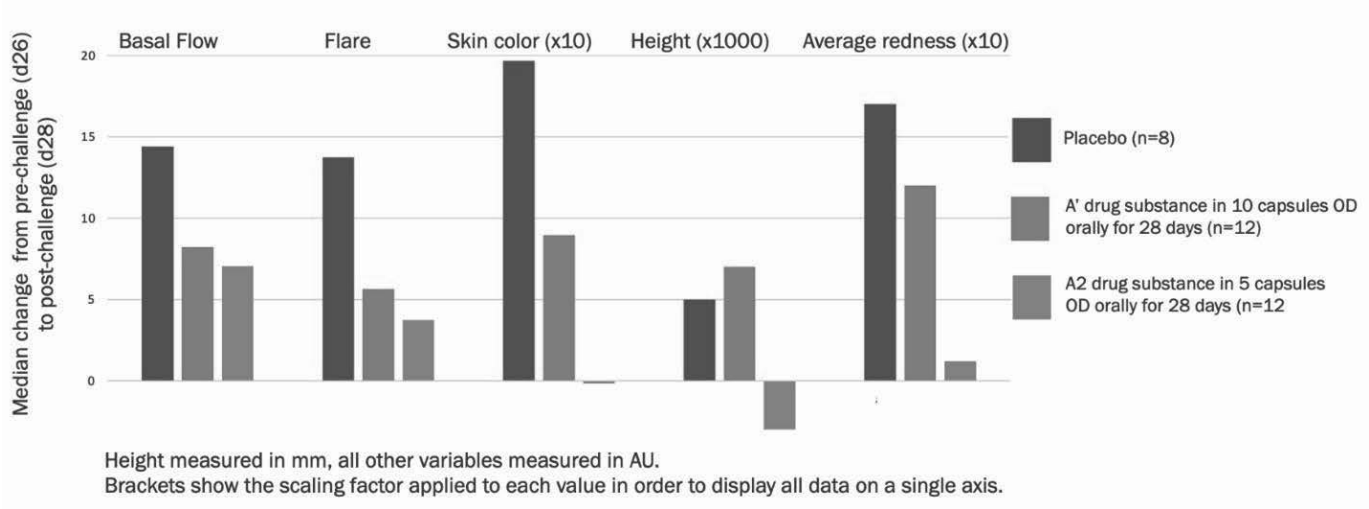
EDP1815 is an investigational oral biologic being developed for the treatment of inflammatory diseases. It is a single strain of Prevotella histicola, selected for its specific pharmacology.

Human Experimental Model of Inflammation

In addition to testing our product candidates in patients with inflammatory disease, we also have employed a human experimental model of inflammation in healthy volunteers. This model is very similar in design to a standard preclinical model of T cell driven inflammation. We have recently used this model to test two different concentrations of EDP1815 to investigate the relative effectiveness of the different concentrations. A total of 32 volunteers were enrolled into the trial and treated with either EDP1815 (n=12 per formulation) or placebo (n=4 per formulation) daily for 28 days. The participants were immunized with an antigen used in preclinical inflammation experiments. After 28 days of daily oral dosing with EDP1815 or placebo, the participants were given a skin challenge with the same antigen, which causes measurable skin inflammation a day later. Inflammation was determined by measuring five parameters in the skin at the challenge site.

The increased concentration of drug results from improvements made in the commercial-scale manufacturing process, referred to as A2. This is the same active drug at four times the concentration compared to a prior manufacturing process, referred to as A'. Twelve participants were dosed with A' EDP1815. Another 12 participants were given the higher concentration A2 EDP185. Eight participants who received a placebo were divided between the two treatment groups. The results are in the figure below.

A2 EDP1815 is more effective than A' at same total dose in human experimental model of inflammation



The higher concentration A2, given in fewer capsules, resulted in numerically superior reductions across the full range of skin scores compared to A' and placebo. A2 and A' were given at the same total daily dose of drug. These results are consistent with preclinical data that showed increased drug concentration resulted in increased activity. This is a key advance in our understanding of how to get more benefit from SINTAX medicine candidates. We plan to evaluate tablets and capsules containing the higher concentration A2 EDP1815 in patients with psoriasis in our on-going Phase 1b trial, and expect to report data in the third quarter of 2021. Results from the Phase 1b trial and our on-going Phase 2 trial in psoriasis will position us to go forward into Phase 3 trials with an optimized dose and formulation of EDP1815, which may further improve on the positive results already seen.

Psoriasis and atopic dermatitis

Phase 2 clinical trial in psoriasis

Based on previously reported positive clinical data in two cohorts of individuals with mild and moderate psoriasis in a Phase 1b clinical trial, we advanced EDP1815 into a Phase 2 dose ranging trial, evaluating three doses of A' EDP1815 in capsules versus placebo in approximately 225 individuals with mild and moderate psoriasis. The primary endpoint of the trial is the mean reduction in Psoriasis Area and Severity Index ("PASI") score at 16 weeks. Other clinical measures of psoriasis are also being evaluated. We initiated the Phase 2 clinical trial in October 2020 and have completed enrollment and, therefore, now plan to report topline data for all patients in the study in the third quarter of 2021. Clinical data from this trial, if positive, may enable us to advance directly into Phase 3 registrational trials, subject to end of Phase 2 discussions with regulatory agencies.

We intend to evaluate EDP1815 in additional inflammatory disease indications, depending on the results from the Phase 2 trial. Potential indications include psoriatic arthritis, axial spondylarthritis and rheumatoid arthritis.

Phase 1b clinical trial in atopic dermatitis

In November 2018, we initiated our ongoing Phase 1b double-blind placebo-controlled dose-escalating safety and tolerability trial of EDP1815 in healthy volunteers and individuals with mild or moderate psoriasis or atopic dermatitis. The primary endpoint of the phase 1b trial is safety and tolerability.

In December 2020 and January 2021, we reported positive clinical data from our Phase 1b trial in a cohort of patients with mild and moderate atopic dermatitis (n=24), randomized 2:1 to receive EDP1815 in capsules or placebo for 56 days. EDP1815 was well-tolerated with no treatment-related adverse events of moderate or severe intensity, and no serious adverse events. Secondary endpoints included a range of established markers of clinical efficacy in atopic dermatitis, such the Eczema Area and Severity Index ("EASI"), the Investigator's Global Assessment times body surface area ("IGA* BSA"), and the SCORing Atopic Dermatitis ("SCORAD") scores.

Table 1

Clinical Measure	Treatment Difference between EDP1815 and Placebo Percentage Change at Day 56*
EASI	52% (p=0.062)
IGA*BSA	65% (p=0.022)
SCORAD	55% (p=0.043)

*Least Squares Mean Percentage Change From Baseline. Note that the Phase 1b trial was not powered to detect statistically significant outcomes on efficacy endpoints: p-values presented are nominal values presented for illustrative purposes only.

The data showed consistent improvements in percentage change from baseline compared to placebo for all three clinical scores: EASI, IGA*BSA, and SCORAD. In addition, 7 out of 16 (44%) patients treated with EDP1815 achieved an outcome of a 50% improvement from baseline in EASI score by day 70, compared with 0% in the placebo group, showing sustained improvement in those patients responding to EDP1815.

In addition to physician-reported clinical outcomes, this trial also assessed patient-reported outcomes. Treatment with EDP1815 resulted in clinically meaningful improvement in the Dermatology Life Quality Index ("DLQI") and Patient-Oriented Eczema Measure ("POEM"). These patient-reported outcomes capture the important impact of the disease on patients, including the domains of itch and sleep, both of which saw improvements in patients receiving EDP1815 in the trial. All five measures of itch within the Pruritus-Numerical Rating Scale ("Pruritus-NRS"), SCORAD, POEM, and DLQI showed greater improvements in the treated group at day 56 compared with placebo. We believe these results provide further evidence that modulating SINTAX has the potential to drive significant clinical benefit without the need for systemic exposure.

Subject to regulatory approval, we anticipate initiation of a Phase 2 trial of EDP1815 in atopic dermatitis in the third quarter of 2021.

COVID-19

EDP1815 is being evaluated in two ongoing clinical studies for the treatment of hospitalized COVID-19 patients. The first is a Phase 2 double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of EDP1815 for the treatment of individuals diagnosed with COVID-19 early in the course of their disease. The trial initially will evaluate 60 individuals to determine if early intervention with EDP1815 can prevent the progression of COVID-19 symptoms and the development of COVID-Related complications. Individuals who have presented at the emergency room within the last 36 hours and tested positive for SARS-CoV-2 are randomized 1:1 to receive the capsule formulation of EDP1815 or placebo for 14 days, along with the standard of care. The primary endpoint is reduced requirements for oxygen therapy, as measured by the ratio of oxygen saturation (SpO2) / fraction of inspired oxygen (FiO2). Key secondary endpoints include total symptom duration, progression along the World Health Organization ("WHO") scale of disease severity, and mortality. The trial is being led by Reynold A. Panettieri, Jr., M.D., Vice Chancellor for Translational Medicine and Science at Rutgers Biomedical and Health Sciences and Professor of Medicine at Rutgers Robert Wood Johnson Medical School.

EDP1815 is also included as a treatment arm in the TACTIC-E clinical trial. TACTIC-E is a Phase 2/3 randomized trial, sponsored by Cambridge University Hospitals NHS Foundation Trust, that is expected to evaluate up to 469 patients per arm at Addenbrooke's Hospital and other leading clinical centers in the United Kingdom and select international sites. The trial is investigating the safety and efficacy of certain experimental therapies in the prevention and treatment of life-threatening complications associated with COVID-19 in hospitalized individuals at early stages of the disease. The trial is enrolling individuals with COVID-19 who have identified risk factors for developing severe complications and are at risk of progression to the intensive care unit or death. The primary outcome measure of the trial is time to incidence (up to day 14) of any one of the following: death, mechanical ventilation, extracorporeal membrane oxygenation, cardiovascular organ support, renal failure, hemofiltration or dialysis. Secondary outcome measures include duration of stay in hospital, duration of oxygen therapy, changes in biomarkers associated with COVID-19 progression, and time to clinical improvement.

As a result of the varying infection rates and resulting hospitalizations that have occurred with the pandemic, we experienced slower than expected enrollment early on in both trials and now expect to report data from the clinical trial conducted at the Robert Wood Johnson University Hospital and interim safety data and futility

analysis from TACTIC-E in the second quarter of 2021. In order to expedite patient recruitment and expand access to potential therapies for COVID-19, new trial sites have been opened for TACTIC-E, including in the United Kingdom and Mexico.

If EDP1815 is successfully developed and approved as a treatment for COVID-19, we believe that we could rapidly scale the manufacturing of EDP1815 to supply the drug at a reasonable cost. If approved and established as effective for early intervention, we expect that oral EDP1815 could also be useful in the outpatient setting to control the community impact of the COVID-19 pandemic. If the Phase 2 trials are successful in COVID-19, we plan to investigate EDP1815 as a potential therapy for other diseases, such as influenza infection, in which hyperinflammation and cytokine storm can play a key role.

EDP1867

EDP1867 is an inactivated investigational oral biologic being developed for the treatment of inflammatory diseases. EDP1867 was selected from a broad screen of single strains of microbes in *in vitro* cellular assays and *in vivo* models of inflammation. In preclinical studies EDP1867 was shown to resolve multiple pathways of inflammation. This observed activity suggests a number of possible initial clinical indications to pursue for EDP1867, including TH2-dependent inflammation, which underlies atopic diseases and a large spectrum of asthma. We initiated our first Phase 1b clinical trial of EDP1867 in healthy volunteers and patients with moderate atopic dermatitis in February of 2021 and expect to report interim data in the fourth quarter of 2021.

EDP2939

EDP2939 is an EV investigational oral biologic being developed for the treatment of inflammatory diseases. EDP2939 is the first EV product candidate we have nominated in our inflammation program and we anticipate initiation of clinical development in 2022.

Inflammation Preclinical Data

Each of our product candidates in our inflammation program have demonstrated the potential to simultaneously impact multiple pathways and associated cytokines in preclinical assays, suggesting that they may have broader applicability than individual cytokine-directed therapies. In addition, anti-inflammatory cytokines such as IL-10 and IL-27 can inhibit the production of pro-inflammatory cytokines. Certain of our product candidates induced increased production of IL-10 and IL-27 in preclinical assays. Importantly, pre-clinical experiments and human biomarker data from the EDP1815 Phase 1b clinical trial in patients with psoriasis, suggest that SINTAX medicines are inflammation resolving and are not immunosuppressive.

Inflammation Development Strategy

We selected mild-to-moderate psoriasis and atopic dermatitis, the most common type of eczema, as indications for first-in-human studies based upon our preclinical data, unmet 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 topical steroids, which either inadequately control inflammation, are not safe for long-term use, or are inconvenient and burdensome in application, leading to poor adherence and reduced efficacy in a real-world setting. 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 majority of eligible patients do not receive biologics. Many patients are uncomfortable with high-cost, injectable antibody therapies or with the toxicity concerns and monitoring requirements of systemic immunosuppressants. There is a large need across the spectrum of disease severity, and especially for midline, pre-biologic patients, for a safe and well-tolerated oral medicine that resolves the systemic inflammation that drives psoriasis and atopic dermatitis.

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 SINTAX medicines 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.

Oncology Portfolio

We are developing SINTAX medicines for the treatment of multiple cancer types.

EDP1908

In December 2020, we announced EDP1908 as our lead product candidate in oncology following presentation of preclinical data at the Society for Immunotherapy for Cancer meeting in November 2020. Preclinical data presented showed that orally administered EDP1908, an EV, resulted in superior tumor growth control versus either the parent microbial strain or anti-PD-1 therapy, with an observed dose-dependent reduction in tumor growth. We anticipate initiation of clinical development in 2022.

Preclinical data suggests that EDP1908 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 inhibitors. Research suggests that checkpoint inhibition prevents the downregulation of the immune system induced by tumors. In preclinical models, we observed that EDP1908 stimulated upregulation of the immune response to tumors. Oral administration of EDP1908 in preclinical mouse models resulted in robust, dose-dependent anti-tumor activity superior to that of anti-PD-1 using different immune mechanisms. The effects were at least comparable to those reported in the literature for intratumorally administered immune stimulators.

We believe that EDP1908, and possibly additional EV product candidates, have the potential to broaden the base of cancer immunotherapy and augment current standard-of-care therapies. Treatment with EDP1908 in syngeneic mice suggested a variety of potential effects on innate and adaptive immunity, including activated IFNγ-positive cytolytic and helper lymphocytes, dendritic cells, and interferon gamma-induced protein 10 (IP-10) in the tumor microenvironment. Fluorescent biodistribution analysis showed that EDP1908 was not detected outside the gastrointestinal tract. These data suggest that EDP1908 activated innate immunity locally on host immune cells in the gut and triggered distal immune responses within the tumor microenvironment, with no apparent adverse safety or tolerability issues. We believe that oral administration of EDP1908 has the potential to offer an improved safety profile compared to systemically - or intratumorally-administered immunotherapy agents as well as broader potential for combination regimens with existing therapies.

Manufacturing

We have developed proprietary methods for the manufacture of pharmacologically active whole microbe and EVs that are scalable and transferable to cGMP manufacturing facilities. Microbes are isolated, grown and purified in a manner analogous to the manufacture of pharmaceutical drugs. The whole microbe and EV manufacturing process produces drug substance in a powder form that makes our product 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 our product candidates. We expect that these controlled manufacturing processes and analytical methods will allow us to produce and release cGMP-compliant 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 use third-party contract manufacturing organizations (“CMOs”) for the production of materials for clinical studies. Our internal personnel have cGMP manufacturing experience to ensure efficient technology transfer and oversee the development and manufacturing activities

conducted by our CMOs. Our agreements with CMOs include confidentiality and intellectual property provisions to protect our proprietary rights to our SINTAX medicine candidates.

We expect our CMOs to meet manufacturing requirements and drug supply required by our clinical studies. In some instances, we have reserved resources from CMOs for the development and manufacture of our product 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 CMOs at the appropriate time. In anticipation of a possible near-term need for commercial supplies of EDP1815, we have established relationships with CMOs who have the capacity to rapidly scale the manufacturing of EDP1815.

Process development and manufacturing are critical for the development of whole microbe and EV product candidates. We believe our internal expertise and external partnerships have allowed us to address unique challenges associated with whole microbe and EV 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 SINTAX medicines address these three challenges. Many human commensals are strict anaerobes with no 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 robust manufacturing processes. We continue to optimize processes across a wide range of parameters in fermentation and formulation.

Our manufacturing processes consist of drug substance and drug product manufacturing. We have established expertise across all aspects of drug substance manufacturing 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.

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, and methods for patient selection created or identified from our ongoing development of our product candidates, as well as discoveries based on our proprietary platforms. 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 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 (the "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 March 5, 2021, our patent portfolio consisted of twelve issued U.S. patents, one European patent, one Singaporean patent, and 51 patent families, which include composition, method of use, formulation, and manufacturing process claims. Additionally, a Notice of Allowance has been received for one application in the United States. Of the U.S. patents in our portfolio, seven are owned by us, and five are exclusively licensed from the Mayo Clinic Foundation for Medical Education and Research, an affiliate of Mayo Clinic, (the "Mayo Clinic"). The European patent is owned by us, and the Singaporean patent is exclusively licensed from the University of Chicago. Of the patent families in our portfolio, 49 are owned by us, one is exclusively licensed to us from the University of Chicago and one is exclusively licensed to us from the Mayo Clinic.

The patent portfolio includes patents and applications covering the following:

- Formulation platforms in which applications that issue as a patent are expected to expire in 2038 to 2041.
- Manufacturing platforms in which applications that issue as a patent are expected to expire in 2041.
- Modality platforms in which applications that issue as a patent are expected to expire in 2038 to 2041.
- Inflammation portfolio:
    - EDP1815, consisting of five issued U.S. patents in-licensed from the Mayo Clinic, covering compositions and methods of use (the patents from the Mayo Clinic are expected to expire in 2030) and ten patent families we own directed to compositions, methods of use, formulations and manufacturing processes. Any applications claiming priority to these applications we own that issue as patents are expected to expire in 2040 to 2041;
    - EDP1867, consisting of six patent families we own directed to compositions, methods of use and formulations. Any applications claiming priority to these applications that issue as patents are expected to expire in 2039 and 2041; and
    - EDP2939, consisting of two patent families we own 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 2042.
- Oncology portfolio:
    - EDP1908, consisting of one patent family we own directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2041.

- An oral oncology platform exclusively licensed from the University of Chicago, consisting of 24 pending applications and one issued patent in Singapore. Patents in this family are expected to expire in 2036.

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 manufacturing agreements 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. 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 $0.5 million 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 expiration 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 the Mayo Clinic

In August 2017, we entered into an agreement with the 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 the 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 the 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 five issued U.S. patents. Issued claims cover compositions containing microbes from a specified species and methods of using these compositions to treat autoimmune and inflammatory diseases. EDP1815, one of our lead candidates in the inflammation program, contains the microbial strain licensed from the 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 the Mayo Clinic an upfront payment of $0.2 million. Beginning on the second anniversary of the effective date, we owe the 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. The Mayo Clinic is entitled to future clinical, approval and sales milestones. In addition, we have agreed to pay the Mayo Clinic future milestone payments totaling a maximum of $1.0 million upon achievement of specific development milestones and $56 million upon achievement of specific regulatory and commercial milestones.

The 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 the 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 sublicensees. We must obtain the Mayo Clinic's permission to grant any fully paid-up, royalty-free or exclusive sublicenses. We have no financial obligations to the Mayo Clinic related to sublicenses.

The Mayo Clinic has the responsibility to prepare, file, prosecute or abandon its patent rights. We may provide prior comment and advice to the Mayo Clinic and we are responsible for reimbursing the 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 the 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 ("Biose"). Under this agreement, Biose reserved manufacturing resources for the manufacture of our drug substance according to a specified schedule of manufacturing runs over a three-year period. We were 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 did not use committed manufacturing resources, we were required to pay Biose for these resources unless Biose was able to re-sell unused runs.

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

The term of the agreement was three years from the effective date. We had the right to terminate the agreement at any time with prior notice within a specified period to Biose, or if there was a change of control of Biose that adversely affected our interest. In the event that we terminated at will, we were 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 had the right to terminate if the other party

materially breached the agreement and did not cure such breach within a specified period or if either party became bankrupt or insolvent, or was dissolved or liquidated. The agreement expired on February 15, 2021 in accordance with its terms.

Sacco Collaboration Agreement

In July 2019, we entered into a collaboration agreement with Sacco S.r.l. ("Sacco"), an affiliate of one of our contract manufacturing organizations. Pursuant to the agreement, Sacco has agreed that it and its affiliates will, on an exclusive and worldwide basis for and on behalf of us, manufacture and supply single strain, non-genetically modified microbes intended for oral delivery or oral use in pharmaceutical products for a period of five years. Sacco and its affiliates may not manufacture and supply single strain, non-genetically modified microbes for oral delivery or oral use in pharmaceutical products for itself or other parties, with the exception of pre-existing products for pre-existing customers. Under the terms of the agreement, we have agreed to pay annual fees in the mid six digits to Sacco during the exclusivity period.

The agreement will remain in effect during the exclusivity period and may be terminated by (i) us upon written notice to Sacco if an independent third-party representative concludes following an audit that Sacco or its affiliates are not in compliance with the exclusivity provisions of the agreement, (ii) Sacco upon written notice to us if the manufacturing relationship has been inactive for a period of six consecutive months and there are no services scheduled to be performed or products scheduled to be supplied within the next six months, or (iii) either party in the event of a material breach of the agreement by the other party that remains uncured for 20 business days or the insolvency of the other party.

Cambrex Master Services Agreement

In December 2020, we entered into a development and clinical master services agreement with Halo Pharmaceutical, Inc. d/b/a Cambrex Whippany (“Cambrex”). Pursuant to the agreement, Cambrex has agreed that it will perform manufacturing process development, manufacturing, packaging, related analytical and storage services for us, as mutually agreed by the parties from time to time in work orders. Under the terms of the agreement, we have agreed to pay service fees to Cambrex and to reimburse Cambrex for purchasing excipients, components, consumables, raw materials, packaging and other items necessary for Cambrex to perform the services, as mutually agreed in a work order. We will supply active pharmaceutical ingredients to Cambrex to enable it to perform the services.

At our request or upon expiration or termination of the agreement, Cambrex has agreed to provide technical assistance to us, at our cost, to implement the technology transfer of the manufacturing processes developed by Cambrex under the agreement to us and of related analytical testing methodologies to us or a third party designated by us.

Unless earlier terminated, the agreement will expire on the later of (i) five years from the effective date or (ii) six months after the expiration or termination of all work orders. We may terminate the agreement or any work order at any time upon 60 days or 5 business days, respectively, prior written notice to Cambrex. In addition, either party may terminate for an uncured material default or if the other party becomes bankrupt or insolvent.

The agreement contains customary representations, warranties and covenants by Evelo, indemnification obligations of Evelo and Cambrex, and other obligations of the parties.

Collaboration

Merck-MSD International GmbH

In November 2018, we entered into a clinical trial collaboration agreement with Merck under which we are sponsoring and conducting 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.

In autoimmune or inflammatory diseases, we may be challenged by a wide range of competitors. In later, more severe stages of disease, the majority of competition will stem from companies marketing or developing injectable biologics and novel small molecule therapies, such as AbbVie Inc., Johnson & Johnson, Pfizer Inc, Novartis International A.G., Regeneron Pharmaceuticals, Inc. Sanofi S.A., Bristol-Myers Squibb, and Amgen Inc. Potentially competing mechanisms of action include TNF, IL-4, IL-17, IL-23, JAK, TYK2, and PDE4 inhibitors. Novel delivery of biologics, particularly via oral administration, and the entry of biosimilars will also add to competition within the therapeutic area. In more mild disease segments, we may face competition from companies marketing or developing topical formulations of small molecules for inflammatory skin diseases, including Pfizer Inc., Arcutis Biotherapeutics Inc., and Dermavant Sciences Ltd.

Significant competition exists in the immuno-oncology field, where we are developing product candidates. Although our SINTAX medicine 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 SINTAX medicines 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., Merck, Pfizer Inc., Regeneron Pharmaceuticals Inc.; and

- ***Cell therapy***: Bristol Myers Squibb, Gilead Sciences, Inc., and Novartis International A.G.

Government Regulation

Government Regulation in the United States

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 ("BLA") and licensure, which constitutes approval, by the FDA before being marketed in the United States.

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 ("GLP") requirements;
- submission to the FDA of an investigational new drug application ("IND") which must become effective before clinical trials in the United States may begin;
- approval by an institutional review board ("IRB"), or ethics committee at each clinical site before the clinical trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the product candidate for each proposed indication, conducted in accordance with the FDA's good clinical practice ("GCP") requirements;
- preparation and submission to the FDA of a BLA after completion of all pivotal trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product candidate is produced to assess compliance with cGMP regulations, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of the BLA prior to any commercial marketing, sale or shipment of the product.

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. An IND is a request for authorization from the FDA to administer an investigational new drug to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical trials. 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. 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 clinical trials 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.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. 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 IRB for each investigator site proposing to participate in a clinical trial must also review and approve the clinical trial and its informed consent form 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 or that the trial is unlikely to meet its stated objectives. Some clinical trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

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

- *Phase 1* - the investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These trials 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* - the investigational product is administered 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. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- *Phase 3* - the investigational product is administered 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. Concurrent with clinical trials, biotechnology 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.

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.

BLA Submission and FDA Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, 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 BLA must include all relevant data available from preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee unless a waiver is granted, and the sponsor of an approved BLA is also subject to an annual program fee. 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, 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 BLAs designated 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. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy ("REMS"), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. 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 of the product based on the results of these post-marketing studies.

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.

For example, a product candidate 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 applies to the combination of the product candidate and the specific indication for which it is being studied. 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 FDA may review portions of the marketing application before the sponsor submits the complete application, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

In addition, a product candidate 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 product candidate 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 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 candidate submitted to the FDA for approval, including a product candidate 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 BLA is eligible for Priority Review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive 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. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing clinical trials or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Accelerated Approval do not change the standards for approval but may expedite the development or review process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

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 record keeping, 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 pursuant to FDA approvals remain 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 BLA sponsors and their 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, untitled 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;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; 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. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. 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 "ACA", the Biologics Price Competition and Innovation Act (the "BPCIA") established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway provides legal authority for the FDA to review and approve biosimilar biologics based on their similarity to an existing brand product, referred to as a reference product, including the possible designation of a biosimilar as interchangeable with a brand product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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 a reference product 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. 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, a biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric clinical trial in accordance with an FDA-issued "Written Request" for such a trial. The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

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 drugs and biologics. For instance, in the European Economic Area (the "EEA") (comprised of the 27 European Union Member States plus Iceland, Liechtenstein and Norway) medicinal products must be authorized for marketing by using either a centralized authorization procedure or national authorization procedures.

Centralized procedure-Under the centralized procedure, following the opining of the European Medicines Agency (“EMA”) Committee for Medicinal Products for Human Use ("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 (the "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 European Union during a period of eight years from the date on which the reference product was first authorized in the European Union. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the European Union until ten years have elapsed from the initial authorization of the reference product in the European Union. 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 European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition. 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 European Union 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 and the related national implementing provisions of the individual European Union Member States govern the system for the approval of clinical trials in the European Union (the "EU"). Under this system, an applicant must obtain prior approval from the competent national authority of the 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, or 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 Member State and further detailed in applicable guidance documents.

In April 2014, a new Clinical Trials Regulation, (EU) No 536/2014, (the "Clinical Trials Regulation") was adopted. The Clinical Trial Regulation is expected to enter into force by the end of 2021 but this could be delayed. The Clinical Trials Regulation is directly applicable in all the European Union Member States and will supersede the Clinical Trials Directive 2001/20/EC. The 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 "European Union 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 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 Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

Other Healthcare Laws

Pharmaceutical manufacturers are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, the U.S. federal anti-kickback, fraud and abuse, false claims, consumer fraud, pricing reporting, data privacy and security, and transparency laws and regulations related to payments and other transfer of value made to physicians and other healthcare providers, as well as similar state and foreign laws in the jurisdictions outside the U.S. Violation of any such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

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 which third-party payors and governments 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.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. The ACA substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; creates a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. By way of example, in 2017, Congress enacted the Tax Act, which eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a Texas U.S. District Court Judge ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal or replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year, which will remain in effect through 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, absent additional congressional action. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

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 $69.6 million and $63.1 million for the years ended December 31, 2020 and 2019 respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development in 2021 as we continue to advance our product candidates through clinical development.

Employees

As of March 5, 2021, we had 90 full-time employees, including 40 with M.D. or Ph.D. degrees. Of those full-time employees, 67 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 relationships 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 on Form 10-K, and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We file electronically with the U.S. Securities and Exchange Commission (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. Our net loss was $93.7 million and $85.5 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $292.5 million. Through December 31, 2020, we have financed our operations through proceeds from equity offerings of our common stock, private placements of our preferred stock and borrowings under loan and security agreements. We have devoted substantially all of our financial resources and efforts to developing our platform, identifying potential product candidates and conducting preclinical and clinical trials. We are in the early stages of developing our product candidates, and we have not completed the development of any product candidate. 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 initiate more and larger clinical trials of our product candidates;
- seek to enhance our 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 operations as 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 FDA or the EMA or other regulatory authorities to perform preclinical studies or clinical trials 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.

During the first quarter of 2021 we raised net proceeds of $82.2 million from the issuance of common stock exclusive of certain other fees payable by us. We expect that our existing cash and cash equivalents as of

December 31, 2020, together with the net proceeds raised in the first quarter of 2021 from the issuance of our common stock will enable us to fund our planned operating expenses and capital expenditure requirements into the third quarter of 2022. 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 EDP1815, EDP1867, EDP2939 and EDP1908;
- 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. Additionally, market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. 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 or cease our operations. 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 ("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 have not yet demonstrated our ability to successfully complete a Phase 2 clinical trial or a Phase 3 or other pivotal clinical trial, obtain regulatory approvals to commercialize a product, 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 agreements 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.

Our loan and security agreement dated July 19, 2019 (as amended, the “2019 Credit Facility”) with K2 Health Ventures LLC ("K2HV") for $45.0 million is secured by a lien covering substantially all of our personal property, excluding intellectual property. Contemporaneous with the closing of the first tranche of funding under the 2019 Credit Facility, we repaid the entire $15.0 million loan balance outstanding under our prior loan and security agreement with Pacific Western Bank. As of December 31, 2020, the outstanding principal balance under the 2019 Credit Facility was $30.0 million, resulting from the closing of the first tranche of funding which occurred on July 19, 2019 and second tranche of funding which occurred on July 14, 2020. The third tranche expired on January 15, 2021. The 2019 Credit Facility contains customary representations, warranties, affirmative and negative covenants and events of default applicable to us and our subsidiaries.

If we default under the 2019 Credit Facility, K2HV may accelerate all of our repayment obligations and exercise all of their rights and remedies under the 2019 Credit Facility and applicable law, 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. K2HV could declare a default upon the occurrence of any event, among others, that they interpret as a material adverse effect or a change of control as delineated under the 2019 Credit Facility, payment defaults, or breaches of covenants 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 technology platform to harness the small intestinal axis, with an initial focus on developing therapies in immunology, specifically inflammatory diseases, and also oncology. While we believe our preclinical studies and clinical trials 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 oral biologics, 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 CMOs, 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 an 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 designed to act on cells in the small intestine to produce systemic therapeutic effects with limited systemic exposure. This biological interaction between the small intestine 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 EDP1815, EDP1867, EDP2939 and EDP1908 have the potential to work by modulating systemic responses via interactions with cells in the small intestine. 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 activity at the site of disease. This may be because our understanding of the mechanisms of the small intestine do not work in humans the way we believe they do. Despite there being strong academic literature to support the concept and our observations in preclinical studies in mice, these principles and the ability to use pharmaceutical preparations derived from single strains of microbes to modulate the immune system and other systems has not yet been proven in humans.

Our product candidates are an unproven approach to therapeutic intervention.

All of our product candidates are based on targeting SINTAX. 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 product

candidates 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 singe strains of microbes, 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 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 EDP1815, EDP1867, EDP2939 and EDP1908 are designed to work by modulating the immune system. While we have observed in preclinical studies that our product candidates have limited systemic exposure, the pharmacological immune effects we induce are systemic. Systemic immunomodulation from taking our product candidates 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 product candidates 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 bacteria. 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 our product candidates. 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, EU Competent Authorities or comparable foreign regulatory authorities, the IRBs at the institutions in which our clinical trials are conducted, or ethics committees, or the data safety monitoring board 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 our product candidates, and may negatively impact regulatory approval of, or demand for, our potential products.

Our 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 therapeutic microbes. 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 therapeutic microbes, 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 product candidates require that we manufacture from master cell banks ("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. 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 clinical trials, investigational drug products are being delivered in a capsule for targeted release in the small intestine. This formulation has not previously been clinically tested, nor are we able to dose mice with a capsule for targeted release in the small intestine. Our ongoing 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 trials, and we cannot be certain that we will not face similar setbacks.

The results from early clinical trials of product candidates may not predict the results that will be obtained in subsequent subjects or in subsequent human clinical trials of that product candidate. There can be no assurance that this trial will ultimately be successful or support further clinical advancement of this product candidate.

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 with respect to biological products in the United States, to market any of our product candidates. Requirements for us to conduct more clinical trials than we anticipate for a given product candidate 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 CROs, CMOs and other 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.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States, such as the EMA. We are developing our product candidates, EDP1815 and EDP1867, to treat inflammatory diseases, beginning with psoriasis and atopic dermatitis. There are a limited number of patients from which to draw for clinical trials.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the trial 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.

The COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials, and finances.

In 2020, a strain of novel coronavirus disease, COVID-19, was declared a pandemic and spread across the world, including throughout the United States, Europe and Asia. The pandemic and government measures taken in response have had and continue to have a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19, we have adopted and continue to employ several temporary business practices, including telecommuting and staggered work shifts in our laboratories, to protect our employees while continuing business operations. In addition, due to the COVID-19 pandemic, enrollment of new patients into, and the retention of existing patients in, our on-going clinical trials have been and continue to be impacted, due primarily to lower patient participation. As a result of the COVID-19 pandemic, we may continue to experience disruptions and face new disruptions that could severely impact our business, preclinical studies and clinical trials, and finances including:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruptions in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;

- interruptions of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by governments, employers and others or interruption of clinical trial subject visits and study procedures (such as skin biopsies that are deemed non-essential activities), which may impact the integrity of subject data and clinical trials endpoints;

- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;

- interruptions or delays in the operations of the FDA and EMA, which may impact review and approval timelines;

- interruptions of, or delays in receiving, supplies of our product candidates from our CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;

- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;

- refusal of the FDA to accept data from clinical trials in affected geographies;

- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and

- delays or difficulties with equity offerings due to disruptions and uncertainties in securities markets.

The COVID-19 pandemic continues to evolve. The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the COVID-19 pandemic could materially affect our business.

We may conduct clinical trials for our product candidates in sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We may in the future choose to conduct clinical trials outside the United States for our product candidates. Although the FDA may accept data from clinical trials conducted outside the United States not conducted under IND, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be conducted in accordance with GCP, and the FDA must also be able to validate the data from the study through an on-site inspection if necessary. In general, the patient population for any clinical trials conducted outside of the United States must be representative of the population for which we intend to seek approval for the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials of our product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

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

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings

and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

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

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

If 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, by the EU legislative bodies, 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 clinical trials than those conducted by a sponsor, especially for novel product candidates such as our product candidates. 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 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 SINTAX medicines and their interactions with cells in the small intestine 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 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.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the global pandemic of COVID-19, on March 10, 2020 the FDA temporarily postponed most foreign inspections of manufacturing facilities and products. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to our Dependence on Third Parties and Manufacturing

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 CROs, clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials.

Our reliance on these third parties for research and development activities will reduce our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and welfare of trial participants are protected. Other countries' regulatory agencies also have requirements for clinical trials with which we must comply. We also 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 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 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. Some of 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 sources of clinical supplies for both drug substance and drug 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. Moreover, as a result of the COVID-19 pandemic, third-party manufacturers may be affected, which could disrupt their activities and, as a result, we could face difficulties and delays in the manufacture of our product candidates, which may negatively affect our preclinical and clinical development activities.

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 clinical trials, 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, 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 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 coverage and an adequate level of reimbursement for our products by third-party payors. 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. In addition, reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. 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 BPCIA 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.

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;
- 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. 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;
- the federal Health Insurance Portability and Accountability Act of 1996 ("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, certain other healthcare professionals beginning in 2022, and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members; manufacturers are required to submit reports to the government by the 90th day of each calendar year;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to our business practices, including but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, pricing information or marketing expenditures; and

- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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, the ACA was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA 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;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;

- extension of manufacturers' Medicaid rebate liability;

- expansion of eligibility criteria for Medicaid programs;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. For example, the Tax Cuts and Jobs Acts (the "TCJA") was enacted, which, among other things, removed penalties for not complying with the individual mandate to carry health insurance. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unclear how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal or replace the ACA will affect the law or our business

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, 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 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. 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.

Although we have numerous patent applications pending, 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 issued 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 or may develop 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, the standards that the USPTO and other jurisdictions use to grant patents are not always applied predictably or uniformly and can change. Similarly, the ultimate degree of protection that will be afforded to biotechnology inventions, including ours, in the United States and other jurisdictions, remains uncertain and is dependent upon the scope of the protection decided upon by patent offices, courts, and lawmakers.

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 issued 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 the patent

laws and/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 USPTO or become involved in derivation, reexamination, inter partes review, ex partes reexamination, 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 February 2021, the European Patent Office informed us of a notice of opposition by a third party for a patent issued to us. The patent at issue does not relate to our current product candidates.

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 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. 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 patent law in the United States and other jurisdictions 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. Patent reform legislation in the United States, including the Leahy-Smith America Invents Act (the" Leahy-Smith Act"), signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These included provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet 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 make it more difficult to obtain patent protection for our inventions and 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 harm our business, results of operations 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. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Supreme 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. 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. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Europe's planned Unified Patent Court may particularly present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court.

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.

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 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 some 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 (e.g. the COVID-19 pandemic), 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, or other anti-bribery and anti-corruption laws.

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

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the European Union and ratified a trade and cooperation agreement governing its future relationship with the European Union. The agreement, which is being applied provisionally from January 1, 2021 until it is ratified by the European Parliament and the Council of the European Union, addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. Because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the European Union as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

These developments, or the perception that any related developments could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict our access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of common stock.

The uncertainty regarding new or modified arrangements between the United Kingdom and other countries following the withdrawal 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 us 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.

Risks associated with data privacy issues, including evolving laws, regulations and associated compliance efforts, may adversely impact our business and financial results.

Legislation in various countries around the world with regard to cybersecurity, privacy and data protection is rapidly expanding and creating a complex compliance environment. We are 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. By way of example, the General Data Protection Regulation (the “GDPR”), which became effective in May 2018, has caused more stringent data protection requirements in the EU and the EEA. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects how their personal data is to be used; imposes limitations on retention of personal data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data

processing activities. We are subject to the supervision of local data protection authorities in those EU jurisdictions where we have business operations or are otherwise subject to the GDPR. Certain breaches of the GDPR requirements could result in substantial fines, which can be up to four percent of worldwide revenue or 20 million Euros, whichever is greater. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, as well as potential civil claims, including class action type litigation where individuals suffered harm. Relatedly, following the United Kingdom's withdrawal from the EEA and the EU, and the expiration of the transition period, from January 1, 2021, companies have to comply with both the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. On January 1, 2021, the United Kingdom became a third country for the purposes of the GDPR. Similarly, California has enacted the California Consumer Privacy Act (the "CCPA"), which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Additionally, the California Privacy Rights Act (the "CPRA") was recently enacted in California. The CPRA will impose additional data protection obligations on covered companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. The CCPA and CPRA may increase our compliance costs and potential liability, and similar laws have been proposed at the federal level and in other states. These laws and regulations are constantly evolving and may be interpreted, applied, created, or amended in a manner that could seriously harm 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;

- speculative trading in and short sales of our stock, as well as trading phenomena such as the “short squeeze”;

- 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 December 31, 2020, our executive officers, directors and stockholders who own more than 5% of our outstanding common stock and their respective affiliates hold, in the aggregate, shares representing approximately 65% of our outstanding voting stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. 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. Moreover, holders of an aggregate of approximately 18.4 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 Jumpstart Our Business Startups Act of 2012, (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, or December 31, 2023, (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;

- 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 of the Sarbanes-Oxley Act of 2002 ("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.

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 tax credits to offset future taxable income or tax liabilities may be subject to certain limitations.

As of December 31, 2020, we had approximately $133.7 million and $129.4 million of Federal and state Net Operating Losses ("NOLs"), respectively. The Federal NOLs include $49.9 million which expire at various dates through 2037, and $83.8 million which carryforward indefinitely. The state NOLs expire at various dates through 2040. As of December 31, 2020, we had federal and state research credits of $5.0 million and $2.6 million, respectively, which expire at various dates through 2040. A portion of these NOLs and the tax credit carryforwards could expire unused and be unavailable to offset future income or tax liabilities, respectively. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs or tax credits to offset future taxable income or tax liabilities. 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 tax 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 tax credits may also be impaired under state law. Our ability to utilize our NOLs or tax credits is also conditioned upon our attaining profitability and generating U.S. federal and state taxable income. We have incurred significant net losses since our inception; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOLs or tax credits. Even if we were to generate net taxable income, the deductibility of federal NOLs generated after December 31, 2017 is limited to 80% of taxable income with respect to taxable years beginning after December 31, 2020. Accordingly, we may not be able to utilize a material portion of our NOLs or tax credits, and we may be required to pay U.S. federal income taxes due to the 80% limitation on deductibility of NOLs even if we have NOLs that are otherwise available for use.

General Risk Factors

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 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, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are 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, 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 preclinical studies or clinical trials 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.

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 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

From time to time, we may be involved in claims and proceedings arising in the course of our business. The outcome of any such claim or proceeding, regardless of the merits, is inherently uncertain. We are not subject to any material legal proceedings.

On February 12, 2021, the European Patent Office issued a Communication of a Notice of Opposition for European patent EP 3223834, which is held by us. We are currently evaluating the options available to us and deciding next steps with respect to this matter. The patent at issue does not relate to any of our current product candidates, and receipt of this communication and/or any subsequent proceeding is not expected to affect any of our current development plans.

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 is traded on the Nasdaq Global Select Market under the symbol “EVLO.”

Holders of Record

As of March 5, 2021, there were approximately 31 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.

Item 6. Selected Financial Data

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, and are not required to provide this information.

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 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 important factors, including without limitation those set forth under "Summary Risk Factors" and 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." A discussion of the year ended December 31, 2019 compared to the year ended December 31, 2018, as well as a discussion of our 2018 fiscal year, specifically, has been reported previously in our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on February 14, 2020, under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Overview

We are discovering and developing a new class of oral biologics that are intended to act on cells in the small intestine to produce therapeutic effects throughout the body. The target cells in the small intestine play a central role in governing human immune, metabolic and neurological systems. We refer to this biology as the small intestinal axis, or SINTAX™. We have built a platform to discover and develop novel oral medicines which target the small intestinal axis. By harnessing the small intestinal axis, we have the potential to transform healthcare via medicines that have the potential to be effective, safe, convenient and affordable and to thereby treat patients at all stages of diseases and to treat patients globally.

Our first product candidates are orally delivered pharmaceutical preparations of naturally occurring, specific single strains of microbes. In preclinical models, our product candidates engaged immune cells in the small intestine and drove changes in systemic biology without any observed systemic exposure. We have observed in early clinical trials and preclinical studies that our approach led to modulated immune responses throughout the body by acting on the small intestinal axis. Our most advanced product candidate, EDP1815 is being developed for the treatment of inflammatory diseases and the hyperinflammatory response associated with COVID-19. Additional product candidates include EDP1867 and EDP2939 for the treatment of inflammatory disease and EDP1908 for the treatment of cancer.

Impact of COVID-19

On March 11, 2020, the WHO declared the COVID-19 outbreak a pandemic. The outbreak has resulted in governments around the world implementing stringent measures to help control the spread of the virus, including quarantines, "shelter in place" and "stay at home" orders, travel restrictions, business closures and curtailments, and school closures.

The COVID-19 pandemic has had, and for an extended period of time is expected to have, negative impacts on our operations and supply chain. Our ability to continue to operate without any significant negative impacts will, in part, depend on our ability to protect our employees and our supply chain. We have endeavored to follow recommended actions of government and health authorities to protect our employees with particular measures in place for those working in our laboratories, such as staggered work shifts and flexible schedules, and telecommuting for office workers. We are working with our CMOs to minimize delays and disruptions to scheduled manufacturing batch runs for our product candidates and to ensure conformity to product specifications.

The COVID-19 pandemic has impacted and continues to impact our enrollment of new patients into, and the retention of existing patients in, our ongoing clinical trials, due primarily to lower patient participation. The pandemic likely will impact enrollment and retention of patients in new and existing clinical trials. We continue to recruit individuals in line with the local and national guidelines of the clinical research sites. We are keeping in close contact with our CROs and clinical sites to provide support and guidance to ensure the safety of the patients in our clinical trials. We have prioritized our drug supply operations to secure the re-supply of patients currently enrolled in our clinical trials.

The extent to which the COVID-19 pandemic impacts our business and finances will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, travel restrictions and social distancing in the United States, the United Kingdom and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States, the United Kingdom and other countries to contain and treat the disease. See “Risk Factors — The COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials and finances.” in Part I, Item 1A of this Annually Report on Form 10-K.

Clinical Programs

We are advancing SINTAX medicines 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 multiple product candidates into clinical trials for a range of diseases.

EDP1815, a whole-microbe candidate for inflammatory diseases

EDP1815 is in clinical development for psoriasis, atopic dermatitis and COVID-19.

Psoriasis

Based on previously reported positive clinical data in two cohorts of individuals with mild and moderate psoriasis in a Phase 1b clinical trial, we have advanced EDP1815 into a Phase 2 dose ranging trial, evaluating three doses of A' EDP1815 in capsules versus placebo in approximately 225 individuals with mild and moderate psoriasis. The primary endpoint of the trial is the mean reduction in PASI score at 16 weeks. Other clinical measures of psoriasis are also being evaluated. We initiated the Phase 2 clinical trial in October 2020 and have completed enrollment and, therefore, now plan to report topline data in the third quarter of 2021. Clinical data from this trial, if positive, may enable us to advance directly into Phase 3 registrational trials, subject to end of Phase 2 discussions with regulatory agencies.

We intend to evaluate EDP1815 in additional inflammatory disease indications, depending on the results from the Phase 2 trial. Potential indications include psoriatic arthritis, axial spondylarthritis and rheumatoid arthritis.

Atopic Dermatitis

In November 2018, we initiated our ongoing Phase 1b double-blind placebo-controlled dose-escalating safety and tolerability trial of EDP1815 in healthy volunteers and individuals with mild and moderate psoriasis or atopic dermatitis. The primary endpoint of the phase 1b trial is safety and tolerability.

In December 2020 and January 2021, we reported positive clinical data from a cohort of patients with mild and moderate atopic dermatitis (n=24), randomized 2:1 to receive EDP1815 in capsules or placebo for 56 days. Atopic dermatitis is the most common type of eczema. EDP1815 was well-tolerated with no treatment-related adverse events of moderate or severe intensity, and no serious adverse events. Secondary endpoints included a range of established markers of clinical efficacy in atopic dermatitis, such EASI, IGA* BSA, and SCORAD scores.

The data showed consistent improvements in percentage change from baseline compared to placebo for all three clinical scores: EASI, IGA*BSA, and SCORAD. In addition, 7 out of 16 (44%) patients treated with EDP1815 achieved an outcome of a 50% improvement from baseline in EASI score by day 70, compared with 0% in the placebo group, showing sustained improvement in those patients responding to EDP1815.

In addition to physician-reported clinical outcomes, this trial also assessed patient-reported outcomes. Treatment with EDP1815 resulted in clinically meaningful improvement in the DLQI and POEM. These patient-reported outcomes capture the important impact of the disease on patients, including the domains of itch and sleep, both of which saw improvements in patients receiving EDP1815 in the trial. All five measures of itch within the Pruritus-NRS, SCORAD, POEM, and DLQI showed greater improvements in the treated group at day 56 compared with placebo. These results provide further evidence that modulating SINTAX can drive significant clinical benefit without the need for systemic exposure.

Subject to regulatory approval, we anticipate initiation of a Phase 2 trial of EDP1815 in atopic dermatitis in the third quarter of 2021.

COVID-19

EDP1815 is being evaluated in two ongoing clinical trials for the treatment of hospitalized COVID-19 patients. The first is a Phase 2 double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of EDP1815 for the treatment of individuals diagnosed with COVID-19 early in the course of their disease. The clinical trial initially will evaluate 60 individuals to determine if early intervention with EDP1815 can prevent the progression of COVID-19 symptoms and the development of COVID-Related complications. Individuals who have presented at the emergency room within the last 36 hours and tested positive for SARS-CoV-2 are randomized 1:1 to receive the capsule formulation of EDP1815 targeted for release in the small intestine or placebo for 14 days, along with the standard of care. The primary endpoint is reduced requirements for oxygen therapy, as measured by the ratio of oxygen saturation (SpO2) / fraction of inspired oxygen (FiO2). Key secondary endpoints include total symptom duration, progression along the WHO scale of disease severity, and mortality. The trial is led by Reynold A. Panettieri, Jr., M.D., Vice Chancellor for Translational Medicine and Science at Rutgers Biomedical and Health Sciences and Professor of Medicine at Rutgers Robert Wood Johnson Medical School.

EDP1815 is also included as a treatment arm in the TACTIC-E clinical trial. TACTIC-E is a Phase 2/3 randomized trial, sponsored by Cambridge University Hospitals NHS Foundation Trust, that is expected to evaluate up to 469 patients per arm at Addenbrooke's Hospital and other leading clinical centers in the United Kingdom and select international sites. The trial is investigating the safety and efficacy of certain experimental therapies in the prevention and treatment of life-threatening complications associated with COVID-19 in hospitalized individuals at early stages of the disease. The trial is enrolling individuals with COVID-19 who have identified risk factors for developing severe complications and are at risk of progression to the intensive care unit or death. The primary outcome measure of the trial is time to incidence (up to day 14) of any one of the following: death, mechanical ventilation, extracorporeal membrane oxygenation, cardiovascular organ support, renal failure, hemofiltration or dialysis. Secondary outcome measures include duration of stay in hospital, duration of oxygen therapy, changes in biomarkers associated with COVID-19 progression, and time to clinical improvement.

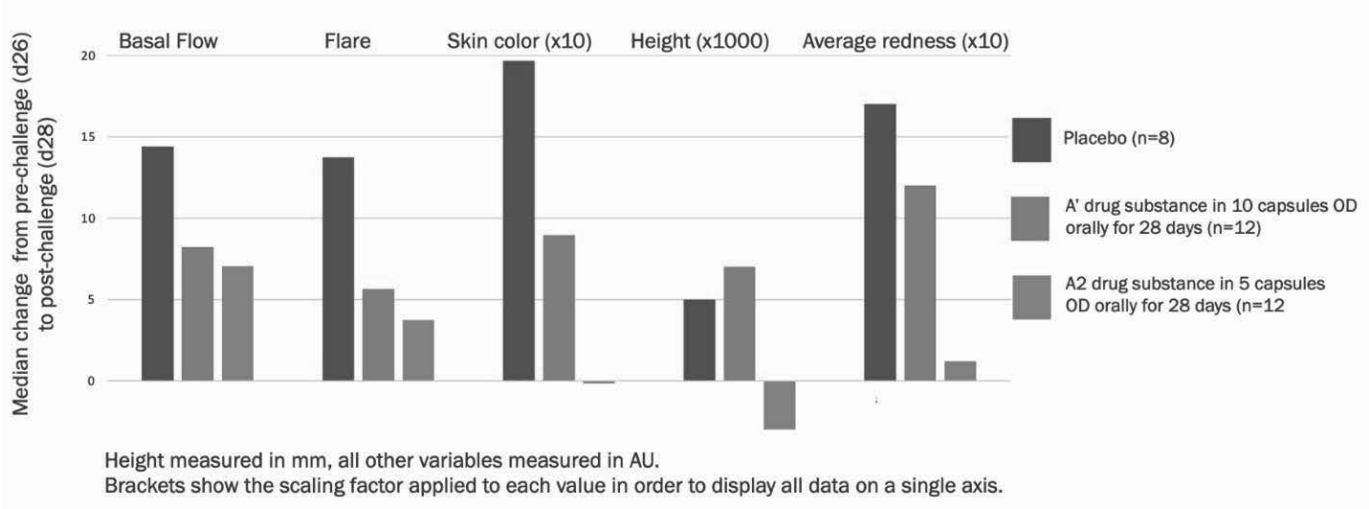
As a result of the varying infection rates and resulting hospitalizations that have occurred with the pandemic, we experienced slower than expected enrollment early on in both trials and now expect to report data from the clinical trial conducted at the Robert Wood Johnson University Hospital and interim safety data and futility analysis from TACTIC-E in the second quarter of 2021. In order to expedite patient recruitment and expand access to potential therapies for COVID-19, new trial sites have been opened for TACTIC-E, including in the United Kingdom and Mexico.

Human Experimental Model of Inflammation

In addition to testing our product candidates in patients with inflammatory disease, we also have employed a human experimental model of inflammation in healthy volunteers. This model is very similar in design to a standard preclinical model of T cell driven inflammation. We have recently used this model to test two different concentrations of EDP1815 to investigate the relative effectiveness of the different concentrations. A total of 32 volunteers were enrolled into the trial and treated with either EDP1815 (n=12 per formulation) or placebo (n=4 per formulation) daily for 28 days. The participants were immunized with an antigen used in preclinical inflammation experiments. After 28 days of daily oral dosing with EDP1815 or placebo, the participants were given a skin challenge with the same antigen, which causes measurable skin inflammation a day later. Inflammation was determined by measuring five parameters in the skin at the challenge site.

The increased concentration of drug results from improvements made in the commercial-scale manufacturing process, referred to as A2. This is the same active drug at four times the concentration compared to a prior manufacturing process, referred to as A'. Twelve participants were dosed with A' EDP1815. Another 12 participants were given the higher concentration A2 EDP185. Eight participants who received a placebo were divided between the two treatment groups. The results are in the figure below.

A2 EDP1815 is more effective than A' at same total dose in human experimental model of inflammation



The higher concentration A2, given in fewer capsules, resulted in numerically superior reductions across the full range of skin scores compared to A' and placebo. A2 and A' were given at the same total daily dose of drug. These results are consistent with preclinical data that showed increased drug concentration resulted in increased activity. This is a key advance in our understanding of how to get more benefit from SINTAX medicine candidates. We plan to evaluate tablets and capsules containing the higher concentration A2 EDP1815 in patients with psoriasis in our on-going Phase 1b trial, and expect to report data in the third quarter of 2021. Results from the Phase 1b trial and our on-going Phase 2 trial in psoriasis will position us to go forward into Phase 3 trials with an optimized dose and formulation of EDP1815, which may further improve on the positive results already seen.

EDP1867- a whole-microbe candidate for inflammatory diseases

EDP1867 is an inactivated investigational oral biologic being developed for the treatment of inflammatory diseases. EDP1867 was selected from a broad screen of single strains of microbes in *in vitro* cellular assays and *in vivo* models of inflammation. In preclinical studies EDP1867 was shown to resolve multiple pathways of inflammation. This observed activity suggests a number of possible initial clinical indications for EDP1867, including TH2-dependent inflammation which underlies atopic diseases and a large spectrum of asthma. We initiated our first Phase 1b clinical trial of EDP1867 in healthy volunteers and patients with moderate atopic dermatitis in February of 2021 and expect to report interim data in the fourth quarter of 2021.

EDP2939- an extracellular vesicle (EV) candidate for inflammatory diseases

EDP2939 is an EV investigational oral biologic being developed for the treatment of inflammatory diseases. EDP2939 is the first EV product candidate we have nominated in our inflammation program and we anticipate initiation of clinical development in 2022.

EDP1908- an EV candidate for oncology

In December 2020, we announced EDP1908 as our lead candidate in oncology following presentation of preclinical data at the Society for Immunotherapy for Cancer meeting in November 2020. Preclinical data presented showed that orally administered EDP1908, an EV, resulted in superior tumor growth control versus the parent microbial strain or anti-PD-1 therapy, with an observed dose-dependent reduction in tumor growth. We anticipate initiation of clinical development in 2022.

Financing

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 loan and security agreements with financial institutions.

Through December 31, 2020, we have received gross proceeds of $332.0 million through the issuance of our common stock, convertible preferred stock and borrowings under our loan and security agreements.

On July 19, 2019 we entered into a loan and security agreement, as amended, with K2HV providing for up to $45.0 million in potential debt financing, the proceeds of which were used to prepay our entire existing outstanding loan balance, and additional amounts are intended for the advancement of our research and development activities related to our pipeline of oral biologics and for general corporate purposes. Under terms of the 2019 Credit Facility, the aggregate principal amount of $45.0 million was available in three tranches of term loans of $20.0 million, $10.0 million, and $15.0 million, respectively. At closing on July 19, 2019, we borrowed $20.0 million, representing the first tranche under the 2019 Credit Facility. On July 14, 2020, we drew down the second tranche of $10.0 million and availability of the third tranche expired on January 15, 2021. Interest on the outstanding loan balance accrues at a variable rate equal to the greater of (i) 8.65% and (ii) the prime rate as published in the Wall Street Journal, plus 3.15%. We are required to make monthly interest-only payments through February 2022. Subsequent to the interest-only period, we are required to make equal monthly principal payments plus any accrued interest until the loans mature in August 2024. Upon final payment or prepayment of the loans, we are required to pay a final payment equal to 4.3% of the loans borrowed.

In June 2020, we sold 13,800,000 shares of our common stock in an underwritten public offering at a public offering price of $3.75 per share, for gross proceeds of $51.8 million and net proceeds of $48.4 million, after deducting underwriting discounts and commission and other offering expenses payable by us.

For the year ended December 31, 2020, pursuant to the June 2019 sales agreement with Cowen and Company, LLC, we sold 1,232,131 shares of our common stock, in “at-the-market” offerings under a registration statement on Form S-3 that we previously filed with the SEC with offering prices ranging between $4.25 to $11.15 per share for gross proceeds of $6.8 million and net proceeds of $6.6 million, after deducting commission and other offering expenses payable by us. In January 2021, we issued 139,734 additional shares of our common stock with offering prices ranging between of $12.54 and $13.17 per share for gross proceeds of $1.8 million and net proceeds of $1.7 million, after deducting commission and other offering expenses payable by us.

On February 2, 2021, we sold 5,175,000 shares of our common stock in an underwritten public offering at a public offering price of $15.00 per share, including the underwriters' exercise of their option to purchase 675,000 shares to cover over-allotment, generating gross proceeds of $77.6 million and net proceeds of $73.0 million, after deducting underwriting discounts and commissions, exclusive of other offering expenses payable by us.

On January 28, 2021, we entered into a stock purchase agreement with ALJ Health Care & Life Sciences Company Limited ("ALJ"), pursuant to which on February 2, 2021, ALJ purchased $7.5 million of our common stock in a private placement at a purchase price of $15.00 per share. The sale of these 500,000 shares was not registered under the Securities Act.

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, 2020 and 2019 our net loss was $93.7 million and $85.5 million, respectively. As of December 31, 2020, we had an accumulated deficit of $292.5 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 clinical trials for EDP1815 and EDP1867;
- initiate additional clinical trials for EDP1815;
- initiate or advance the clinical development of additional 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, 2020, our principal source of liquidity is cash and cash equivalents, which totaled approximately $68.9 million. During the first quarter of 2021 we raised net proceeds of $82.2 million from the issuance of common stock exclusive of certain other fees payable by us. We expect that our existing cash and cash equivalents as of December 31, 2020, together with the net proceeds raised in the first quarter of 2021 from the issuance of our common stock, will enable us to fund our planned operating expenses and capital expenditure requirements into the third quarter of 2022. 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 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 and develop the first set of clinical assets. Our platform and program expenses consist principally of costs, such as preclinical research, process development research, clinical and preclinical manufacturing activity costs, clinical development costs, licensing expense as well as an allocation of certain indirect costs, facility and office related expenses. 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 EDP1815 and EDP1867, initiate additional clinical trials of other product candidates, including EDP2939 and EDP1908, 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 IND-enabling toxicology studies;
- our ability to establish and maintain agreements with CMOs 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 (Expense) Income, 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 (Expense) Income, Net

For the year ended December 31, 2020, other income (expense), net primarily consists of foreign currency gains and government grants related to our operations in the United Kingdom.

Income Taxes

Income tax expense primarily relates to tax expense at our UK subsidiary.

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, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2020	2019	
Operating expenses:			
Research and development	$ 69,616	$ 63,128	$ 6,488
General and administrative	22,270	23,229	(959)
Total operating expenses	91,886	86,357	5,529
Loss from operations	(91,886)	(86,357)	(5,529)
Other (expense) income:			
Interest (expense) income, net	(2,109)	1,049	(3,158)
Other income, net	738	26	712
Other (expense) income, net	(1,371)	1,075	(2,446)
Net loss before income taxes	(93,257)	(85,282)	(7,975)
Income tax expense	(409)	(190)	(219)
Net loss	$ (93,666)	$ (85,472)	$ (8,194)

Research and Development Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2020	2019	
Platform expenses	$ 11,487	$ 10,468	$ 1,019
Inflammation programs	30,467	25,161	5,306
Oncology programs	5,487	9,226	(3,739)
Research and development personnel costs (including stock-based compensation)	22,175	18,273	3,902
Total research and development expenses	$ 69,616	$ 63,128	$ 6,488

Research and development expenses were $69.6 million for the year ended December 31, 2020, compared to $63.1 million for the year ended December 31, 2019. The increase of $6.5 million was primarily driven by a $5.3 million increase in inflammation program costs due to the progression of EDP1815 to Phase 2, the addition of COVID-19 studies utilizing EDP-1815, and costs incurred in contract manufacturing to enable EDP1867 Phase 1 clinical trials partially offset by the closeout of the EDP1066 program. In addition, personnel costs increased by $3.9 million due to increases in clinical development and technical operations headcount to support increased clinical program activities. Finally, there was a $1.0 million increase for platform expenses which is in line with our strategy to maximize the potential of our platform. These increases were partially offset by a $3.7 million decrease in our oncology program costs, primarily related to the clinical trial stage and the impact of the COVID-19 pandemic on patient recruitment. Overall, 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 EDP1815 and EDP1867, initiate new clinical trials, potentially expand into additional therapeutic areas, continue discovery and development efforts for additional product candidates, hire additional research and development personnel, and seek to increase manufacturing capabilities.

General and Administrative Expenses (in thousands):

	Year Ended December 31,		Increase/ (Decrease)
	2020	2019	
General and administrative personnel costs (including stock-based compensation)	$ 12,261	$ 12,345	$ (84)
Professional fees	5,513	6,725	(1,212)
Facility costs, office expense and other	4,496	4,159	337
Total general and administrative expenses	$ 22,270	$ 23,229	$ (959)

General and administrative expenses were $22.3 million for the year ended December 31, 2020, compared to $23.2 million for the year ended December 31, 2019. The decrease of $1.0 million was primarily driven by $1.2 million lower cost associated with legal, consulting and other professional fees, partially offset by higher IT, facilities and other office expenses costs. We expect this decrease to be temporary and general and administrative expenses to increase due to higher personnel and related costs, professional, legal, and patent fees and consulting expenses in support of our continued growth.

Other (Expense) Income, Net

Other income (expense), net for the year ended December 31, 2020 was expense of $1.4 million compared to income of $1.1 million for the year ended December 31, 2019. This decrease was primarily driven by a decrease in interest income as a result of lower interest rates and a lower cash and cash equivalent balance and an increase in interest expense as a result of a higher interest rate on a greater principal balance from the 2019 Credit Facility, partially offset by foreign currency gains and a grant related to our operations in the United Kingdom.

Net Loss

Net loss was $93.7 million for the year ended December 31, 2020, compared to $85.5 million for the year ended December 31, 2019. The increase of $8.2 million was primarily the result of the increase in research and development expenses and decrease in other income (expense), net discussed above, partially offset by the decrease in general and administrative expenses discussed above.

Liquidity and Capital Resources

To date, we have financed our operations primarily with the proceeds from issuance of our common stock combined with proceeds from previous sales of our convertible preferred stock to our equity investors and borrowings under loan and security agreements. From our inception through December 31, 2020, we have received gross proceeds of $332.0 million from such transactions, including $30.0 million borrowed under the 2019 Credit Facility. As of December 31, 2020, we had cash and cash equivalents of $68.9 million and an accumulated deficit of $292.5 million. During the first quarter of 2021 we raised net proceeds of $82.2 million from the issuance of common stock exclusive of certain other fees payable by us. We expect that our existing cash and cash equivalents as of December 31, 2020, together with the net proceeds raised in the first quarter of 2021 from the issuance of our common stock, will enable us to fund our planned operating expenses and capital expenditure requirements into the third quarter of 2022.

On June 3, 2019, we filed a Registration Statement on Form S-3 (File No. 333-231911) (the “Shelf”) with the SEC under which we can offer from time to time common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in an aggregate amount of up to $200.0 million over a period of up to three years from the date of its effectiveness on June 6, 2019. We also simultaneously entered into a sales agreement with Cowen and Company, LLC, as sales agent, providing for the offering, issuance and sale by us of up to an aggregate $50.0 million of our common stock from time to time in “at-the-market” offerings under the Shelf. For the year ended December 31, 2020, we had issued 1,232,131 shares of our common stock with offering prices ranging between $4.25 to $11.15 per share for gross proceeds of $6.8 million and net proceeds of $6.6 million, after deducting commission and other offering expenses payable by us. In January 2021, we issued 139,734 additional shares of our common stock with offering prices ranging between $12.54 and $13.17 per share for gross proceeds of $1.8 million and net proceeds of $1.7 million, after deducting commission and other offering expenses payable by us.

On February 2, 2021, we sold 5,175,000 shares of our common stock in an underwritten public offering at a public offering price of $15.00 per share, including the underwriters' exercise of their option to purchase 675,000 shares to cover over-allotment, generating gross proceeds of $77.6 million and net proceeds of underwriting discounts and commission of $73.0 million, exclusive of certain other offering expenses payable by us.

On January 28, 2021, we entered into a stock purchase agreement with ALJ, pursuant to which on February 2, 2021, ALJ purchased $7.5 million of our common stock in a private placement at a purchase price of $15.00 per share. The sale of such shares will not be registered under the Securities Act.

Debt financing

On July 19, 2019 we entered into the 2019 Credit Facility with K2HV providing for up to $45.0 million of current and future potential debt financing. The aggregate principal amount was available in three tranches of term loans of $20.0 million, $10.0 million, and $15.0 million, respectively. At closing on July 19, 2019, we borrowed $20.0 million,

representing the first tranche under the 2019 Credit Facility. On July 14, 2020, we drew down the second tranche of $10.0 million and availability of the third tranche expired on January 15, 2021.

Interest on the outstanding loan balance will accrue at a variable rate equal to the greater of (i) 8.65% and (ii) the prime rate as published in the Wall Street Journal, plus 3.15%. We are required to make monthly interest-only payments through February 2022. Subsequent to the interest-only period, we are required to make equal monthly principal payments plus any accrued interest until the loans mature in August 2024. Upon final payment or prepayment of the loans, we are required to pay a final payment equal to 4.3% of the loans borrowed. We have an option to prepay the loans in whole, subject to a prepayment fee of 2% of the amount prepaid or, if the prepayment occurs after the 18-month anniversary of the funding date of the loans, 1% of the amount prepaid.

Contemporaneous with the closing of the first tranche of funding described above, we repaid the entire $15.0 million loan balance outstanding under an existing loan and security agreement with a separate financial institution. In accordance with the agreement underlying the prior debt facility, we paid an additional 0.5% prepayment fee as additional expense.

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 $93.7 million and $85.5 million for the years ended December 31, 2020 and 2019, 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,	
	2020	**2019**
Cash used in operating activities	$ (73,063)	$ (71,980)
Cash (used in)/provided by investing activities	(1,315)	51,970
Cash provided by financing activities	65,465	4,992
Net decrease in cash, cash equivalents and restricted cash	$ (8,913)	$ (15,018)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2020, was $73.1 million, primarily due to our net loss of $93.7 million. This was partially offset by non-cash charges, including stock-based compensation expense of $8.5 million, depreciation expense of $2.0 million, lease expense of $2.0 million and reduction in working capital of $7.8 million.

Net cash used in operating activities for the year ended December 31, 2019, was $72.0 million, primarily due to our net loss of $85.5 million. This was partially offset by non-cash charges, including stock-based compensation expense of $8.2 million, depreciation expense of $1.8 million, and reduction in working capital of $3.5 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2020, was $1.3 million, primarily due to the purchase of capital equipment.

Net cash provided by investing activities for the year ended December 31, 2019, was $52.0 million, primarily consisting of maturity of investments totaling $55.0 million, slightly offset by the purchase of capital equipment totaling $3.0 million during the year.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $65.5 million, primarily due to proceeds from issuance of commons stock totaling $55.0 million, issuance of long-term debt under our 2019 Credit Facility totaling $10.0 million and proceeds from the issuance of common stock in connection with the exercise of options totaling $0.5 million.

Net cash provided by financing activities for the year ended December 31, 2019 was $5.0 million, primarily due to proceeds from the issuance of long-term debt under our 2019 Credit Facility and proceeds from the issuance of common stock in connection with the exercise of options totaling $0.5 million, partially offset by the repayment of our prior debt facility.

Funding Requirements

We have incurred losses and cumulative negative cash flows from operations since our inception. As of December 31, 2020, we had an accumulated deficit of $292.5 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 EDP1815;
- 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.

During the first quarter of 2021 we raised net proceeds of $82.2 million from the issuance of common stock exclusive of certain other fees payable by us. We expect that our cash and cash equivalents as of December 31, 2020 together with the net proceeds raised in the first quarter of 2021 from the issuance of our common stock, will enable us to fund our planned operating expenses and capital expenditure requirements into the third quarter of 2022. 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 EDP1815 and EDP1867, 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 clinical studies of EDP1815 and EDP1867;
- 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. 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 2019 Credit Facility with K2HV preclude us from paying dividends on our equity securities without their 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

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, and are not required to provide this information.

Off-Balance Sheet Arrangements

As of December 31, 2020, 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 of the grant. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. Prior to January 1, 2020, we accounted for these awards in accordance with the provisions of ASC Subtopic 505-50, Equity-Based Payments to Non-employees (“ASC 505-50”). Under ASC 505-50, share-based awards to nonemployees were subject to periodic fair value re-measurement at the end of each financial reporting period prior to completion of the service.

As discussed in Note 2 (Significant Accounting Policies) to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K under the heading “New Accounting Pronouncements - Adopted during the current period,” we adopted ASU No. 2018-07, Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting (Topic 718), on January 1, 2020. As a result, our accounting for nonemployee awards is now generally consistent with that of employee awards. Beginning on January 1, 2020, the measurement date for nonemployee awards is the date of grant without any subsequent changes in the fair value of the award.

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.

Item 7A. Quantitative and Qualitative Disclosure about Market Risk

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, and are not required to provide this information.

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, as defined under 13a-15(e) and 15d-15(e) under the Exchange Act. Based on that evaluation, our principal executive officer and principal financial officer concluded that, as of December 31, 2020, our disclosure controls and procedures as of such date were 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

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the framework in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2020.

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 1: Election of Directors,” “Executive Officers” and “Corporate Governance” of our proxy statement for our 2021 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020, 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 2021 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020, 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 2021 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020, 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, 2020, regarding our common stock that may be issued under: (1) the Evelo Biosciences, Inc. 2015 Stock Incentive Plan (the "2015 Plan"); (2) Evelo Biosciences, Inc. 2018 Incentive Award Plan, (the "2018 Plan"); and (3) the Evelo Biosciences, Inc. 2018 Employee Stock Purchase Plan (the “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)	3,114,275		$ 4.05	—	
2018 Plan (2)	3,780,387	(3)	$ 8.77	951,621	
ESPP (4)	—		$ —	307,753	(5)
Equity Compensation Plans not approved by Stockholders	—		$ —	—	
Total	6,894,662		$ 6.64	1,259,374	

(1) In connection with the initial public offering of shares of our common stock in May 2018 (the “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.

(3) Includes 3,496,387 outstanding options to purchase stock under the 2018 Plan and 284,000 restricted stock units (RSUs) under the 2018 Plan.

(4) Pursuant to the terms of the ESPP, the number of shares of common stock that may be issued under the ESPP will automatically increase on each January 1, until and including January 1, 2028, by an amount equal to the lesser of (A) 1% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by the board of directors. The board of directors determined that, as to the January 1, 2020 increase, no shares be added to the number of shares reserved under the ESPP.

(5) Includes 307,753 shares available for issuance under the ESPP, of which 27,587 were issued on January 31, 2021.

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 2021 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020, 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 2021 annual meeting of stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020, 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	
4.3	Description of Capital Stock	10-K	001-38473	10.3	2/14/2020	
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, as amended	10-K	001-38473	10.3	2/14/2020	
10.4#	Non-Employee Director Compensation Program, as amended	10-K	001-38473	10.4	2/14/2020	
10.5#	Executive Severance Plan, as amended	10-K	001-38473	10.5	2/14/2020	
10.6#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-224278	10.6	4/30/18	
10.7	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	
10.8#	Terms and Conditions of Employment between Evelo Biosciences (UK) Limited and Duncan McHale, M.B.B.S., Ph.D., effective as of May 1, 2019	8-K	001-38473	10.1	4/25/19	
10.9#	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	

10.10#	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	
10.11#	Letter Agreement, dated September 16, 2019, between Evelo Biosciences, Inc. and David R. Epstein, as amended	10-Q	001-38473	10.2	10/30/20	
10.12#	Consulting Agreement, dated September 16, 2019, between Evelo Biosciences, Inc. and David R. Epstein, as amended	10-Q	001-38473	10.3	10/30/20	
10.13	Master Services Agreement, dated September 1, 2018, between Evelo Biosciences, Inc. and Weatherden Ltd	10-K	001-38473	10.12	2/15/19	
10.14†	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	
10.15†	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	
10.16††	Collaboration Agreement between Evelo Biosciences, Inc. and Sacco S.r.l. dated July 9, 2019	10-Q	001-38473	10.4	8/6/19	
10.17††	Development and Clinical Master Services Agreement between Evelo Biosciences, Inc. and Halo Pharmaceutical, Inc. d/b/a Cambrex Whippany dated December 17, 2020					*
10.18	Loan and Security Agreement by and among Evelo Biosciences, Inc. and the other borrowers party thereto, the lenders party thereto, K2 HealthVentures LLC, as administrative agent for such lenders, and Ankura Trust Company, LLC, as collateral agent for such lenders, dated July 19, 2019, as amended	10-Q	001-38473	10.3	8/6/19	
10.19	Second Amendment to Loan and Security Agreement dated as of May 15, 2020 by and among Evelo Biosciences, Inc., the lenders party thereto and K2 HealthVentures LLC, as administrative agent for such lenders.	8-K	001-38473	10.1	5/18/20	
10.20	Third Amendment to Loan and Security Agreement dated as of July 8, 2020 by and among Evelo Biosciences, Inc., the lenders party thereto and K2 HealthVentures LLC, as administrative agent for such lenders	10-Q	001-38473	10.2	7/31/20	
21.1	Subsidiaries of Evelo Biosciences, Inc.	10-K	001-38473	21.1	2/14/2020	
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	Inline XBRL Instance Document - the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*

104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* 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.

†† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

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: March 9, 2021

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 and principal financial officer)	March 9, 2021
/s/ Xiaoli (Jacqueline) Liu Xiaoli (Jacqueline) Liu	VP of Finance and Controller (principal accounting officer)	March 9, 2021
/s/ David R. Epstein David R. Epstein	Chairman of the Board of Directors	March 9, 2021
/s/ Juan Andres Juan Andres	Director	March 9, 2021
/s/ Ara Darzi Lord Ara Darzi	Director	March 9, 2021
/s/ John A. Hohneker John A. Hohneker, M.D.	Director	March 9, 2021
/s/ Theodose Melas-Kyriazi Theodose Melas-Kyriazi	Director	March 9, 2021
/s/ David P. Perry David P. Perry	Director	March 9, 2021
/s/ Nancy A. Simonian Nancy A. Simonian, M.D.	Director	March 9, 2021

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, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Adoption of ASU No. 2016-02

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2020 due to the adoption of Accounting Standards Update (ASU) No. 2016-02 Leases (Topic 842), and the related amendments.

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
March 9, 2021

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

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	$ 68,857	$ 77,833
Prepaid expenses and other current assets	2,123	3,176
Total current assets	70,980	81,009
Property and equipment, net	7,478	8,341
Right of use asset - operating lease	10,757	—
Other assets	1,424	1,570
Total assets	$ 90,639	$ 90,920
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,442	$ 620
Accrued expenses	16,254	8,758
Operating lease liability, current portion	1,674	—
Other current liabilities	463	365
Total current liabilities	19,833	9,743
Noncurrent liabilities:		
Long-term debt	30,048	19,634
Operating lease liability, net of current portion	9,989	—
Deferred rent, net of current portion	—	1,148
Other noncurrent liabilities	284	198
Total liabilities	60,154	30,723
Commitments and contingencies (Note 9)		
Stockholder's equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2020 and 2019, respectively	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 47,488,505 and 32,232,258 shares issued and 47,470,119 and 32,170,605 shares outstanding at December 31, 2020 and 2019, respectively	47	32
Additional paid-in capital	322,957	259,018
Accumulated deficit	(292,519)	(198,853)
Total stockholders' equity	30,485	60,197
Total liabilities and stockholders' equity	$ 90,639	$ 90,920

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,	
	2020	**2019**
Operating expenses:		
Research and development	$ 69,616	$ 63,128
General and administrative	22,270	23,229
Total operating expenses	91,886	86,357
Loss from operations	(91,886)	(86,357)
Other (expense) income:		
Interest (expense) income, net	(2,109)	1,049
Other income, net	738	26
Other (expense) income, net	(1,371)	1,075
Loss before income taxes	(93,257)	(85,282)
Income tax expense	(409)	(190)
Net loss	$ (93,666)	$ (85,472)
Weighted-average number of common shares outstanding, basic and diluted	39,479,197	32,031,862
Net loss per share, basic and diluted	$ (2.37)	$ (2.67)
Comprehensive loss:		
Net loss	$ (93,666)	$ (85,472)
Other comprehensive loss:		
Unrealized gain on investments, net of tax of $0	—	18
Comprehensive loss	$ (93,666)	$ (85,454)

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

Evelo Biosciences, Inc.
Consolidated Statements of Stockholders' Equity
(In thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount				
Balance-January 1, 2019	31,825,769	$ 32	$ 250,316	$ (18)	$ (113,381)	$ 136,949
Vesting of restricted common stock	64,118	—	26	—	—	26
Exercise of stock options	280,718	—	511	—	—	511
Stock-based compensation expense	—	—	8,165	—	—	8,165
Unrealized gain on investments	—	—	—	18	—	18
Net loss	—	—	—	—	(85,472)	(85,472)
Balance-December 31, 2019	32,170,605	$ 32	$ 259,018	$ —	$ (198,853)	$ 60,197
Issuance of common stock, net of fees	15,032,131	15	54,979	—	—	54,994
Vesting of restricted common stock	43,267	—	21	—	—	21
Issuance of common stock under the Employee Stock Purchase Plan	28,603	—	92	—	—	92
Exercise of stock options	195,513	—	379	—	—	379
Stock-based compensation expense	—	—	8,468	—	—	8,468
Net loss	—	—	—	—	(93,666)	(93,666)
Balance-December 31, 2020	47,470,119	$ 47	$ 322,957	$ —	$ (292,519)	$ 30,485

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,	
	2020	2019
Operating activities		
Net loss	$ (93,666)	$ (85,472)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	8,468	8,165
Depreciation expense	2,026	1,764
Net accretion of discount on marketable securities	—	(164)
Non-cash interest expense	374	255
Non-cash lease expense	1,976	—
Gain on sale of fixed assets	(6)	(2)
Prepaid expenses and other current assets	1,503	372
Accounts payable	837	(585)
Accrued expenses and other current liabilities	7,438	3,694
Operating lease liabilities	(2,218)	—
Other liabilities	205	(7)
Net cash used in operating activities	(73,063)	(71,980)
Investing activities		
Proceeds from sales and maturities of investments	—	55,000
Purchases of property and equipment	(1,321)	(3,032)
Proceeds from the sale of fixed assets	6	2
Net cash (used in) provided by investing activities	(1,315)	51,970
Financing activities		
Net proceeds from the issuance of common stock, net of issuance cost	54,994	—
Net proceeds from the issuance of long-term debt	10,000	19,481
Proceeds from issuance of common stock under employee stock purchase plan and the exercise of stock options, restricted common stock	471	511
Repayment of long-term debt	—	(15,000)
Net cash provided by financing activities	65,465	4,992
Net increase in cash, cash equivalents and restricted cash	(8,913)	(15,018)
Cash, cash equivalents and restricted cash – beginning of year	79,333	94,351
Cash, cash equivalents and restricted cash – end of year	$ 70,420	$ 79,333
Supplemental disclosure of cash flow information		
Cash paid for interest	$ 2,172	$ 1,166
Cash paid for taxes	$ 20	$ —
Noncash investing and financing activities		
Property and equipment additions in accounts payable and accrued expenses	$ 178	$ 246
Public offering cost in accrued expenses	$ 111	$ —

The accompanying notes are an integral part of these 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 is discovering and developing oral biologics that act on cells in the small intestine with systemic therapeutic effects. The Company is advancing these oral biologics with the aim of treating a broad range of immune mediated diseases with an initial focus on inflammatory diseases and oncology. The Company is headquartered in Cambridge, Massachusetts.

Since inception, the Company has devoted 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.

To date, the Company has financed operations primarily with the proceeds from issuance of common stock combined with proceeds from previous sales of convertible preferred stock to equity investors and debt financing.

On June 3, 2019, the Company filed a Registration Statement on Form S-3 (File No. 333-231911) (the “Shelf”) with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of its effectiveness on June 6, 2019. The Company also simultaneously entered into a sales agreement (the "ATM") with Cowen and Company, LLC, as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate $50.0 million of its common stock from time to time in “at-the-market” offerings under the Shelf. For the year ended December 31, 2020, the Company sold 1,232,131 common shares under the ATM with offering prices ranging between $4.25 to $11.15 per share for gross proceeds of $6.8 million and net proceeds of $6.6 million, after deducting commission and other offering expenses payable by us. In January 2021, the Company issued 139,734 additional shares of common stock under the ATM with offering prices ranging between $12.54 and $13.17 per share for gross proceeds of $1.8 million and net proceeds of $1.7 million, after deducting commission and other offering expenses.

In June 2020, the Company sold 13,800,000 shares of its common stock in an underwritten public offering at a public offering price of $3.75 per share, including the underwriters' exercise of their option to purchase 1,800,000 shares to cover over-allotment, generating gross proceeds of $51.8 million and net proceeds of $48.4 million, after deducting underwriting discounts and commission and other offering expenses payable by the Company.

On July 14, 2020, the Company drew down the second tranche of $10.0 million available under the 2019 Credit Facility. Refer to Note 7, Loan and Security Agreement, to this Annual Report on Form 10-K for more information.

On February 2, 2021, the Company sold 5,175,000 shares of its common stock in an underwritten public offering at a public offering price of $15.00 per share, including the underwriters' exercise of their option to purchase 675,000 shares to cover over-allotment, generating gross proceeds of $77.6 million and net proceeds of underwriting discounts and commission of $73.0 million, exclusive of other offering expenses payable by the Company.

On January 28, 2021, the Company entered into a stock purchase agreement with ALJ Health Care & Life Science Company Limited ("ALJ"), pursuant to which on February 2, 2021, ALJ purchased $7.5 million of our common stock in a private placement at a purchase price of $15.00 per share, equal to the public offering price per share at which our common stock was sold to the public as referred above. The sale of such shares will not be registered under the Securities Act.

In accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The Company has incurred recurring losses since its inception, including net losses of $93.7 million and $85.5 million for the years ended December 31, 2020 and 2019, respectively. In addition, as of December 31, 2020, the

Company had an accumulated deficit of $292.5 million. The Company expects to continue to generate operating losses for the foreseeable future.

The Company previously identified conditions and events that raised substantial doubt about its ability to continue as a going concern. During the first quarter of 2021 we raised net proceeds of $82.2 million from the issuance of common stock exclusive of certain other fees payable by us. The Company expects that its cash and cash equivalents as of December 31, 2020 of $68.9 million together with the net proceeds raised from the issuances of common stock in the first quarter of 2021, will be sufficient to fund the operating expenditures and capital expenditure requirements necessary to advance its research efforts and clinical trials for at least one year from the date of issuance of these consolidated financial statements. The future viability of the Company beyond one year from the date of issuance of these consolidated financial statements is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or 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 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 subsidiaries. All intercompany transactions and balances 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 Note 16, Subsequent Event, to this Annual Report on Form 10-K.

Emerging Growth Company Status

Evelo is an “emerging growth company,” as defined in 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 its IPO 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; it has more than $700.0 million in market value of its stock held by non-affiliates (and has been a public company for at least 12 months and has filed one annual report on Form 10-K), or it has issued 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 and cash equivalents. The Company places its cash and cash equivalents in primarily two custodian accounts at accredited financial institutions. Such deposits have and will continue to exceed federally insured limits.

As of December 31, 2020, and 2019, 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 that are excluded from net loss. The Company's only element of other comprehensive loss is unrealized gains on available-for-sale

investments. For the year ended December 31, 2020 comprehensive loss was equal to net loss. Comprehensive loss totaled $85.5 million for the years ended December 31, 2019, and was not significantly different than 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. The Company's restricted cash consists of restricted cash in connection with a lease for the Company's office and laboratory premises and deposits held in relation to the Company's credit card facility. As of December 31, 2020 the Company had $0.3 million in current restricted cash within prepaid expenses and other current assets in the consolidated balance sheet. The Company had no current restricted cash at December 31, 2019. As of December 31, 2020 and 2019, the Company had noncurrent restricted cash of $1.3 million and $1.5 million, respectively, which were included within other assets in the consolidated balance sheets. The following reconciles cash, cash equivalents and restricted cash as of December 31, 2020 and 2019, as presented on the Company's consolidated statements of cash flows, to its related consolidated balance sheet accounts (in thousands):

	December 31,	
	2020	**2019**
Cash and cash equivalents:		
Cash	$ 4,487	$ 1,634
Money market funds	64,370	76,199
Total cash and cash equivalents	68,857	77,833
Restricted cash	1,563	1,500
Cash, cash equivalents and restricted cash	$ 70,420	$ 79,333

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.

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 (used/new)	3/5 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 material impairment charges during the years presented.

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. Prior to January 1, 2020, we accounted for these awards in accordance with the provisions of ASC Subtopic 505-50, Equity-Based Payments to Non-employees ("ASC 505-50"). Under ASC 505-50, share-based awards to nonemployees were subject to periodic fair value re-measurement at the end of each financial reporting period prior to completion of the service.

As discussed in below under the heading "New Accounting Pronouncements - Adopted during the current period," the Company adopted ASU No. 2018-07, Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting (Topic 718), on January 1, 2020. As a result, the Company's accounting for nonemployee awards is now generally consistent with that of employee awards. Beginning on January 1, 2020, the measurement date for nonemployee awards is the date of grant without any subsequent changes in the fair value of the award.

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

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share 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 stock options, common stock from Employee Stock Purchase Plan (the "ESPP") 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.

New Accounting Pronouncements

Adopted during the current period

Leases

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 accounting guidance requires recognition of all long-term lease assets and lease liabilities by lessees and sets forth new disclosure requirements for those lease assets and liabilities. It requires lessees to recognize right-of-use assets and lease liabilities on the balance sheet using a modified retrospective approach at the beginning of the earliest comparative period in the financial statements for all leases with a term of greater than 12 months regardless of classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The FASB subsequently issued several ASUs amending the new standard. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2018 for most public entities. The Company adopted this new standard on January 1, 2020 using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840.

ASU 2016-02 provides a number of optional practical expedients in transition. The Company elected to adopt the 'package of practical expedients', which permits the Company (i) not to reassess whether expired existing contracts are or contain leases, (ii) not to reassess the classification of expired or existing leases, and (iii) not to reassess initial direct costs for any existing leases. The Company will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases using classification criteria that are substantially similar to the previous guidance. Adoption of this standard resulted in the recognition of a right-of-use asset and a lease liability on the Company’s January 1, 2020 consolidated balance sheet of $12.7 million and $13.9 million, respectively. There was no material impact resulting from the adoption on the Company’s consolidated statement of operations for the year ended December 31, 2020. For leases with terms greater than 12 months, the Company records the related right-of-use asset and lease liability at the present value of lease payments over the term. As the Company’s leases do not provide readily determinable implicit interest rates, the Company utilized its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. In transition to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates. The application of the new standard required netting of unamortized balance of lease incentives and deferred lease obligation to the right-of-use asset at the adoption date. The Company’s operating leases include rental escalation clauses that are factored into the determination of lease payments when appropriate. The Company does not separate lease and non-lease components of contracts. Refer to Note 3, Leases, to this Annual Report on Form 10-K for additional information.

Share-Based Compensation

In June 2018, the FASB issued ASU No. 2018-07, Stock-based Compensation: Improvements to Nonemployee Share-based Payment Accounting (Topic 718) ("ASU 2018-07"), which amends the existing accounting standards for share-based payments to nonemployees. This ASU aligns much of the guidance on measuring and classifying nonemployee awards with that of awards to employees. Under the new guidance, the measurement of nonemployee equity awards is fixed on the grant date. Entities will apply the ASU by recognizing a cumulative-effect adjustment, if any, to retained earnings as of the beginning of the annual period of adoption. The Company adopted ASU 2018-07 on January 1, 2020. The adoption of this standard did not have a material impact to this Annual Report on Form 10-K.

To be adopted in future periods

In December 2019, the FASB issued ASU No. 2019 -12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. The new standard includes several provisions which simplify accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and increasing consistency and clarity for the users of financial statements. This standard will be effective for the Company on January 1, 2021. Early adoption is permitted. The adoption of this guidance is not expected to have a material impact on the Company’s financial position and results of operations.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments, which has been subsequently amended by ASU No.

2018-19, ASU No. 2019-04, ASU No. 2019-05, ASU No. 2019-10, ASU No. 2019-11 and ASU No. 2020-03 ("ASU 2016-13"). The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for the Company on January 1, 2023, with early adoption permitted. The Company is currently evaluating the potential impact that this standard may have on its financial position and results of operations, as well as the timing of its adoption of this standard.

On August 5, 2020, the FASB issued ASU 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU-2020-06"), which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. ASU 2020-06 eliminates the beneficial conversion and cash conversion accounting models in ASC 470-20 that require separate accounting for embedded conversion features from convertible instruments. As a result, after adopting the ASU's guidance, entities will not separately present in equity an embedded conversion feature in such debt. Additionally, the guidance simplifies the evaluation of whether a contract in the issuer's own equity can be classified in equity or an embedded feature qualifies for the derivative scope exception. Although the guidance is not effective until 2022, early adoption of ASU 2020-06 is permitted for all entities for fiscal years beginning after December 15, 2020. The Company is currently evaluating the impact of this new guidance on the Company's consolidated financial statements and related disclosures.

3. Leases

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 maintained an additional separate operating lease for office and laboratory space that expired in May 2020. The leases require security deposits, which the Company has primarily met with letters of credit from a financial institution that is 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 expired in April 2020. The minimum rental payments received under this agreement totaled $0.2 million for the year ended December 31, 2020 and were equivalent to the minimum payments due from the Company to the landlord.

The Company recorded rent expense of $2.9 million for both years ended December 31, 2020 and 2019, which are net of sublease rental income of $0.3 million and $0.5 million. Sublease rental income is inclusive of rental payments, taxes, and operating expenses.

The minimum aggregate future lease commitments at December 31, 2020, are as follows (in thousands):

	Amount
2021	$ 2,727
2022	3,062
2023	3,154
2024	3,249
2025	2,491
Total lease payments	14,683
Less imputed interest	(3,020)
Total	$ 11,663

Other information:	
Operating cash flows used for operating leases	$ 3,334
Weighted-average remaining lease term (in years)	5 years
Weighted-average discount rate	9.5%

Under the prior lease accounting guidance, minimum rental commitments under non-cancelable leases as of December 31, 2019 were as follows (in thousands):

	Amount
2021	$ 2,973
2022	3,062
2023	3,154
2024	3,249
2025	2,492
Total lease payments	$ 14,930

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, 2020 and 2019 (in thousands):

Description	December 31, 2020	(Level 1)	(Level 2)	(Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 64,370	$ 64,370	$ —	$ —
Total	$ 64,370	$ 64,370	$ —	$ —

Description	December 31, 2019	(Level 1)	(Level 2)	(Level 3)
Assets:				
Money market funds included within cash and cash equivalents	$ 76,199	$ 76,199	$ —	$ —
Total	$ 76,199	$ 76,199	$ —	$ —

As of December 31, 2020 and 2019, the Company's cash equivalents 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.

5. Property and Equipment, Net

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

	December 31, 2020	December 31, 2019
Property and equipment:		
Lab equipment	$ 8,831	$ 7,479
Leasehold improvements	2,157	2,014
Furniture and fixtures	822	750
Computers and software	230	204
Office equipment	3	9
Construction-in-process	1,078	1,594
Property and equipment	13,121	12,050
Less: accumulated depreciation	(5,643)	(3,709)
Property and equipment, net	$ 7,478	$ 8,341

The Company recognized $2.0 million and $1.8 million of depreciation expense for the years ended December 31, 2020 and 2019, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2020	December 31, 2019
Accrued external research and development expenses	$ 9,394	$ 4,583
Accrued payroll and related expenses	5,620	3,149
Accrued professional fees	604	659
Accrued other	636	367
Total accrued expenses	$ 16,254	$ 8,758

7. Loan and Security Agreement

2016 Credit Facility

In 2016, the Company entered into a credit facility (the “2016 Credit Facility”) with a bank that allowed the Company to borrow up to $15.0 million. Borrowings under the 2016 Credit Facility were secured by a lien on all Company assets, excluding intellectual property. The Company borrowed the entire $15.0 million available under the 2016 Credit Facility prior to its extinguishment in July 2019 as discussed in further detail below.

The 2016 Credit Facility contained 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 were no financial covenants associated with the agreement.

2019 Credit Facility

On July 19, 2019, the Company entered into a loan and security agreement (as amended, the "2019 Credit Facility") with K2 HealthVentures LLC and others (collectively, "K2HV") pursuant to which the K2HV agreed to make term loans in an aggregate principal amount of up to $45.0 million available to the Company in three tranches. The initial tranche of $20.0 million was funded upon closing on July 19, 2019. As amended on May 15, 2020, the second tranche of $10.0 million was available to be funded between December 1, 2019 and July 15, 2020 and was drawn down on July 14, 2020. The third tranche of $15.0 million expired on January 15, 2021. Borrowings under the 2019 Credit Facility are collateralized by substantially all of the Company's personal property, excluding intellectual property, and the Company pledged its equity interests in its subsidiaries, subject to certain limitations with respect to its foreign subsidiaries.

Interest on the outstanding loan balance will accrue at a variable annual rate equal to the greater of (i) 8.65% and (ii) the prime rate plus 3.15%. The Company is required to make interest-only payments on the loans on a monthly basis through February 28, 2022. Subsequent to the interest only periods, the Company is required to make equal monthly payments of principal plus interest until the loans mature on August 1, 2024. Upon final payment or prepayment of the loans, the Company must pay a final payment equal to 4.3% of the loans borrowed, which is being accrued to interest expense over the term of the loan using the effective-interest method. The Company incurred fees associated with establishing the 2019 Credit Facility of $0.4 million. The Company has an option to prepay the loans in whole, subject to a prepayment fee of 2% of the amount prepaid or, if the prepayment occurs after the 18-month anniversary of the funding date of the loans, 1% of the amount prepaid.

The 2019 Credit Facility contains customary representations, warranties and covenants and also includes customary events of default, including payment defaults, breaches of covenants, change of control and occurrence of a material adverse effect. The Company has determined that the risk of subjective acceleration under the material adverse events clause was remote and therefore has classified the long-term portion of the outstanding principal in non-current liabilities. Upon the occurrence and continuation of an event of default, a default interest rate of an additional 5% per annum may be applied to the outstanding loan balances, and the administrative agent, collateral agent, and lenders may declare all outstanding obligations immediately due and payable and exercise all of their rights and remedies as set forth in the 2019 Credit Facility and under applicable law. As of December 31, 2020, the Company was in compliance with all covenants under the 2019 Credit Facility.

The Company used the proceeds from the initial $20.0 million tranche to prepay on July 19, 2019 the full $15.0 million loan balance outstanding under the 2016 Credit Facility .

The Company has the following minimum aggregate future loan payments at December 31, 2020 (in thousands):

	Amount
2021	$ 2,631
2022	11,603
2023	13,387
2024	10,259
Total minimum payments	$ 37,880
Less amounts representing interest and discount	(7,832)
Long-term debt	$ 30,048

Interest expense related to the Company's 2016 Credit Facility was approximately $0.5 million, for the year ended December 31, 2019.

Interest expense related to the Company's 2019 Credit Facility was approximately $2.6 million and $0.8 million for the year ended December 31, 2020 and 2019.

8. 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 the Mayo Foundation for Medical Education and Research, an affiliate of Mayo Clinic (the “Mayo Clinic”). Under the 2016 Mayo License Agreement, the Mayo Clinic was entitled to certain participation rights in connection with the issuance and sale of preferred stock that was issued prior to the Company’s public offering and warrants which were issued in 2016 and exercised in 2018.

On August 6, 2017, the Company and the Mayo Clinic entered into a license agreement (“2017 Mayo License Agreement”). Under the 2017 Mayo License Agreement, the Mayo Clinic granted the Company (i) an exclusive, worldwide, sublicensable license under the Mayo Clinic’s rights to certain intellectual property and microbial strains and (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 will pay 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 the Mayo Clinic 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, 2020, 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. As of December 31, 2020, the Company has incurred milestone payments to date totaling approximately $0.4 million under the agreement of which no amounts are currently due.

9. Commitments and Contingencies

Collaboration Agreement with Sacco S.r.l.

In July 2019, the Company entered into an agreement with Sacco S.r.l. ("Sacco"), an affiliate of one of the Company’s existing contract manufacturing organizations, pursuant to which and subject to certain exceptions for pre-existing products for pre-existing customers, Sacco will manufacture and supply single strain, non-genetically modified microbes intended for oral delivery or oral use in pharmaceutical products exclusively for the Company for a period of five years. Sacco may terminate the agreement if the provision of manufacturing services has been, or is scheduled to be, inactive for a period of six consecutive months. The Company has agreed to pay Sacco an aggregate of €3.0 million, €0.6 million annually, during the exclusivity period. The Company has incurred annual exclusivity fees to date totaling approximately €1.2 million, and no amounts are currently due as of the year ended December 31, 2020.

Agreement with Biose Industrie

On February 15, 2018, the Company entered into an agreement with Biose Industrie (“Biose”), a French corporation, in which Biose agreed to exclusively manufacture certain microbial biotherapeutic products for the Company and reserved 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 those microbial biotherapeutics 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, 2020, aggregate minimum payments over the remaining contract life total approximately $0.7 million. The agreement expired on February 15, 2021 in accordance with its terms.

Litigation and Other Proceedings

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.

On February 12, 2021, the European Patent Office issued a Communication of a Notice of Opposition for European patent EP 3223834, which is held by the Company. The Company is currently evaluating its available options and deciding next steps with respect to this matter. The patent at issue does not relate to any of the Company's current product candidates, and receipt of this communication and/or any subsequent proceeding is not expected to affect any of the Company's current development plans.

10. Stockholders' Equity

Common Stock

On June 3, 2019, the Company filed a Shelf with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million for a period of up to three years from the date of the filing. The Company also simultaneously entered into the ATM, providing for the offering, issuance and sale by the Company of up to an aggregate $50.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf. For the year ended December 31, 2020, pursuant to the ATM, the Company sold 1,232,131 shares of its common stock, with offering prices ranging between $4.25 to $11.15 per share for gross proceeds of $6.8 million and net proceeds of $6.6 million, after deducting commission and other offering expenses payable by us.

In June 2020, the Company sold 13,800,000 shares of its common stock pursuant to the Shelf in an underwritten public offering at a public offering price of $3.75 per share, for gross proceeds of $51.8 million and net proceeds of $48.4 million, after deducting underwriting discounts and commission and other offering expenses payable by the Company.

11. 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 initially allowed 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, on January 1, 2021, 2020 and 2019 the number of shares authorized for issuance under the 2018 Incentive Plan was increased by 1,898,805 shares, 1,286,824 shares and 1,273,031 shares, respectively. 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, 2020, equity-based incentive awards

covering 4,376,182 options of the Company's common stock and 284,000 restricted stock units have been issued under the 2018 Plan, of which 875,155 options have been canceled and 4,640 options have been exercised. As of December 31, 2020, 951,621 shares of common stock are available for future grant under the 2018 Plan, which includes 832,101 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 equity award agreements, including vesting requirements, were 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 effectiveness 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, 2020, an aggregate of 5,758,518 options and other equity awards had been granted under the 2015 Plan, of which 1,376,141 have been exercised, 1,268,110 have been canceled and 18,468 have been repurchased as of December 31, 2020. 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

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

	Year Ended December 31,	
	2020	2019
Research and development	$ 4,487	$ 3,648
General and administrative	3,981	4,517
Total stock-based compensation expense	$ 8,468	$ 8,165

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, 2019	5,691,474	$ 6.99		
Granted	2,161,356	$ 6.06		
Exercised	(195,513)	$ 1.94		
Canceled	(1,046,655)	$ 8.80		
Options outstanding at December 31, 2020	6,610,662	$ 6.55	7.53	$ 38,815
Exercisable at December 31, 2020	3,671,175	$ 5.52	6.77	$ 25,332
Vested and expected to vest as of December 31, 2020	6,610,662	$ 6.55	7.53	$ 38,815

(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.

The Company had 2,957,873 unvested stock options outstanding as of December 31, 2020. The weighted-average fair value of options granted during the years ended December 31, 2020 and 2019 was $4.14 and $7.46,

respectively. The aggregate intrinsic value of options exercised during the years ended December 31, 2020 and 2019 was $0.9 million and $1.8 million, respectively.

When utilizing the Black-Scholes option-pricing model to determine the grant date fair value of stock options granted to employees or non-employees, the Company used the following weighted average, or ranges of, assumptions:

Employee option grants

	Year Ended December 31,	
	2020	**2019**
Risk-free interest rate	1.11 %	2.28 %
Expected life (in years)	6.05	6.02
Volatility	79.6 %	76.2 %
Expected dividend rate	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.

Non-employee option grants

	Year Ended December 31,	
	2020	**2019**
Risk-free interest rate	0.38 %	1.98 %
Expected life (in years)	5.21	7.63
Volatility	78.9 %	76.0 %
Expected dividend rate	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.

As of December 31, 2020, total unrecognized stock-based compensation expense relating to unvested stock options was $14.4 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 2.12 years.

On November 4, 2020, 284,000 RSUs were granted to certain employees of the Company under the 2018 Plan with a weighted average grant date fair value of $4.41. Each award of RSUs vests as to 25% on the first anniversary of the grant date, 25% of the RSUs on the second anniversary of the grant date and 50% of the RSUs on the third anniversary of the grant date, subject to the grantees continuing service. As of December 31, 2020, none of the restricted stock units had vested. Stock-based compensation expense related to RSUs was immaterial for the year ended December 31, 2020.

2018 Employee Stock Purchase Plan

The Company's board of directors adopted on April 18, 2018, and the Company’s stockholders approved, 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. The Company's board of directors determined not to increase the number of shares that may be issued under the ESPP on January 1, 2020. The Company's board of directors has authorized an initial offering period under the ESPP commencing on February 1, 2020. Accordingly, on January 1, 2021, the number of shares authorized for issuance under the ESPP was increased by 474,701 shares.

The compensation expense recognized related to the ESPP for the year ended December 31, 2020 was $0.1 million. There was a total of 28,603 shares purchased under the ESPP during the year ended December 31, 2020.

12. Income Taxes

The Company has recorded a tax provision of $0.4 million and $0.2 million for the year ended December 31, 2020 and 2019, respectively. The Company did not record a tax benefit for the periods presented due to the losses incurred and the need for a full valuation allowance on net deferred tax assets. The tax expense recorded for the December 31, 2020 and 2019 period primarily relates to current tax expense at the Company's UK subsidiary. 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 in the United States with a small profit generated by the Company's subsidiary in the United Kingdom.

	December 31,	
	2020	2019
U.S. federal tax statutory rate	21.0 %	21.0 %
State taxes, net of federal benefit	6.8 %	7.0 %
Non-deductible stock compensation	(1.0)%	(0.6)%
Other non-deductible expenses	(0.4)%	(0.4)%
Credits	1.8 %	1.6 %
Change in valuation allowance	(28.6)%	(29.1)%
Other	— %	0.3 %
Total	(0.4)%	(0.2)%

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 36,256	$ 25,895
Research and development credits	7,092	4,856
Capitalized research and development, patent and start-up costs	34,452	22,101
Accrued expenses	1,370	1,006
Stock based compensation	3,443	2,335
Operating lease liability	3,186	—
Right of use asset - operating lease	(2,939)	—
Depreciation	(208)	(295)
Deferred tax assets before valuation allowance	82,652	55,898
Valuation allowance	(82,652)	(55,898)
Net deferred tax assets	$ —	$ —

As of December 31, 2020, the Company had approximately $133.7 million and $129.4 million of Federal and state Net Operating Losses ("NOLs"), respectively. The Federal NOLs include $49.9 million which expire at various dates through 2037, and $83.8 million which carryforward indefinitely. The state NOLs expire at various dates through 2040. As of December 31, 2020, the Company had federal and state research credits of $5.0 million and $2.6 million, respectively, which expire at various dates through 2040.

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 Code, 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 our stock ownership, some of which may be outside the Company's control. As a result, the Company's ability to use our 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 Federal NOLs generated post tax reform will have an indefinite life, are not subject to carryback provisions and limited to 80% of income in any year after 2020.

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, 2020 and 2019, respectively. The valuation allowance increased by $26.8 million in 2020 primarily due to increases in net operating losses and research and development credits.

As of December 31, 2020 and 2019, 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.

13. 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, common stock from the ESPP and restricted common stock, outstanding during the period determined using the 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,	
	2020	2019
Unvested common stock from early exercise of options	18,386	61,653
Stock options to purchase common stock	6,610,662	5,691,474
RSUs	284,000	—
Common stock from the ESPP	24,508	—
Total	6,937,556	5,753,127

14. Related Party Transactions

The Company receives clinical advisory services from Weatherden Ltd. ("Weatherden") under agreements that were entered into during 2017 and 2018. Duncan McHale, the Company's Chief Medical Officer is a part owner of Weatherden. During the years ended December 31, 2020 and 2019, the Company paid Weatherden $0.6 million and $1.0 million, respectively. As of December 31, 2020 an immaterial amount was due to Weatherden. As of December 31, 2019, the amount due to Weatherden under the supply of service agreement totaled approximately $0.2 million.

In June 2018, the Company entered into a subleasing arrangement with Ring Therapeutics, Inc. (formerly VL46, Inc.), an affiliate of one of its stockholders, Flagship Venture Funds. Under the terms of the sublease, the Company invoiced Ring Therapeutics for an aggregate $0.9 million in rent payments which were due during the period from July 1, 2018 through April 30, 2020, the sublease expiration date, plus related taxes and lease operating costs. For the year ended December 31, 2020, $0.3 million related to this sublease, inclusive of rent payments,

taxes and operating expenses, has been recorded as an offset to operating expense within the consolidated statements of operations and comprehensive loss.

The Company entered into a consulting agreement with David Epstein (as amended, the "Consulting Agreement"), the Company's Chairman of the Board, effective September 16, 2019 pursuant to which Mr. Epstein will provide strategic advisory and other consulting services to the Company. As amended on October 15, 2020, the Agreement will continue until June 30, 2021 unless terminated earlier by either Mr. Epstein or the Company upon 30 days' notice, or 24 hours' notice by the non-breaching party in the event of a breach. In accordance with the terms of the Consulting Agreement, on September 16, 2019, Mr. Epstein was granted an option to purchase 75,000 shares of the Company's common stock, which award vests in 36 equal monthly installments subject to his continued provision of consulting services to the Company pursuant to the Consulting Agreement on the applicable vesting dates. Under the Consulting Agreement, Mr. Epstein also is entitled to receive (i) an annual equity award on each anniversary of the effective date of the Consulting Agreement in the form of an option to purchase shares of the Company's common stock having an aggregate grant date fair market value equal to approximately $0.2 million, as determined by the Board in its discretion based on customary option pricing methodologies, which award vests in 12 equal monthly installments following the grant date, subject to his continued provision of consulting services to the Company pursuant to the Consulting Agreement on the applicable vesting date, and (ii) an aggregate annual cash consulting fee of $0.3 million for his consulting services. All of the foregoing options, to the extent then outstanding, will be subject to accelerated vesting upon the occurrence of a change in control of the Company. On October 11, 2020, in connection with the commencement of his second year of service as a consultant to the Company, Mr. Epstein was granted an annual equity award in the form of an option to purchase 44,743 shares of the Company's common stock, which award vests in nine equal monthly installments, in each case subject to his continued provision of consulting services to the Company pursuant to the Consulting Agreement on the applicable vesting dates.

15. Defined Contribution Plan

The Company provides benefits under certain retirement benefit plans. The Company's most significant defined contribution plan is in the United States, which is administered through a third-party administrator. Under the U.S. defined contribution plan employees may elect to defer up to 85.0% of their compensation per year (subject to a maximum limit prescribed by federal tax law) and the Company matches a portion of such employee contributions. For the years ended December 31, 2020 and 2019 the Company's matching contribution expense totaled $0.3 million and $0.2 million, respectively.

16. Subsequent Event

In January 2021, pursuant to the ATM, the Company issued 139,734 shares of its common stock in an "at-the-market" offering under the Company's previously filed Shelf, with offering prices ranging between $12.54 and $13.17 per share for gross proceeds of $1.8 million and net proceeds of $1.7 million, after deducting commission and other offering expenses payable by the Company.

On February 2, 2021, the Company sold 5,175,000 shares of its common stock in an underwritten public offering at a public offering price of $15.00 per share, including the underwriters' exercise of their option to purchase 675,000 shares to cover over-allotment, generating gross proceeds of $77.6 million and net proceeds of underwriting discounts and commission of $73.0 million, exclusive of other offering expenses payable by the Company.

On January 28, 2021, the Company entered into a stock purchase agreement with ALJ, pursuant to which on February 2, 2021, ALJ purchased $7.5 million of our common stock in a private placement at a purchase price of $15.00 per share, equal to the public offering price per share at which our common stock was sold to the public as referred above. The sale of such shares will not be registered under the Securities Act.

Board of Directors

Juan Andres
Chief Technical Operations and Quality Officer, Moderna, Inc.

Professor the Lord Ara Darzi of Denham
Paul Hamlyn Chair of Surgery and Director of the Hamlyn Centre, Imperial College London

David R. Epstein
Executive Partner, Flagship Pioneering

Balkrishan (Simba) Gill, Ph.D.
President & Chief Executive Officer, Evelo Biosciences, Inc.

John A. Hohneker, M.D.
Former Chief Executive Officer, Anokion SA

Julie H. McHugh
Former Chief Operating Officer, Endo Health Solutions, Inc.

Theodose Melas-Kyriazi
Chief Financial Officer, Levitronix Technologies LLC

David P. Perry
Executive Chairman and Co-Founder Better Therapeutics, Inc.

Nancy A. Simonian, M.D.
President and Chief Executive Officer, Syros Pharmaceuticals, Inc.

Executive Officers

Balkrishan (Simba) Gill, Ph.D.
Chief Executive Officer, President and Treasurer

Mark Bodmer, Ph.D.
Chief Scientific Officer and President of Research and Development

Daniel S. Char
General Counsel and Secretary

Duncan McHale, M.B.B.S, Ph.D.
Chief Medical Officer

Jonathan Zung, Ph.D.
Chief Development Officer

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Stock Exchange

Evelo Biosciences, Inc.'s common stock shares are listed and traded on the Nasdaq Global Select Market under the ticker symbol "EVLO"

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