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

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2019
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE TRANSITION PERIOD FROM _ TO _

COMMISSION FILE NUMBER 001-38501

AXCELLA HEALTH INC.
(Exact name of registrant as specified in its charter)

Delaware	26-3321056
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
840 Memorial Drive Cambridge, Massachusetts **(Address of principal executive offices)**	02139 **(Zip Code)**

(857) 320-2200
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock	AXLA	The Nasdaq Global Market

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

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $107,368,972 as of June 28, 2019 (based on a closing price of $9.31 per share as quoted by the Nasdaq Global Market as of such date). In determining the market value of non-affiliate common stock, shares of the registrant's common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 19, 2020, the registrant had 23,188,816 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive proxy statement for its 2020 annual meeting of shareholders, or the Proxy Statement, 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 end of December 31, 2019. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

In this Annual Report on Form 10-K, or Annual Report, we use the following defined terms:

"product candidate" to refer to one of our investigational product candidates.

"development platform" to refer to our proprietary human-focused development platform.

"dose" to refer to the exposure amount of a product candidate in Clinical Trials and Clinical Studies.

"non-drug" to refer to a non-therapeutic use of a product candidate. Such use may be as a food product or dietary supplement.

"Clinical Trial" to refer to a human clinical study of a drug product candidate subject to the requirements for an effective Investigational New Drug application, or an IND.

"Clinical Study" to refer to Institutional Review Board-Approved, or IRB-Approved, clinical studies conducted in humans with our product candidates under U.S. Food and Drug Administration, or the FDA, regulations and guidance supporting research with food outside of an IND (prior to any decision to develop a product candidate as a drug product candidate under an IND or a non-drug product candidate). In these food studies, based on our understanding of FDA regulations and guidance, we evaluate in humans, including individuals with disease, a product candidate for safety, tolerability and effects on the normal structures and functions of the body. These studies are not designed or intended to evaluate a product candidate's ability to diagnose, cure, mitigate, treat or prevent a disease as these would be evaluated in Clinical Trials if we decide to develop a product candidate as a drug or therapeutic.

This Annual Report contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may", "will", "should", "expects", "intends", "plans", "anticipates", "believes", "estimates", "predicts", "potential", "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product development activities, preclinical studies, Clinical Studies and Clinical Trials, including statements regarding the timing of initiation and completion of preclinical studies, Clinical Studies or Clinical Trials and related preparatory work, and the timing of the availability of the results of these preclinical studies, Clinical Studies and Clinical Trials;
- our ability to obtain funding for our operations, including funding necessary to complete further development of our initial product candidates, and if successful, commercialization of these candidates as drug or non-drug products;
- the potential for our identified research priorities to advance our development platform, development programs or product candidates;
- our ability to obtain and maintain regulatory approval or find alternate regulatory commercialization pathways from the FDA, the European Medicines Agency, or the EMA, and other comparable regulatory authorities for our product candidates, and any related restrictions, limitations or warnings in the label of an approved product candidate;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates, development platform and the type of such protection;

- our ability and the potential to successfully manufacture our product candidates for preclinical studies, Clinical Studies and Clinical Trials and for commercial use, if approved;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets, either alone or in combination with others;
- the rate and degree of market acceptance of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to enter into a collaboration, partnership, or other agreement with a third party on reasonable terms or at all to develop one or more product candidates or commercialize any of our product candidates, if approved;
- our ability to secure sufficient manufacturing and supply chain capacity;
- the success of competing products or therapies that are or may become available;
- our ability to attract and retain key scientific, management or other necessary personnel;
- our estimates regarding expenses for both product development and as a public company, future revenue, capital requirements and needs for additional financing;
- the potential for faults in our internal controls;
- the effect of the COVID-19 outbreak on any of the foregoing; and
- other risks and uncertainties, including those discussed in Part I, Item 1A, Risk Factors in this Annual Report.

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other 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 these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part I, Item 1A, Risk Factors and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. 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.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Annual Report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

PART I

Except where the context otherwise requires or where otherwise indicated, the terms "Axcella," "Axcella Health," "we," "us," "our," "our company," "the company," and "our business" refer to Axcella Health Inc. and its consolidated subsidiary.

Item 1. Business

Overview

We are a clinical-stage biotechnology company focused on leveraging endogenous metabolic modulators, or EMMs, to pioneer a new approach for treating complex diseases and improving health. Our product candidates are comprised of multiple EMMs that are engineered in distinct combinations and ratios with the goal of simultaneously impacting multiple biological pathways. Our pipeline includes lead therapeutic candidates for non-alcoholic steatohepatitis, or NASH, and the reduction in risk of overt hepatic encephalopathy, or OHE, recurrence. Additional muscle- and blood-related programs are in earlier-stage development.

Using our development platform, we have efficiently designed a pipeline of product candidates that are comprised of amino acids and their derivatives. These orally administered compositions are designed to have the potential for multifactorial effects, and their constituents have a general history of safe use.

Once we design a product candidate, we decide whether to initially evaluate it in (i) a non-investigational new drug application, or non-IND, Institutional Review Board, or IRB, approved clinical study under U.S. Food and Drug Administration, or the FDA, regulations and guidance supporting research with food (as noted herein, the term food also includes dietary supplements) or (ii) in a clinical trial under an IND. In this Annual Report, we refer to our non-IND Clinical Studies as "Clinical Studies" and our planned IND-enabled Clinical Trials as "Clinical Trials." A Clinical Study allows us to evaluate a product candidate's safety, tolerability and permissible secondary endpoints (e.g. impact on normal structures and functions of the body, including metabolic pathways), before we determine the next steps in its development. Our Clinical Studies are conducted at reputable medical centers following Good Clinical Practices, or GCPs, including IRB approval and monitoring, by qualified investigators, including key opinion leaders in their fields. Subsequent development options for a product candidate we initially investigate in a Clinical Study include but are not limited to conducting future research in a Clinical Trial for an identified therapeutic indication, continuing research in another Clinical Study, out-licensing the product candidate, or terminating development.

In 2018, we completed three Clinical Studies. In all three studies, our product candidates were found to be generally well tolerated, and we generated structure and function biomarker data suggesting clinically relevant changes in liver and muscle metabolic pathways. We believe our ability to generate these human data at an early stage of development via initial Clinical Studies (i) significantly reduces the translational uncertainty typically seen when transitioning from animal studies to human studies, (ii) enables us to make high-insight, capital-efficient product candidate development decisions and (iii) for product candidates we initially research in Clinical Studies and subsequently decide to investigate for potential therapeutic indications, increases their probability of Clinical Trial success.

We currently have three Clinical Studies underway:

- AXA1665-002: A placebo-controlled, randomized, parallel-arm study assessing the impact of two doses of AXA1665 on safety, tolerability and structure/function secondary endpoints in approximately 60 subjects with mild and moderate hepatic insufficiency;
- AXA1125-003: A placebo-controlled, randomized, parallel-arm study assessing the impact of AXA1125 and two doses AXA1957 on safety, tolerability and structure/function secondary endpoints in approximately 105 adult subjects with non-alcoholic fatty liver disease, or NAFLD; and
- AXA4010-001: A sequential and staged cohort study assessing the impact of AXA4010 on safety, tolerability and blood structure/function secondary endpoints in approximately 24 subjects (up to 16 adults and eight adolescents) with sickle cell disease.

In March 2020, as a result of resource reallocations at clinical sites from clinical studies and trials toward COVID-19 detection and treatment, enrollment and dosing in our AXA1957-002 pediatric Clinical Study was temporarily suspended. AXA1957-002 is a placebo-controlled, randomized, parallel-arm Clinical Study assessing the impact of one dose of AXA1957 on safety, tolerability and structure/function secondary endpoints in approximately 30 adolescent subjects with fatty liver.

Based in part on our Clinical Study results to date, along with other relevant information, in 2019, we decided to pursue future development for AXA1665 and AXA1125/AXA1957 in Clinical Trials, subject to data readouts from ongoing Clinical Studies and FDA allowance of INDs, to study their potential to modulate key pathogenic pathways associated with OHE and NASH. As a result, in 2019 we declared AXA1665, AXA1125 and AXA1957 as our first therapeutic product candidates. We have yet to make a development decision for our other product candidates, AXA2678 and AXA4010.

On March 6, 2019, we had a face-to-face pre-IND meeting with the FDA for AXA1665 during which we discussed clinical endpoints, assessment tools and other matters relating to a potential IND-opening Clinical Trial for AXA1665 in the complications of cirrhosis, including hepatic encephalopathy, or HE, and sarcopenia or muscle wasting in cirrhosis. Based on FDA comments received at this meeting, we believe that additional toxicology work would not be required prior to commencing a Clinical Trial for AXA1665. Assuming supportive data from our ongoing Clinical Study of AXA1665 and FDA feedback, we plan to initiate a potential Phase 2b/3 registrational Clinical Trial in the fourth quarter of 2020. We anticipate interacting with the FDA again in 2020 prior to a formal IND submission for AXA1665.

About Endogenous Metabolic Modulators (EMMs)

EMMs encompass a broad set of molecular families, including amino acids, bile acids other intermediary substrates and hormones. Together, these molecules can serve as master regulators and signaling agents, driving multiple pathways to elicit multifactorial effects that integrate basic cellular functioning to impact fundamental biologies. Such biologies include cellular bioenergetics (e.g., tricarboxylic acid cycle and electron transport chain), nutrient handling (e.g., de novo lipogenesis, or metabolic formation of fat, gluconeogenesis, or the generation of glucose from certain non-carbohydrate carbon substrates, and proteogenesis, or protein formation), nutrient sensing via master regulators (e.g., via mammalian target of rapamycin, or mTOR, 5' AMP-activated protein kinase, or AMPK, fibroblast growth factor 21, or FGF21, and peroxisome proliferator-activated receptors, or PPARs), immune response and inflammation, reactive oxygen response, vascular function, neurotransmitter signaling, tissue repair, and autophagy.

Metabolic dysregulation results from a disruption in human homeostasis that is core to optimal functioning and consequently, health. Maintenance of this equilibrium requires an orchestration of multiple metabolic pathways and inter-organ signaling, evolved over billions of years, and is carried out by signaling intermediates and endogenous mediators. EMMs are a critical subset of such endogenous elements that regulate metabolic function.

The loss of homeostasis can be manifested in many conditions and complex diseases, including Type 2 diabetes, or T2D, NASH/NAFLD, and muscle atrophy. As an example, dysregulation in the metabolic processes and pathways controlled by the liver such as de novo lipogenesis or gluconeogenesis can lead to an inability to adequately handle fuel substrates such as fats or carbohydrates. This ultimately results in fatty liver, insulin resistance and buildup of toxic waste products, such as ammonia. Similarly, a complex cascade of fuel dysregulation within skeletal muscles, a key organ involved in glucose disposal and utilization of amino acids as substrates for protein synthesis, can result in insulin resistance, intramuscular fat infiltration and muscle mass loss, thus decreasing muscle function. Muscle mass loss, or sarcopenia, is increasingly recognized as a critical determinant of end organ function linked to clinical outcomes and overall survival, such as in end-stage liver disease (cirrhotic sarcopenia) or in end-stage renal disease (uremic sarcopenia).

Consequently, restoring homeostasis and healthy metabolism benefits from a multifactorial approach. We believe that our EMM compositions have the potential to address systems-wide metabolic dysregulation to restore, improve, support and/or maintain homeostasis. In recent decades, extensive data have been generated demonstrating amino acids' role as fundamental building blocks of life. More recently, their roles in nutrient sensing and cellular signaling have been elucidated not only with individual amino acids, such as a leucine sensor on mTOR, but also in combinations. Additionally, amino acids have a long history of general safe use in foods and dietary supplements. We believe our approach in developing EMM compositions has the potential to bring about a transformation in treating complex diseases and/or supporting health.

Our EMM Composition Design and Nonclinical Research Approach

Design Approach

Our development platform allows us to efficiently design and test EMM compositions that simultaneously target multiple biologies and metabolic pathways. This platform integrates advanced analytics of metabolic regulation and dysregulation to interrogate data in our proprietary databases, which we refer to as Axcella Database, or AxcellaDB, and Axcella Knowledge Base, or AxcellaKB. Our human primary cell systems also directly test the multiple biologies that are particularly disease-related and drive metabolic dysregulation. All of this is supported by what we believe to be the world's leading EMM safety database. The data and learnings generated through this process further inform our design methodology, increasing our development platform's efficiency for the development of subsequent product candidates.

AxcellaDB, our proprietary database, synthesizes a combination of data from published scientific and medical literature, our in vitro models, and our human Clinical Studies. Through advanced analytics, we investigate novel, causal connections among EMMs, biology, health and disease. We believe this enables us to take a systems biology approach to product candidate discovery and development. Ultimately, we envision utilizing AxcellaKB and its internal machine learning capabilities to identify EMM compositions, predict their effects on biology and identify new target areas for our platform.

Nonclinical Research

We test EMM compositions and hypothesized synergies in normal and disease-specific human primary cell models. We conduct our model systems in environments that aim to simulate physiological levels of biofluids and nutrients. These models include multiple cell types that we use to deconstruct dysregulated metabolism or disease conditions to isolate effects of EMM compositions on subsets of metabolic pathways. The throughput of these models enables us to test product candidates as well as combinations of the individual constituents to identify and better understand their interactions.

Pharmacokinetic, or PK, literature, experiments and modeling inform our EMM compositions (i.e. amounts and ratios). We are able to evaluate EMM plasma exposure, supra-physiological exposures, windows of exposure administration amounts, the characterization of critical PK behaviors across molecule classes, and the implications of physiological compartmental distribution. We believe these data can be used to refine product candidate designs.

Our Clinical Approach and Development Path Decision Making

Once a product candidate is designed, we then decide whether to evaluate the candidate in a Clinical Study or under a Clinical Trial. To date, we have initially conducted clinical investigations of our product candidates in Clinical Studies. Going forward, we may conduct initial clinical investigations of future product candidates under Clinical Trials.

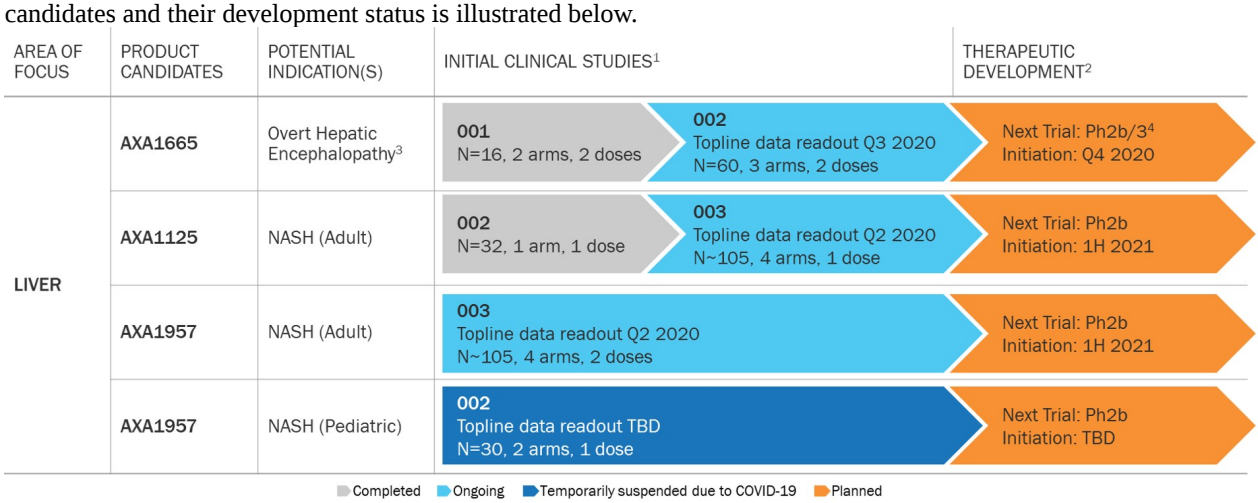
We conduct our Clinical Studies under the FDA's September 2013 Guidance for Clinical Investigators, Sponsors, and IRBs entitled "Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND ," which we believe allows for Clinical Studies to be conducted to assess a food product's safety, tolerability and effect on normal structures or functions in humans in healthy and diseased subjects. Our current product candidates comprise amino acids and their derivatives, which may be deemed generally recognized as safe (GRAS) when used in Clinical Studies. We select the amounts of the amino acids and derivatives used in our product candidates based upon doses previously found in third-party clinical studies and third-party clinical trials to be tolerable with no significant safety concerns. Therefore, we believe we can study our product candidates in Clinical Studies as food and dietary supplements. See "*FDA regulation of conventional food*" for further information.

Our Clinical Studies include a substantial number of biomarkers that may inform biologies relevant to the healthy structures and functions of the body but are not designed or intended to evaluate a product candidate's ability to diagnose, cure, mitigate, treat or prevent a disease or other health condition. They are conducted at reputable medical centers following GCPs, including IRB approval and monitoring, by qualified investigators, including key opinion leaders in their fields. Using a combination of data from these Clinical Studies and/or other relevant information, we decide whether to advance the product candidate's development in a therapeutic path under a Clinical Trial, further research the product candidate in another Clinical Study, out-license commercialization rights to the product candidate, or terminate its development. We may decide to partner with other companies in the development or commercialization of our product candidates.

In 2019, we determined that our lead compounds, AXA1665, AXA1125 and AXA1957, will be pursued as therapeutic product candidates, meaning that subject to final data readouts from ongoing Clinical Studies and FDA allowance of INDs, any future assessment of these product candidates will be made in Clinical Trials. These Clinical Trials would therefore be designed to evaluate each product candidate's ability to diagnose, cure, mitigate, treat or prevent targeted diseases (OHE for AXA1665 and NASH for AXA1125 and AXA1957).

Our Therapeutic Pipeline

We have developed a wholly-owned therapeutic pipeline currently consisting of three product candidates. An overview of these product candidates and their development status is illustrated below.



1. Initial Clinical Studies refers to Non-IND Clinical Studies initiated prior to a development path decision.
2. Planned Clinical Trial, contingent upon final data readouts from ongoing Clinical Studies and allowance by the FDA.
3. Indication expected to be reduction in risk of overt hepatic encephalopathy recurrence.
4. We believe that this has the potential to serve as a registrational Clinical Trial, contingent upon final data readout from ongoing Clinical Study and allowance by the FDA.

AXA1665 for the Reduction in Risk of Overt Hepatic Encephalopathy (OHE) Recurrence

The initial proposed indication for an AXA1665 Clinical Trial is expected to be for the reduction in risk of OHE recurrence in adult patients with liver cirrhosis. We expect the proposed primary endpoint for our Clinical Trial to be time to breakthrough episode of OHE. We expect our proposed key secondary endpoints to be assessments related to physical function. We expect to discuss our proposed trial design and endpoints with the FDA in 2020.

About OHE and Cirrhosis

Long-term damage to the liver from various causes, such as alcohol, hepatitis B or C viral infections, NASH or autoimmune hepatitis, can lead to permanent scarring, a condition called cirrhosis. Prevalence of cirrhosis in the United States is approximately 0.27%, corresponding to approximately 633,000 adults, of which 69% reported that they were unaware of having liver disease. Decompensated cirrhosis is a serious systemic disease with multi-organ dysfunction, resulting in a variety of significant complications, including HE, bacterial infections, gastrointestinal bleeding, renal impairment and ascites, which is the build-up of excess fluid in the abdomen. Transition from compensated cirrhosis to decompensated cirrhosis occurs at a rate of approximately 5% to 7% per year.

HE is one of the most common complications of cirrhosis with multiple contributing factors, such as amino acid imbalance, ammonia toxicity, muscle wasting, infections and constipation, all of which ultimately result in diminished brain function. Emerging data suggest that muscle mass and function are key independent factors associated with progression to and severity of HE. It is estimated that up 40% to 60% of cirrhosis subjects have sarcopenia and, separately, 40% have HE symptoms. OHE refers to the presence of neurological abnormalities that are clinically apparent and do not require specialized psychometric testing. By contrast, minimal, or covert, HE is less severe and requires specialized testing for its diagnosis, including psychometric tests. OHE is well-established as a significant cause of morbidity and mortality in the cirrhotic population and is an area that continues to have unmet medical needs.

Furthermore, muscle depletion and muscle fat infiltration occurring during cirrhosis independently increase the risk of both overt and minimal HE with increased mortality. Decline in muscle mass can also hamper the alternative pathway of ammonia detoxification, and hyperammonemia may further worsen sarcopenia, generating a vicious cycle. The highly interdependent complications of cirrhosis, sarcopenia and HE, constitute a significant disease burden and can have an impact on irreversible morbidity and mortality in cirrhotic patients. We estimate that approximately 63,000 to 130,000 individuals may be affected at any given time with both cirrhotic sarcopenia and OHE in the United States.

While there are three approved therapies for HE, there is still a need for additional HE treatment options, particularly those that have the potential to address the systemic complications of cirrhosis, including frailty.

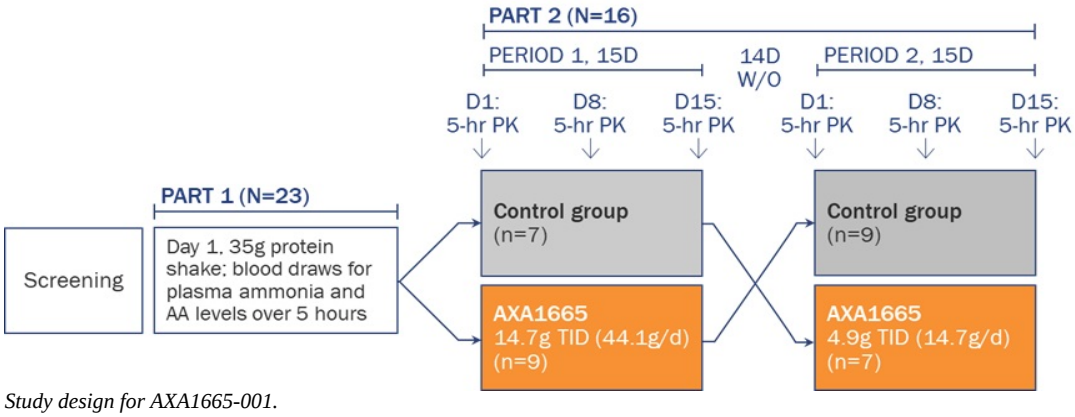
Design of AXA1665

AXA1665 is a composition of eight amino acids and derivatives that is designed to target multiple metabolic pathways intersecting key organ systems (liver, muscle and gut) key to support and maintain liver health.

Underlying Biology	**AXA1665 Design Objectives**
Plasma amino acid imbalance	Maximize proteogenesis and reduce systemic aromatic amino acids
Dysregulated ammonia handling	Stimulate urea cycle function, intestinal and renal nitrogen metabolism, and induce intramuscular ammonia detoxification
Muscle wasting	Increase muscle protein synthesis by addressing metabolic demand and stimulating mTORC1

Completed Clinical Study AXA1665-001

AXA1665-001 was a two-part, 15-day controlled crossover Clinical Study with 23 adult subjects designed to assess AXA1665's safety, tolerability and impact on normal liver structure and function in subjects with mild and moderate hepatic insufficiency (Child-Pugh Class A and B). The study included two doses of AXA1665 (44.1g/day and 14.7g/day).



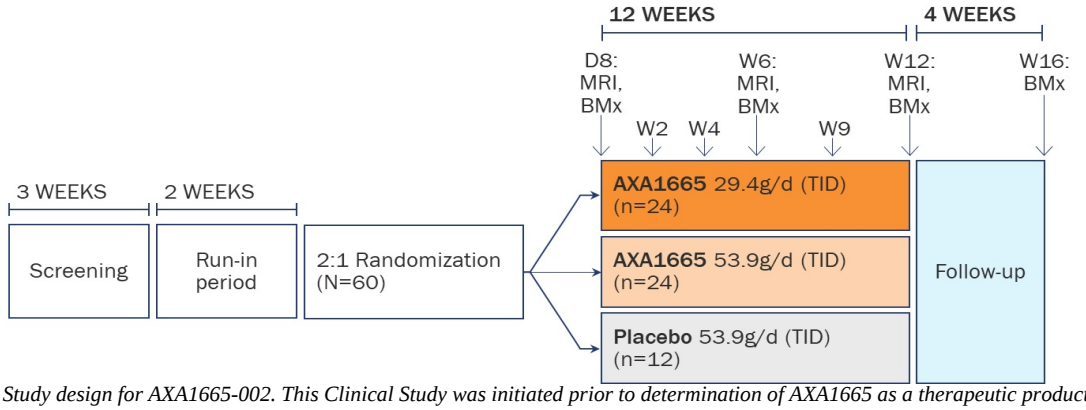
Study design for AXA1665-001.

AXA1665 was found to be generally well tolerated in the study. There were no product-related adverse events, or AEs, observed in Part 1 of the study. No AEs were serious or led to discontinuation from the study. There were five AEs, specifically neck pain, posterior shoulder pain, gastroesophageal reflux disease, or GERD, rib pain and headache, observed in four subjects in Part 2, all of which were considered unlikely to be related to AXA1665. All of the AEs resolved spontaneously, including GERD, which self-resolved within a day. There were no clinically significant changes in vital signs, ECGs or standard safety clinical laboratory parameters.

Most AXA1665 constituent amino acids, or AAs, demonstrated dose-dependent systemic exposures. At Day 15, fasted Fischer (branched-chain AA to aromatic AA) and valine-to-phenylalanine ratios, or FR and VPR respectively, dose-dependently increased (AXA1665 14.7g three times per day, or TID, control-adjusted change: 44.3±2.7% and 47.2±3.9%, respectively; $p<0.0001$). Despite provision of additional nitrogen with AXA1665 14.7g TID, mean fasted plasma ammonia concentration at Day 15 decreased by 21.1% versus 3.8% (control). AXA1665 14.7g TID produced a leaner body composition (decreased percentage body fat and increased percentage lean body mass) coupled with significantly decreased Liver Frailty Index, or LFI, at Day 15 versus control (−0.70±0.15 vs −0.14±0.17; $p<0.05$).

Ongoing Clinical Study AXA1665-002

AXA1665-002 is an ongoing 12-week (with a four-week follow-up) randomized, placebo-controlled Clinical Study to assess AXA1665's safety, tolerability and impact on normal liver and muscle structures and functions in approximately 60 subjects with mild (Child A) and moderate (Child B) hepatic insufficiency.



Study design for AXA1665-002. This Clinical Study was initiated prior to determination of AXA1665 as a therapeutic product candidate.

The assessments in AXA1665-002 include:

Primary	
Safety & tolerability	Clinical AEs, vital signs, ECGs, clinical laboratory parameters, including standard chemistry and hematology panels, plasma ammonia, albumin, total protein and other liver function tests
Secondary	
PK of AXA1665 constituents and endogenous amino acid levels Physiological assessments	FR* and VPR* Normal Structure • Body composition via MRI to assess lean and fat mass compartments, including thigh muscle volumes, intramuscular fat Normal Function • Physical (LFI*; gait speed) • Cognitive (Stroop test; PHES; CFF) • Health-related questionnaires

** FR, VPR and LFI are believed to have prognostic significance in subjects with cirrhosis and end-stage liver disease based on emerging scientific literature. PHES = psychometric hepatic encephalopathy score; CFF = critical flicker frequency.*

Enrollment in AXA1665-002 was completed in February 2020, and AXA1665 continues to be generally safe and well tolerated through week 12 to date. Top-line data from this Clinical Study is anticipated in the third quarter of 2020.

AXA1125 and AXA1957 for Nonalcoholic steatohepatitis (NASH)

Given the significant unmet need in NASH, the data that we generated from our non-clinical studies and Clinical Studies and the potential of multifactorial interventions using EMMs in liver disease, we made the decision in 2019 to develop AXA1125 and/or AXA1957 as therapeutic candidates for NASH. As such, our intent is to conduct any subsequent clinical investigations of these product candidates under IND, subject to final data readouts from ongoing

Clinical Studies and input from the FDA. Following the completion of our AXA1125-003 Clinical Study, we expect to engage with the FDA to discuss next steps in this program.

About NAFLD and NASH

We anticipate seeking an initial indication for AXA1125 and/or AXA1957 for the treatment of noncirrhotic NASH. While the pathologies of NAFLD and NASH manifest primarily in the liver, they are systemic diseases driven by multifactorial systemic dysregulation of pathways associated with metabolism, inflammation and fibrosis. Dysfunctional lipid metabolism associated with insulin resistance and hepatocyte lipotoxicity increases liver cell death. Systemic and chronic inflammation at the cellular and cytokine level drives tissue damage and activates fibrogenic pathways. Activation of stellate cells then causes accumulation of collagen in the liver and leads to progressive fibrosis.

NAFLD is one of the most common causes of liver disease in the United States. It is characterized by excess fat accumulation in the liver, typically resulting from obesity, insulin resistance and diabetes. NAFLD in children is often more severe than in adults.

NAFLD can progress to NASH, which is characterized by necroinflammation and fibrosis, and may ultimately lead to life-threatening conditions such as cirrhosis or liver cancer, requiring liver transplant. With a U.S. prevalence of over 15 million people and a similar prevalence in the five major European countries (France, Germany, Italy, Spain and the United Kingdom), NASH represents a substantial public health issue and a substantial burden on the overall healthcare system. Incidence is expected to continue increasing in parallel with the obesity and T2D epidemics.

A combination of dietary modifications and increased physical activity remains the standard of care for management of NAFLD and NASH. Currently, there are no approved drug therapies for NASH.

The potential exists for the first U.S. approval of a NASH therapy, obeticholic acid, or OCA, in 2020, and other potential therapies are in various earlier stages of development. To date, most compounds in development have focused on single key targets within metabolic, inflammation or fibrosis pathways. Few, however, have demonstrated statistical significance in the FDA's approved endpoints, which are steatohepatitis resolution with no worsening of fibrosis or improvement in liver fibrosis with no worsening of steatohepatitis. As a result, clinicians and biopharmaceutical companies are increasingly evaluating combination approaches to address the broad spectrum of the disease, improve response rates and expand the size of the treatable population. Significant challenges to this approach include the potential compounding of overlapping side effect profiles and high development and treatment costs.

Additionally, there are no approved pharmacologic treatments and few pipeline programs targeting pediatric NASH. Recommended treatment guidelines for this population currently center around lifestyle interventions.

Design of AXA1125 and AXA1957

AXA1125 is a product candidate that contains six amino acids and derivatives. AXA1957 is a product candidate that contains seven amino acids and derivatives. Both product candidates were designed to target multiple metabolic pathways intersecting key organ systems (liver, muscle and gut) to support and maintain liver health. We believe they may ultimately have the potential to impact hepatic histology by simultaneously influencing multiple pathways that affect metabolism, inflammation and fibrogenesis as summarized in the table below.

Underlying Biology	AXA1125/1957 Design Objectives
Metabolism	Lower lipotoxicity, improve insulin sensitivity and maximize mitochondrial function by enhancing fatty acid beta-oxidation via activation of pathways such as PPARα and AMPK
Inflammation	Modulate apoptosis, macrophage function, reduce hepatic inflammatory mediators and improve gut epithelial integrity
Fibrosis	Reduce hepatic stellate cell activation and proliferation and decrease hepatic fibrogenesis by downregulating certain pathways, including TGFβ and Hif1α

Completed Clinical Study AXA1125-001

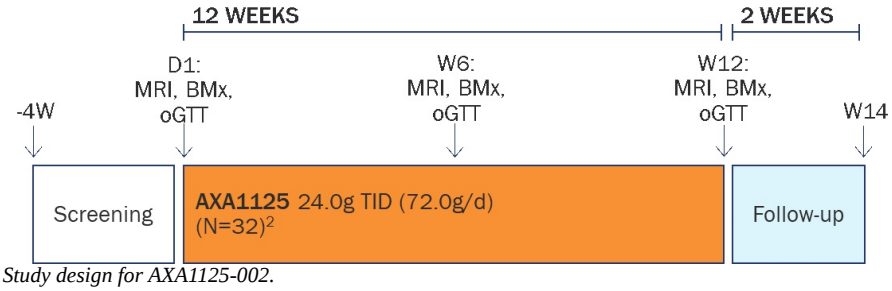
AXA1125-001 was a two-part Clinical Study to assess safety, tolerability and to secondarily explore pharmacokinetics of AXA1125 in normal healthy adult subjects. Part 1 included ten subjects administered a single 24g amount of AXA1125 either 30 minutes before meal (fasted), 30 minutes after meal (fed) or two hours after meal (fed) to assess the effect of meal timing on plasma concentration and exposure of AXA1125 amino acid constituents. Part 2 included ten subjects administered 24g TID (72g/day) for six weeks to assess the safety and tolerability at these amounts over this duration in healthy subjects.

In both Parts 1 and 2, we did not observe any significant safety issues with AXA1125, and it was generally well tolerated with no clinically significant changes in clinical laboratory values, vital signs or ECGs. There were no product-related AEs in Part 1. In Part 2, mild gastrointestinal symptoms of abdominal pain, distention and diarrhea were noted in three of ten subjects that was considered by the study investigator to be study product-related. All AEs were transient, self-limited and resolved with no intervention, and none were serious or led to discontinuation.

The PK data suggested normal PK of the complex amino acid mixture with all of the constituents achieving supra-physiologic concentrations as well as no meaningful impact of meal timing on the amino acid profiles. Average peak amino acid plasma concentrations, or Cmax, and total exposure, or AUC, values were generally similar (within 20% to 30%) and sequentially increased with each AXA1125 consumption regardless of meal timing, with the exception of glutamine. Consumption of AXA1125 in the fed state, either 30 minutes or two hours after a meal, resulted in a 1.1 to 2.5-fold increased AUC of glutamine relative to when AXA1125 was consumed in the fasted state.

Completed Clinical Study AXA1125-002

AXA1125-002 was a pilot single-arm, open-label, 12-week (with a two-week follow-up) multicenter Clinical Study designed to assess the safety, tolerability and normal liver structure and function impact of AXA1125 24g TID (72g/day) in 32 NAFLD adult subjects with T2D.



Study design for AXA1125-002.

All 32 subjects were included in the safety analysis as all received at least one dose of AXA1125. There were four subjects who received AXA1125 6g TID. A subgroup (n=23) was examined who (i) had received the intended amount of AXA1125 (i.e. 24g TID), (ii) had >10% liver fat at baseline (day 1) by magnetic resonance imaging based assessment of proton density fat fraction (MRI-PDFF), and (iii) were compliant and met all the protocol requirements, i.e. the per protocol group.

We did not observe any significant safety issues with AXA1125, and it was generally well tolerated. Among subjects who received at least one dose of AXA1125, the most common product-related AEs were diarrhea in seven (21.9%) subjects, and headaches in five (15.6%) subjects, which were all mild or moderate. There were two serious AEs reported, acute cholecystitis and right toe infection, which were deemed not to be reasonably associated with the study product, and more likely due to subject's preexisting conditions as these complications are quite common with underlying obesity and T2D. Of the four discontinuations from the study due to AEs, none were related to study product. There were no clinically significant abnormalities in physical examination, vital signs, ECG, and in standard clinical safety laboratory (chemistry and hematology) parameters over the course of the 12-week duration.

Only basal (fasted) levels of amino acids were measured in this study. The average plasma concentration of the individual amino acid constituents within AXA1125 in all subjects receiving 24g TID AXA1125 in the basal state (i.e., before ingestion of AXA1125) was not meaningfully changed over 12 weeks as compared to their corresponding baseline (Day 1) levels.

The biological effects of AXA1125 were analyzed on the per-protocol group (as defined above), and the findings are summarized below. Actual observation values for each biomarker at each time point are reported versus imputation of the last observation carried forward, or LOCF.

Metabolism

Lipotoxicity and insulin resistance are generally regarded as metabolic drivers of NAFLD. AXA1125 24g TID administration for 12 weeks tended to decrease the mean liver fat content. In the per protocol group, mean liver fat by PDFF was 18.0% (n=22), 14.8% (n=17) and 13.4% (n=13) at baseline, week 6 and week 12, respectively. Similar directional trends were seen with homeostatic model assessment-insulin resistance, or HOMA IR, with mean HOMA IR of 7.4 (n=22), 3.9 (n=13) and 4.9 (n=14) at baseline, week 6 and week 12, respectively. Effects on liver fat were observed without any accompanying body weight changes despite the provision of approximately 496 additional calories per day via AXA1125 administrations. Subjects did not drastically alter their usual dietary or physical activity patterns during the 12-week study period as assessed by subject food and physical activity diaries. Thus, the observation of body weight neutrality under these circumstances suggests a likely change in nutrient utilization, implicating increased fat oxidation. Assessment of the fasting lipid profile revealed no changes in mean serum levels of total cholesterol, HDL-C, and nonesterified fatty acids, with trends toward slight decreases in LDL-C and triglyceride, or TG, levels. However, beta hydroxybutyrate, or BHB, tended to directionally increase as compared to the corresponding mean pre-administration baseline levels, suggestive of a mild-to-moderate ketotic state. A systematic plasma lipidomic profiling demonstrated a tendency to up-regulate acylcarnitines, a marker of mitochondrial fatty acid oxidation, and downregulate toxic lipid species such as ceramides, sphingomyelins and long-chain TGs. Taken together, we believe these results suggest that AXA1125 over 12 weeks tended to impact lipid handling (lowered liver fat and raised BHB).

Inflammation

After 12 weeks of AXA1125 24g TID administration, there were decreased trends in the mean alanine aminotransferase (ALT) levels. In the per protocol group, the mean ALT (expressed as IU/L) was 47.3 (n=22), 36.9 (n=14) and 32.1 (n=13) at baseline, week 6 and week 12, respectively. Similar directional changes were seen in mean monocyte chemoattractant protein-1 levels (expressed as pg/mL): 305 (n=19), 209 (n=12), and 234 (n=10) at baseline, week 6 and week 12, respectively. The M65 subunit of cytokeratin-18 (expressed as U/L) also declined over the 12-week treatment duration: 884 (n=22), 475 (n=14), and 503 (n=14) at baseline, week 6 and week 12, respectively.

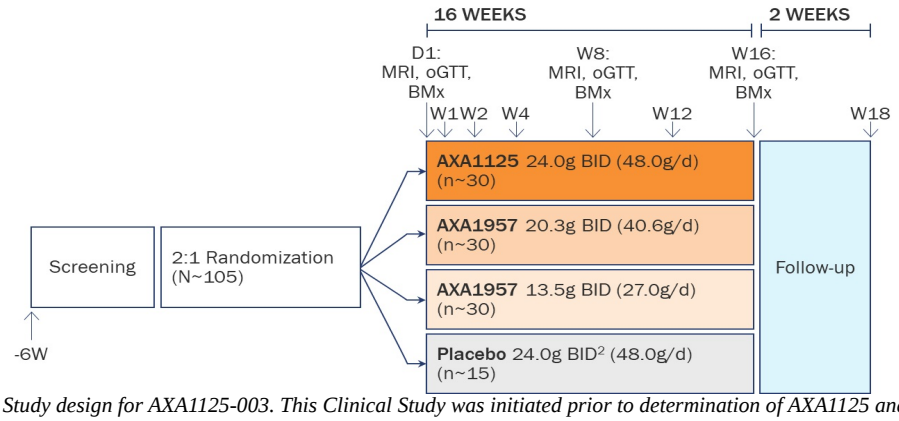
Fibrosis

Change in a key hepatic fibrogenic marker, Pro-C3 (N-terminal type III collagen propeptide), was assessed after 12 weeks of AXA1125 24g TID administration in the per protocol group. Mean pro-C3 (ng/mL) was 21.6 (n=22), 17.7 (n=14), and 16.9 (n=18) at baseline, week 6, and week 12, respectively. We believe changes in the pro-collagen markers were specific to those that indicate a change in hepatic fibrogenesis (i.e., Pro-C3) versus a more generalized change in collagen metabolism, because total procollagen type 1 N-terminal propeptide, or P1NP, considered to be a sensitive marker of bone turnover was not affected by AXA1125. We believe these observations suggest that AXA1125 may selectively impact hepatic fibrogenesis.

Overall, we believe the weight of evidence from these initial results support the directional consistency of changes across both the structural and functional markers associated with liver health. These encouraging results prompted us to design and embark on a randomized placebo-controlled clinical study in a population of NAFLD subjects enriched using noninvasive biomarkers and to further study safety, tolerability and normal structure and function impact.

Ongoing Clinical Study AXA1125-003

AXA1125-003 is an ongoing 16-week (with a two-week follow-up), randomized, single-blind, placebo-controlled, Clinical Study to assess safety, tolerability and impact on the liver structure and function of AXA1125 and AXA1957 in approximately 105 adult subjects with NAFLD. Key inclusion criteria for this study included having at least 10% fat by MRI-PDFF and a corrected T1, or cT1, a measure of liver injury by multiparametric MRI, of at least 830 mSec. Randomization was stratified by the presence or absence of T2D. In this study, subjects receive either AXA1125, two different doses of AXA1957 or a calorie-matched placebo control twice a day, or BID (see figure below). Enrollment of 102 subjects in this study was completed in late 2019.



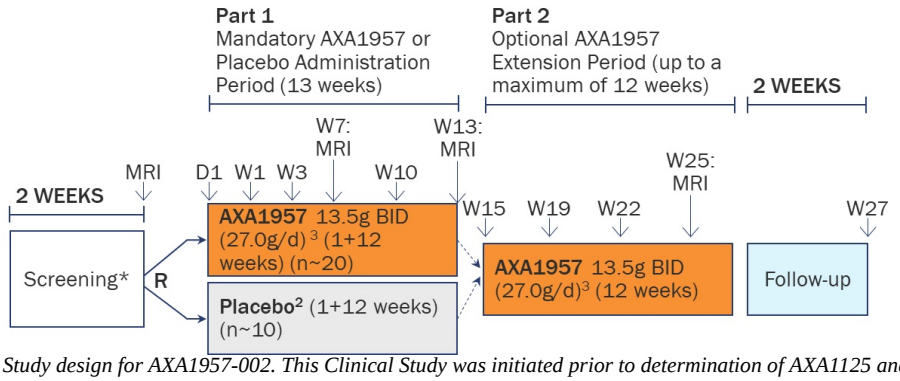
Study design for AXA1125-003. This Clinical Study was initiated prior to determination of AXA1125 and AXA1957 as therapeutic product candidates.

Completion of enrollment in this study was announced in October 2019. In January 2020, we announced positive interim findings from this ongoing study. This interim analysis included data from approximately half of the study population through the full 16 weeks of administration. The analysis showed that AXA1125 and both doses of AXA1957 have been well tolerated to date. Additionally, both AXA1125 and AXA1957 demonstrated clinically relevant responses and directional changes on the three biological nodes: metabolism (MRI-PDFF and HOMA-IR), inflammation (ALT, CK-18, cT1) and fibrogenesis (proC3). The onset of response in some biomarkers was seen as early as the eight-week post-baseline assessment with continued improvement through 16 weeks. We anticipate reporting top-line data from this study in the second quarter of 2020.

Clinical Study AXA1957-002

AXA1957-002 is a placebo-controlled, single-blind, randomized (2:1) controlled Clinical Study to assess safety and tolerability and the physiological impact of AXA1957 on the normal structures and functions of the liver in approximately 30 adolescent (12-17 year old) subjects with NAFLD. Key inclusion criteria include at least 10% liver fat by MRI-PDFF and a cT1 of > 820 mSec. Subjects are stratified by the presence or absence of T2D. This is among the few clinical programs undertaken to date in a population of adolescent subjects with NAFLD.

As a result of resource reallocations at clinical sites involved in AXA1957-002 from clinical studies and trials toward COVID-19 detection and treatment, enrollment and dosing in this Clinical Study was temporarily suspended in March 2020. We continue to view pediatric NASH as a significant area of unmet need and, utilizing the information gathered thus far from AXA1957-002 and the expected top-line data readout from AXA1125-003, we expect to provide an update on our plans for this program at a future date.



Study design for AXA1957-002. This Clinical Study was initiated prior to determination of AXA1125 and AXA1957 as therapeutic product candidates.

Our Early-Stage Pipeline

AXA4010

Overview

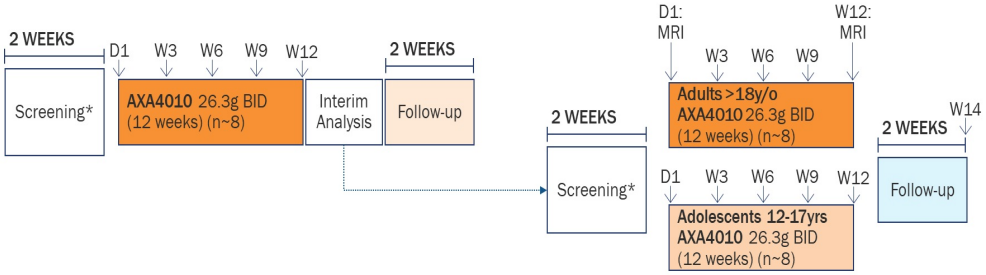
We believe that EMMs have the potential to support and maintain blood health, which is critical to a multitude of metabolic functions throughout the body. Using insights from our Clinical Studies with our other product candidates, cell-based studies of novel EMM compositions, published clinical studies of amino acid interventions on blood physiology, published and in-house metabolic profiling data, and published mechanistic understanding of blood health, we identified key metabolic pathways where we believe amino acid biologies drive key aspects of normal blood health.

AXA4010 is a product candidate that contains 10 amino acids and derivatives in distinct ratios. This product candidate was designed to target multiple biological pathways with the goal of supporting normal structures and functions of the blood.

Underlying Biology	AXA4010 Design Objectives
Blood production & integrity	Promote proliferation and maturation of blood cells during hematopoietic demand Maintain red blood cell, or RBC, form and function against dehydration, rigidity and support oxygen transport; prevent RBC membrane deformability
Plasma and RBC amino acid imbalance	Restore amino acid balance to support RBC metabolism, including substrates for glutathione and nitric oxide synthesis, improve reactive oxygen species and delivery of amino acids to peripheral tissue
Vascular health & inflammation	Defend against vascular adhesion, inflammation and vascular stasis

Ongoing Clinical Study AXA4010-001

AXA4010-001 is an ongoing Clinical Study that is expected to enroll up to 24 subjects ages 12 and older in a staged sequential design of three separate cohorts each for up to 12 weeks (see study design below).



Study design for AXA4010-001.

In addition to safety and tolerability, the study will assess the effects of AXA4010 on normal blood structure and function, including hemolysis, inflammation and vascular physiology. The first cohort will consist of eight adult subjects with sickle cell disease, or SCD, to test whether AXA4010 can impact normal blood and vascular function. Subsequently, additional adult subjects as well as adolescent subjects may be enrolled into the study. SCD is a chronic hemolytic anemia that is associated with inflammation and metabolic derangements that include nitric oxide depletion and oxidative stress. As a result, we believe SCD is an appropriate biological model in which to study AXA4010's potential impact on multiple aspects of blood health. We currently anticipate a data readout from Cohort 1 of this study in the fourth quarter of 2020.

Potential Development Paths for AXA4010

If we were to decide to develop AXA4010 under an IND development path, a potential target indication could be SCD. SCD is an inherited disorder of hemoglobin affecting approximately 100,000 individuals in the United States and 4.4 million worldwide. For many patients, SCD is defined by chronic organ failure punctuated by acute complications and early mortality. Despite the recent approvals of two new therapeutic agents for SCD, voxelotor and crizanlizumab, significant medical needs still remain to adequately address the sequelae of SCD complications due to its inherently complex and multifactorial etiopathogenesis.

If we were to decide to develop AXA4010 as a non-drug product candidate, the target market would be defined by, or with input from, a strategic partner. We believe a non-drug pathway could also represent a significant market opportunity given the potential benefits to overall health by supporting blood health and modulating inflammation. Under a non-drug development path, we or a strategic partner may decide to develop AXA4010 as a dietary supplement to support blood-related structure and function.

AXA2678

Overview

We believe that EMMs have the potential to support and maintain muscle health. Using insights from cell-based studies of novel EMM compositions, published clinical studies of amino acid interventions on muscle physiology, published and in-house metabolic profiling data, and published mechanistic understanding of muscle health, we identified key metabolic pathways where we believe amino acid biologies drive key aspects of normal muscle health.

AXA2678 is a product candidate that contains 10 amino acids and derivatives in distinct ratios. This product candidate was designed to target multiple biological pathways with the goal of maintaining normal muscle structure and function, especially in states of disuse atrophy.

Underlying Biology	**AXA2678 Design Objectives**
Proteostasis and anabolic resistance	Optimize the balance between muscle anabolism via increased muscle protein synthesis and catabolism via decreased muscle protein breakdown Improve muscle insulin resistance Stimulate mitochondrial function and provide anaplerotic substrates for the TCA cycle
Inflammation and vasodilation	Decrease inflammation cascades and reactive oxygen species
Defective myogenesis, the process of forming skeletal muscle fibers, and regeneration	Activate stem cells for muscle growth and differentiation

Completed Clinical Study AXA2678-001

AXA2678-001 was a double-blind, randomized, placebo-controlled Clinical Study in which we examined the safety, tolerability and impact on normal structure and functions of muscle of AXA2678 during single limb immobilization. Twenty healthy young men were randomly assigned (10 per group) to receive AXA2678 or an excipient- and calorie-matched non-amino acid containing placebo for 28 days.

Muscle biopsies were taken on days 1, 8 (immobilization start), 15 (immobilization end), and 28 (post-immobilization recovery). Magnetic resonance imaging, or MRI, was utilized to assess quadricep muscle volume, or Mvol, muscle cross-sectional area, or CSA, and muscle fat fraction (FF: the fraction of muscle occupied by fat). Maximal voluntary leg isometric torque was assessed by dynamometry. Administration of AXA2678 attenuated muscle disuse atrophy compared to placebo ($p < 0.05$) with changes from day 8 to day 15 in placebo: Mvol= $-2.4 \pm 2.3\%$ and 1CSA = $-3.1\% \pm 2.1\%$, both $p < 0.001$ vs. zero; against AXA2678: Mvol: $-0.7 \pm 1.8\%$ and 1CSA: $-0.7 \pm 2.1\%$, both $p > 0.3$ vs. zero; and $p < 0.05$ between treatment conditions for CSA.

During immobilization, muscle FF increased in subjects who received placebo but not AXA2678 (placebo: $12.8 \pm 6.1\%$ vs. AXA2678: $0.4 \pm 3.1\%$; $p< 0.05$). Immobilization resulted in similar reductions in peak leg isometric torque and change in time-to-peak, or TTP, torque in both groups. Recovery (day 15–day 28) of peak torque and TTP torque was also not different between groups, but showed a trend for better recovery in the AXA2678 group.

AXA2678 at 24g TID (72 g/day) was well-tolerated and no clinically significant safety issues were observed over the 28-day administration period. AEs of sore throat were reported in one subject on two separate occasions (on Day 6, and then again on Day 22) taking AXA2678. Another two AEs of stomach gas and nausea were reported simultaneously in one subject taking AXA2678 on Day 12. These AEs were mild, self-resolving within one day and noted as possibly related to AXA2678 administration. No other AEs were reported with AXA2678 or with placebo. There were no clinically meaningful changes noted in routine safety labs (chemistry, hematology), vital signs or ECG.

Potential Development Paths for AXA2678

If we were to decide to develop AXA2678 under an IND development path, we believe it could potentially be investigated for multiple indications characterized by such disuse-related muscle atrophy, including total knee arthroplasty, or TKA, total hip arthroplasty, or THA, hip fracture related myopenia, or HFRM, rotator cuff repairs or injury, and other musculoskeletal atrophy or injuries. In the United States, the market for these conditions each year is upwards of 140,000 patients undergoing TKA, 50,000 undergoing THA, 133,000 recovering from HFRM and 195,000 recovering from rotator cuff injuries annually.

If we were to decide to develop AXA2678 as a non-drug product candidate, the target market likely would be defined by, or with input from, a strategic partner. We believe a non-drug pathway could also represent a significant market opportunity given the potential benefits to muscle health. Under a non-drug development path, we or a strategic partner may decide to develop AXA2678 as a dietary supplement to support muscle-related structure and function.

Additional Potential Opportunities for EMM Compositions

Many EMMs, including amino acids, are well established agents used to support health. Single EMMs and simple EMM combinations also are already approved as treatments for sickle cell disease, dyslipidemia, inborn errors of metabolism and other conditions. We believe EMM compositions have the potential to address a variety of diseases and conditions, including areas related to intermediary substrate metabolism, muscle atrophy, mitochondrial biology, neuroprotection, inflammation and immunology. We intend to continue to target biologies and disease areas driven by regulation of metabolic pathways in which we can potentially leverage the vital role that EMMs play in regulating metabolic function. To date, we have characterized approximately 75 potential therapeutic applications for EMMs based upon data from public databases, and our own metabolic profiling from biorepository samples.

Intellectual Property

We are establishing a broad, global intellectual property portfolio for our pipeline and have already received three issued U.S. patents, including both composition of matter and method of use claims. This is notable considering the speed of our development model and establishes a foundation for the large number of submitted applications for our pipeline (127 patents pending worldwide as of December 31, 2019). Our matrixed approach to IP is inclusive of trade secrets and trademarks and encompasses our product candidates (various constituents and amounts); indications; the development platform; manufacturing processes and technologies; and formulations. In our patents for compositions and methods of use, we seek claims of broad and narrow scope. For instance, some claims cover any composition containing a minimum of specified EMMs with activity, while other claims expressly cover specific product candidates by naming all the EMMs present.

We seek to create a multi-dimensional intellectual property portfolio as a strategic asset that has the potential to provide us with a significant competitive advantage. We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or through collaborations, or licensed from third parties. Our policy is to file patent applications related to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business in the United States and in jurisdictions outside of the United States. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of leveraging EMMs for treating complex diseases and improving health. We additionally rely on regulatory-related protections such as data exclusivity, market exclusivity and patent term extensions when available, and where appropriate, plan to seek and rely on regulatory protection afforded through orphan drug designations. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements. Please see the section on "Risk factors — Risks related to our intellectual property."

As of December 31, 2019, our product candidate-related patent portfolio consisted of 18 patent families, three granted U.S. patents and 127 worldwide patents pending. To date, all of our patent rights are owned by us. Our objective is to continue to expand our portfolio of patents and patent applications to protect our product candidates and certain aspects of our development platform, manufacturing processes, formulations, and insights into amounts, uses, and features of our EMM compositions.

In addition, we own a portfolio of legacy patents and patent applications related to recombinant proteins for nutrition and therapeutics, including 11 granted and three pending U.S. patents, and five granted and five pending foreign patents.

Examples of the product candidate and technology areas covered by our intellectual property portfolio are described below.

Indication-Related Intellectual Property

The indication-related patent rights in our intellectual property portfolio relate to conditions and disorders associated with dysregulated metabolism and provide coverage for product candidates to specifically address those conditions and the associated disease states, as well as structure and function of normal organs in the context of dysregulated metabolism. The indication-related patent applications for our lead programs cover novel product candidate compositions and their uses broadly and, with respect to individual product candidates, in detail. Often, we are able to exemplify even our earliest product candidate inventions with human as well as animal and in vitro data. Each of the indication-related patent rights and applications described below are owned by us and are not licensed from any third party.

Notably, while our intellectual property covers drug and non-drug areas, to date, each initial product candidate has been first tested as a food in order to better understand safety, tolerability and the impact on normal human physiology and metabolic pathways. After such initial testing, a decision may be made to deem the product candidate a drug product candidate, and subsequent studies on disease endpoints are conducted under INDs.

Compositions and Methods for the Treatment of Cirrhosis

Our patent applications cover a class of compositions for cirrhosis, including our drug product candidate AXA1665. Currently, patent rights relating to cirrhosis include two U.S. patent applications, a PCT patent application, and two foreign national patent applications. We expect any granted patent based on this family to expire in 2038, excluding any patent term adjustments or extensions.

A second family of applications directed to unique features and uses of AXA1665 and related compositions currently includes one provisional application. We expect the patent applications in this second family, if issued, to expire in 2040, without taking into account any patent term adjustments or extensions we may obtain.

Compositions and Methods for NAFLD/NASH

Our patent applications cover a class of compositions for fatty liver disease, including our drug product candidates AXA1125 and AXA1957. Currently, patent rights relating to AXA1125 and related compositions and their uses in fatty liver disease include three granted U.S. patents, two U.S. patent applications, and over 40 foreign national patent applications. We expect any granted patent based on this family to expire in 2037, excluding any patent term adjustments or extensions.

A second family of applications directed more specifically to AXA1957 and related compositions and uses currently includes one U.S. patent application, one PCT patent application, and two foreign national patent applications. We expect the patent applications in this second family, if issued, to expire in 2039, without taking into account any patent term adjustments or extensions we may obtain.

Compositions and Methods for Blood and Sickle Cell Disease

Our patent applications cover a class of compositions for blood health and sickle cell disease, including our product candidate AXA4010 and related compositions and uses. Currently, this family of applications includes one U.S. patent application, one PCT patent application, and two foreign national patent applications. We expect any granted patent based on this family to expire in 2039, excluding any patent term adjustments or extensions.

A second family of applications directed to specific, related compositions and uses currently includes one U.S. provisional patent application. We expect the patent applications in this second family, if issued, to expire in 2040, without taking into account any patent term adjustments or extensions we may obtain.

Compositions and Methods for Acute Muscle Atrophy

Our patent applications cover a class of compositions for muscle atrophy, including our product candidate AXA2678. Currently, patent rights relating to muscle atrophy include one U.S. patent application and over 40 foreign national patent applications. We expect any granted patent based on this family to expire in 2037, excluding any patent term adjustments or extensions.

A second family of applications directed to unique features and uses of AXA2678 and related compositions currently includes one U.S. patent application, one PCT patent application, and two foreign national patent applications. We expect the patent applications in this second family, if issued, to expire in 2039, without taking into account any patent term adjustments or extensions we may obtain.

Compositions and Methods for Treatment of Traumatic Brain Injury and Stroke

Our patent applications cover a class of compositions for traumatic brain injury and stroke. Currently, patent rights relating to traumatic brain injury include two U.S. patent applications, one PCT patent application, and six foreign national patent applications. We expect any granted patent based on this portfolio to expire in 2038, excluding any patent term adjustments or extensions.

Additional AXA Combination-Related Patents

We have filed provisional patent applications directed to combinations of particular product candidates (e.g., AXA1957) and EMM combinations with particular NAFLD/NASH drugs and drug candidates, and some novel EMM compositions. We expect the patent applications in this portfolio, if issued, to expire in 2040, without taking into account any patent term adjustments or extensions we may obtain.

Platform-Related Intellectual Property

In addition to the indication-related intellectual property, our intellectual property portfolio also includes know-how and patent applications directed to our development platform and other technologies developed internally. Exemplary platform technologies that are the subject of such patent applications include:

- manufacturing processes for complex EMM compositions (currently one U.S. patent application, one PCT patent application, and two foreign national patent applications);
- taste formulations (currently one U.S. patent application, one PCT patent application, and two foreign national patent applications); and
- unique formulations of candidate compositions (2 separate provisional applications).

Our development platform iterates and integrates data from literature, including patents, in vitro experiments, animal studies and our own Clinical Studies, giving us significant competitive advantages. Our development platform, which is protected by trade secrets, is core to maintaining our first mover advantage. These advantages translate into a unique understanding of metabolism, development of many new product candidates, and creation of intellectual property around our product candidates and development platform technologies.

These development platform technologies, and our intellectual property protection related thereto, are broadly applicable to our product candidates. Our patent applications directed to platform-related technologies, if issued, would expire beginning in 2039, without taking into account any patent term adjustment or extensions we may obtain.

Therapeutic Modality Intellectual Property

Our proprietary knowledge and insights into the behavior of EMMs have yielded inventions related to categories of metabolic dysfunction, such as insulin resistance, inflammation, and fibrosis. Our patent applications directed to these underlying modalities, if issued, would expire in 2039, without taking into account any patent term adjustment or extensions we may obtain.

We continually assess and refine our intellectual property strategy as we develop new platform technologies and product candidates. To that end, we are prepared to file additional patent applications if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. Further, we are prepared to file patent applications, as we consider appropriate under the circumstances, relating to the new technologies that we develop. We will also prosecute patent applications owned by or co-owned with third party licensors. In addition to filing and prosecuting patent applications in the United States, we plan to file counterpart patent applications in additional countries where we believe such foreign filing is likely to be beneficial, including, but not limited to, Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, and South Korea.

Individual patent terms depend upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States and most other countries have patent terms that expire 20 years from the earliest effective filing date. In certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of a regulatory review period, although patent term restoration in the United States applies to a new chemical entity, so may not apply to some EMM compositions. In Europe, any patentee can obtain a supplementary protection certificate, or SPC, on the basis of approval of a therapeutic product covered by the patent based on a full clinical development program. Any restoration period is limited to a maximum restoration time (five years in the United States and Europe) and total effective patent life of the approved drug product (14 years in the United States and 15 years in Europe). The actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and local decisions about the validity and enforceability of the patent.

Regulatory Exclusivity

Under certain circumstances, approval of a drug product by a health authority will result in a period of data exclusivity and/or market exclusivity (together considered as regulatory exclusivity) for the product. Data exclusivity means that no party can file for approval of a drug product based on the original drug approval application data. Market exclusivity (such as orphan drug exclusivity) means that the health authority may not be permitted to give final approval to a drug product for a defined period of time, absent certain conditions. In the United States, five-year data exclusivity is only available upon initial approval of a new chemical entity (NCE), which may not apply to some EMM product compositions. Moreover, if an abbreviated new drug application (ANDA) or 505(b)(2) application is filed with a "Paragraph IV certification" referencing a product protected by NCE exclusivity and Orange Book-listed patent(s), FDA may accept such application for filing four years after the reference product's approval rather than five years. A new drug application with a Paragraph IV certification provides an opportunity for initiating patent litigation, and FDA cannot grant final approval of the application until the earlier of resolution of the patent litigation in the applicant's favor or 30 months from the Paragraph IV notice date. See "*Hatch-Waxman Act and Generic Competition*" for further information. Three-year market exclusivity may also be granted upon approval of applications (including supplements) containing the results of new clinical investigations (other than bioavailability studies), conducted by the applicant and essential to the FDA's approval of new versions or conditions of use of previously approved drugs, such as new indications, delivery mechanisms, dosage forms, strengths, or other conditions of use. However, the scope of such exclusivity is generally limited to the particular basis of the approval (e.g., the new indication or dosage form). In Europe, the period of regulatory exclusivity for a drug product approved based on a full stand-alone dossier consisting of quality, pre-clinical and clinical trial data is 10 years, which consists of eight years of data exclusivity against data cross-referencing of a generic application and two years of market exclusivity where the generic product (even if approved in the first eight years of the protection period) cannot be marketed until the full 10-year exclusivity or protection period has expired. This 10-year of exclusivity or protection period can be cumulatively extended to 11 years even during the first eight years of the protection/exclusivity period, the marketing authorization holder has obtained approval of one or more new therapeutic indications that are held to bring about a significant benefit as compared with existing therapies. We believe that our products, if approved, should be entitled to the full 10 years of regulatory data exclusivity in Europe. Orphan drug exclusivity in the U.S. is seven years. See "*Orphan Drug Designation*" for further information. Conducting a pediatric study in response to, and in compliance with the conditions of, a written request from FDA extends every form of existing regulatory exclusivity as well as patents by 6 months in the U.S. provided that the data is submitted in a timely manner. For orphan indications, the product is eligible for a period of 10 years of orphan market exclusivity in the EU, during which the EU regulatory authorities are not permitted to accept or approve a similar medicinal product in relation to the approved orphan indication. This period can be extended to a maximum of 12 years if the marketing authorization holder has conducted and provided data in compliance with an agreed pediatric investigation plan and has not secured an SPC on the basis of the product approval. Orphan drug exclusivity in Japan is 10 years.

Trademark Protection

As of December 31, 2019, our trademark portfolio contains more than 50 registrations and pending applications. We have trademarks in over 12 countries, including the European Union. For the marks AXCELLA and the Axcella LOGO, we have pending applications in Canada and Brazil as well as International Registrations designating China, the European Union, India, Japan and Russia. In the United States we have a registration for the Axcella LOGO, and pending applications for the AXCELLA and AXCELLA HEALTH marks.

Trade Secrets

We may also rely, in some circumstances, on trade secrets to protect our technology and aspects of our development platform. However, trade secrets are difficult to protect. We seek to protect our trade secret technology, e.g., AxcellaKB, confidential product candidates, and commercial plans in part by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators and advisors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. To learn more about risks related to trade secrets for our proprietary technology, inventions, improvements and products, please see the section on "Risk factors — Risks related to our intellectual property."

Manufacturing

To date, we have rapidly designed and efficiently manufactured product candidates and believe our process is readily scalable. Under our existing agreements with our manufacturers, we have been able to secure initial product candidates to initiate our Clinical Studies in less than three months from identifying the product amount needed. We continue to make enhancements to our product candidates to make them even more consumer-friendly, including in their formulation (e.g., taste and texture), packaging (e.g., easy to open sachets) and administration (e.g., water soluble). Our product candidates are supplied in a dry powder form, which is dissolved in water and then administered orally as an orange-flavored drink. Our formulation enables us to deliver high concentrations of dry powder materials at appropriate administration volumes. This covers a wide range of raw material characteristics, and we believe will enable us to deliver multiple oral dosage forms to meet Clinical Study and Clinical Trial needs, as well as commercial needs.

Any product candidates that we decide to develop as drug candidates under INDs will be manufactured at a well-known contract manufacturing organization (CMO) under pharmaceutical current Good Manufacturing Practices (cGMPs) to produce the dry powder forms in sealed foil sachets. Chemical and microbiological testing of product candidates will be performed by this same CMO per defined product specifications and Certificate of Analysis will be issued for each batch. Chemical and microbiological testing will be performed using validated test methods. We believe these processing steps would enable us to readily provide high quality Clinical Trial Material, or CTM, product to support multiple Clinical Trials conducted under INDs and that are readily scalable to support commercial drug product requirements, if any of our product candidates regulated as drugs receive regulatory approval.

Government regulation

Our ongoing research and development activities and any manufacturing and potential marketing of our product candidates are subject to extensive regulation by numerous governmental authorities in the United States and other countries. The process of obtaining regulatory approvals of drugs for initial and subsequent therapeutic indications or commercialization of non-drug products and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

None of our product candidates have been approved by the FDA for marketing as a drug in the United States, and we have not marketed any product as a food (including dietary supplements) or medical food. In the United States, the FDA regulates drug products as well as non-drug products under the Federal Food, Drug and Cosmetic Act, or the FD&C Act, as amended, its implementing regulations and other laws. The FDA regulates, among other things, the research, development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution and import and export, of these products. If we fail to comply with applicable FDA or other requirements at any time, we may become subject to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, suspension or revocation of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

For our product candidates developed as drugs, the process required by the FDA before such products can be marketed in the United States generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including good laboratory practice, or GLP, requirements and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human Clinical Trials may begin;
- approval by an IRB or independent ethics committee at each Clinical Trial site before each trial may be initiated;
- performance of adequate and well-controlled human Clinical Trials in accordance with applicable IND regulations, GCP requirements and other Clinical Trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a new drug application, or NDA;
- a determination by the FDA within 60 days of its receipt of the NDA, to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA inspection of the Clinical Trial sites that generated the data in support of the NDA and/or us as Clinical Trial sponsor;
- payment of user fees for FDA review of the NDA (unless a fee waiver applies);
- agreement with FDA on the final labeling for the product and the design and implementation of any required Risk Evaluation and Mitigation Strategy (REMS); and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a REMS, and the potential requirement to conduct post-approval studies.

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

Regulation of Drug Product Candidates and Drugs

Preclinical and Clinical Trials for drugs

Once a product candidate is identified for development as a drug, it generally enters the preclinical testing stage. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as in vitro and animal studies to evaluate the potential for adverse events, which must be conducted in accordance with federal regulations and requirements, including GLP requirements. The results of the preclinical studies, together with manufacturing information and analytical data as well as the results of our Clinical Studies, would be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans for a therapeutic indication and must become effective before human Clinical Trials for such purpose may begin. 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 does not ensure that FDA will allow Clinical Trials to commence at all or 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, and IRB approval must be obtained before each Clinical Trial can begin.

Such Clinical Trials involve the administration of the product candidate to human volunteers under the supervision of qualified investigators. Clinical Trials are conducted under protocols detailing, among other things, the objectives of the Clinical Trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol for our product candidates which we decide to market through the drug development pathway must be submitted to the FDA as part of the IND. An IRB for each investigator site proposing to participate in a Clinical Trial must also review and approve the Clinical Trial, including its protocol and 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. Clinical testing of drug product candidates also must satisfy extensive GCP requirements, including requirements for informed consent.

Human Clinical Trials to support NDAs, for marketing approval are typically conducted in three sequential phases, which may overlap or be combined. In certain circumstances, where sufficient evidence of safety and tolerability are collected from preclinical studies and other human experience with a product, subject to discussions and acceptance by the FDA, such as our non-IND human clinical studies, we believe that for the development of such drug candidate, a human Clinical Trial may begin at Phase II, or combined Phase I/II, rather than starting at Phase I. We would expect to discuss with the FDA such proposal to initiate the clinical development program of a drug candidate in a later phase study without first conducting a Phase I Clinical Trial or Trials.

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

Post-approval trials, sometimes referred to as Phase IV Clinical Trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase IV Clinical Trials as a condition of approval of an NDA or, in certain circumstances, post-approval.

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 within 15 calendar days for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Concurrent with Clinical Trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the drug product 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 drug product. FDA may require such testing to occur on a lot-by-lot basis in order to release product for clinical use. 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.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the product available in the United States for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including research tax credits for qualified clinical testing and waiver of application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. Clinically superior means that a drug is shown to provide a significant therapeutic advantage over and above that provided by an approved drug that is otherwise the same drug in one or more of the following ways: greater effectiveness than the approved drug, greater safety in a substantial portion of the target populations, and in unusual cases, where neither greater safety nor greater effectiveness has been shown, a demonstration that the drug otherwise makes a major contribution to patient care. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, 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 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.

Expedited development and review programs for drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions 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, as well as Priority Review, discussed below. In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase I, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and accelerated approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. In addition, if a sponsor submits an NDA for a product intended to treat certain rare pediatric or tropical diseases or for use as a medical countermeasure for a material threat and that meets other eligibility criteria, upon approval, such sponsor may be granted a priority review voucher that can be used for a subsequent NDA. Under priority review, the FDA must review an application in six months compared to ten months for a standard review. Additionally, products for treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments are eligible for accelerated approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. The FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, unless otherwise informed by the FDA, the FDA currently requires, as a condition for accelerated approval, that all advertising and promotional materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the FDA for review during the pre-approval review period, and that after 120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

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 the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process.

U.S. marketing approval for drugs

Assuming successful completion of the required clinical testing of our product candidates for drug uses, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy. The marketing application may include both negative and ambiguous results of preclinical studies and Clinical Trials, as well as positive findings. Data may come from company-sponsored Clinical Trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the United States. Under the Prescription Drug User Fee Act guidelines that are currently in effect, the FDA has a goal of ten months from the 60-day filing date for a standard NDA, for a new molecular entity to review and act on the submission.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Moreover, under the Food and Drug Administration Safety and Innovation Act, a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan (PSP) within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials or other clinical development programs. The FDA also may require submission of a REMS to ensure that the benefits of the drug outweigh its risks. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk-minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it historically has tended to follow such recommendations.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the Sponsor product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more Clinical Trial sites and/or the Clinical Trial sponsor to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and Clinical Trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase IV Clinical Trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

U.S. post-approval requirements for drugs

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. There is also a continuing, annual prescription drug product program user fee.

In addition, drug manufacturers and their subcontractors involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information or information on reduced effectiveness, 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;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or holds on post-approval Clinical Trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or mandated modification of promotional materials and labeling and issuance of corrective information.

Hatch-Waxman Act and Generic Competition

Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, Congress created an abbreviated FDA review process for generic versions of pioneer (brand name) drug products under section 505(j) of the FDCA. Section 505(j) provides for approval of an ANDA that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use, among other things, to a previously approved drug (commonly known as the reference drug). In considering whether to approve such a generic drug product, the FDA requires that an ANDA applicant demonstrate, among other things, that the proposed generic drug product’s active ingredient is the same as that of the reference product, that the proposed generic is bioequivalent to the reference product, that any impurities in the proposed product do not affect the product’s safety or effectiveness, and that its manufacturing processes and methods ensure the consistent potency and purity of its proposed product.

In addition to the ANDA pathway, the Hatch-Waxman Act also established an abbreviated approval pathway under section 505(b)(2) of the FDCA for applications that contain full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2) permits approval of applications other than those for duplicate products and permits reliance for such approvals on literature or on FDA's finding of safety or effectiveness for an approved drug product.

The Hatch-Waxman Act requires NDA applicants and NDA holders to submit certain information about patents related to their drugs for listing in the FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book). ANDA and section 505(b)(2) applicants generally must submit a certification or statement regarding each of the patents listed with the FDA for the reference product. A certification that a listed patent is invalid and/or will not be infringed by the marketing of the ANDA or section 505(b)(2) applicant's product is called a "Paragraph IV certification." If an ANDA or section 505(b)(2) application containing a Paragraph IV certification is submitted to the FDA and accepted as a reviewable filing, the ANDA or section 505(b)(2) applicant then must provide, within 20 days of FDA acceptance, notice to the NDA holder and patent owner stating that the application has been submitted and providing the factual and legal basis for the applicant's opinion that the patent is invalid and/or not infringed. The NDA holder or patent owner then may file suit against the ANDA or section 505(b)(2) applicant for patent infringement. If this is done within 45 days of receiving notice of the Paragraph IV certification, a 30-month stay of the FDA's ability to approve the ANDA or section 505(b)(2) application is triggered. The 30-month stay begins on the date of receipt of the Paragraph IV notice and, in the case where an ANDA or section 505(b)(2) application is submitted before a reference product's NCE exclusivity expires (i.e., four years after approval of the reference product), the 30-month period is extended to ensure that approval of the ANDA or section 505(b)(2) application cannot be granted for 7-1/2 years after initial approval of the reference product. Nevertheless, the FDA may approve the proposed product before the expiration of the 30-month stay (or 7-1/2 year period) if a court finds the patent invalid and/or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

On December 20, 2019, the Further Consolidated Appropriations Act, 2020 (FCAA 2020) became law. Section 610, entitled "Actions for Delays of Generic Drugs and Biological Products", provides generic drug (ANDA and 505(b)(2)) and biosimilar developers with a private right of action to obtain sufficient quantities of reference product from the brand manufacturer, or a generic or biosimilar manufacturer, necessary for approval of the developers' generic or biosimilar product. If a generic drug or biosimilar developer is successful in its suit, the defendant manufacturer would be required to provide sufficient quantities of product on commercially-reasonable, market-based terms and may be required to pay the developer's reasonable attorney's fees and costs as well as financial compensation under certain circumstances. The purpose of section 610 is to promote competition in the market for drugs and biological products by facilitating the timely entry of lower-cost generic and biosimilar products. We cannot determine what effect section 610 of the FCAA 2020 may have on manufacturers that may develop generic or other competing versions of our products if approved as drugs.

Other regulatory matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

Coverage and Reimbursement

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. 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. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Other healthcare and privacy laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

- The Anti-Kickback Statute prohibits for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer, provide or pay any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward referrals, including the purchase, recommendation, order, arrangement or prescription of a good or service, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term ‘‘remuneration’’ has been broadly interpreted to include anything of value. Violations of this law are punishable by imprisonment, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act or federal civil money penalties statute.

- Federal civil and criminal false claims laws, and civil monetary penalty laws including the federal False Claims Act, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented false, fictitious, or fraudulent claims for payment by a federal healthcare program; or knowingly making a false statement or record material to payment of a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly and improperly avoiding, decreasing or knowingly concealing an obligation to pay money to the federal government. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers, with respect to drug products, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product, or promoting a product off-label. Claims that include items or services resulting from a violation of the federal Anti-Kickback Statute are false or fraudulent claims for purposes of the False Claims Act. Any future marketing and activities relating to the reporting of wholesaler or estimated retail prices for drug products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our product and any future product candidates, are subject to scrutiny under this law.
- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or knowingly and willfully falsifying, concealing or covering up by trick or device a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rules published January 2013, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy, security and transmission of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for information related to certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.

- Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope and apply regardless of payor. These laws are enforced by various state agencies and through private actions. Some state laws require pharmaceutical companies implement compliance to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts. Data privacy and security laws and regulations in foreign jurisdictions may also be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, which became effective in May 2018).

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do 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 related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Moreover, on October 17, 2019, the Office of the Inspector General of the Department of Health and Human Services issued a Proposed Rule: Revisions to Safe Harbors under the Anti-Kickback Statute and Civil Monetary Penalty Rules Regarding Beneficiary Inducements to, among other things, add new safe harbors for certain value-based arrangements. Although the value-based proposals would not include pharmaceutical manufacturers among the entities that could permissibly enter into such contracting arrangements, the general trend toward outcomes and value-based contracts in the healthcare industry may continue. It is possible that payors, among other customers, could push manufacturers for novel contracting approaches, including those that would incorporate value-based principles, and these efforts could affect our business. It is unclear at this time whether this proposed rule will be adopted or, if adopted, what effect, if any, it would have on the cost and ability to comply with the federal Anti-Kickback Statute or on our business.

Current and future healthcare reform legislation

In the United States and foreign jurisdictions, there have been and continue to be 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, that we may develop as drugs, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

The ACA, for example, expanded and increased industry rebates for drugs covered under Medicaid programs, made changes to the coverage requirements under the Medicare Part D program, and imposed annual, non-deductible fees on any entity that manufactures or imports certain types of branded prescription drugs and biologics. With the current administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the ACA, which may impact reimbursement for drugs. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the ACA. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 (TCJA) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, 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. This decision was appealed to the U.S. Court of Appeals for the Fifth Circuit. On December 18, 2019, the Fifth Circuit issued an opinion holding that, while the individual mandate was no longer constitutional, the case must be remanded to the District Court to further evaluate whether the mandate can be severed from the ACA or the entire ACA must be stricken down. On January 3, 2020, petitions for certiorari were filed with motions to expedite requesting that the U.S. Supreme Court review the Fifth Circuit’s decision and ultimately decide the constitutionality of the ACA. The U.S. Supreme Court has not yet decided whether to grant the petitions. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal and replace elements of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Additionally, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted:

- The Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2029, unless additional Congressional action is taken.
- The American Taxpayer Relief Act of 2012, among other things, also reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers.

Further, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. In addition, the United States government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs to limit the growth of government paid health care costs. For example, the United States government has passed legislation requiring pharmaceutical manufacturers to provide rebates and discounts to certain entities and governmental payors to participate in federal healthcare programs. Further, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs, and the current administration released a "Blueprint," or plan, to reduce the cost of drugs. The current administration's Blueprint contains certain measures that the U.S. Department of Health and Human Services is already working to implement. For example, on December 23, 2019, the Trump administration, through the FDA, released a proposed rule and draft guidance that set forth two pathways for the legal importation of certain drugs in an effort to control drug costs. Since these pathways are not yet effective and are subject to revision pending receipt of public comments, we cannot determine what effect these pathways may have on our business and financials. Individual states in the United States have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Our revenue and future profitability could be negatively affected by the passage of these laws or similar federal or state legislation and regulations.

Compliance with other federal and state laws or requirements; Changing legal requirements

If any products that we may develop are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to which the company or its products may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects companies to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a company to enter into supply contracts, including government contracts. Any claim or 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. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Other U.S. environmental, health and safety laws and regulations

We may be 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our 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.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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

Government regulation of drugs 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, quality and efficacy and governing, among other things, Clinical Trials, marketing authorization or identification of an alternate regulatory pathway, manufacturing, commercial sales and distribution of our products. For instance, in the European Economic Area, or the EEA (comprised of the 27 EU Member States plus Iceland, Liechtenstein and Norway), medicinal products must be authorized for marketing by using either the centralized authorization procedure or national authorization procedures.

- Centralized procedure — If pursuing marketing authorization of a product candidate for a therapeutic indication under the centralized procedure, following the adoption of a positive opinion of the EMA's Committee for Medicinal Products for Human Use, or, CHMP, the European Commission issues a single marketing authorization in the form of a binding decision 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 considered as of 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 timeframe for completing the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops that ordinarily occur at Day 120 of the procedure.

- National authorization procedures — There are also two other possible routes to authorize products in more than one country in the EEA for therapeutic indications, which fall outside the scope of the mandatory 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.

Following the ratification of the Agreement on the Withdrawal of the United Kingdom from the EU, or Withdrawal Agreement, by the European Parliament and UK Parliament, the UK formally left the EU on January 31, 2020. The Withdrawal Agreement provides for a transition period until December 31, 2020, during which the UK remains in the single market and customs union and the free movement of people will continue, in order to ensure frictionless trade and business continuity until a long-term relationship is agreed between the UK and the EU. During the transition period, EU law and rules continue to apply in the UK. The Withdrawal Agreement envisages that following its departure from the EU on January 31, 2020, the UK can no longer participate in EU institutions and their decision-making. This will mean the UK can no longer be represented on various advisory committees within the EMA during the Centralized procedure. The UK cannot participate in the meetings of Coordination Group on Mutual Recognition and Decentralized procedure and cannot act as a Reference Member State. However, the UK can participate in the Decentralized procedure and Mutual Recognition procedure as a Concerned Member State during the transition period.

At the end of transition, the UK’s relationship with the EU will be determined by the new agreements it has entered into on trade and other areas of cooperation. The new agreements must be reached before the transition period ends. If not, the UK would have to rely on previous international conventions for security cooperation and would trade with the EU on World Trade Organization terms. The exception is Northern Ireland, whose trade in goods with the EU would be covered by the provisions in the Northern Ireland Protocol.

In the EEA, a reference medicinal product is defined as the product which was authorized based on a full stand-alone dossier consisting of quality, preclinical testing and clinical trial data. A reference medicinal product includes those that contain a new active substance which has not been approved in the EU previously. As indicated above, upon grant of a marketing authorization, a reference medicinal product will benefit from eight years of data exclusivity and an additional two years of market exclusivity. The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and Clinical Trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during this exclusivity. The market exclusivity or protection means that even if the generic or biosimilar product is authorized, such a product cannot be marketed in the EU Member States until the full 10-year exclusivity period has expired. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The criteria for designating an "orphan medicinal product" in the EEA are similar in principle to those in the United States. In the EEA a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten-year orphan market exclusivity period, no marketing authorization application shall be accepted, and no marketing authorization shall be granted for a similar medicinal product for the same indication. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough its own approved 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 GCP and the related national implementing provisions of the individual EU Member States govern the system for the approval of Clinical Trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the Clinical Trial is to be conducted. Furthermore, the applicant may only start a Clinical Trial at a specific study site after the competent ethics committee has issued a favorable opinion. The Clinical Trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials foreseen by the regulation, through an independent audit. The regulation becomes applicable six months after the European Commission publishes notice of this confirmation. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all Clinical Trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing Clinical Trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual Clinical Trial. If a Clinical Trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the Clinical Trial. The new Clinical Trials Regulation aims to simplify and streamline the approval of Clinical Trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for Clinical Trial sponsors; and a harmonized procedure for the assessment of applications for Clinical Trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a Clinical Trial has been submitted (Member States concerned). The technical assessment in Part I is led by the “reporting member state” that will form the basis for consideration by the member states concerned by the application during the coordinated review phase of the process. Part II is assessed separately by each Member State concerned. Strict timelines have been established for the assessment of Clinical Trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, previously governed by the provisions of the Data Protection Directive, is now governed by the GDPR, which became effective on May 25, 2018. While the Data Protection Directive did not apply to organizations based outside the EU, the GDPR has expanded its reach to include any business, regardless of its location, that provides goods or services to residents in the European Economic Area. This expansion would incorporate any Clinical Trial activities in European Economic Area. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for "sensitive information" which includes health and genetic information of data subjects residing in the European Economic Area. The GDPR grants individuals the opportunity to object, and requires them to consent, to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies and obtain compensation for damages in the event the individual believes his or her rights have been violated. It requires controllers and processors of personal data to provide information to individuals regarding data processing activities, implement safeguards to protect the security and confidentiality of personal data, provide notice of data breaches, and take certain measures when engaging with third-party processors. Further, the GDPR imposes strict rules on the transfer of personal data out of the European Economic Area to the United States or other regions that have not been deemed to offer "adequate" privacy protections. In addition, the GDPR includes restrictions on cross-border data transfers. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States, which may deviate slightly from the GDPR, may result in fines of up to 4% of annual global revenues, or € 20,000,000, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules, including as implemented by individual countries. Further, the United Kingdom’s decision to leave the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated now that the United Kingdom has left the EU.

There is significant uncertainty related to the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is not clear if the authorities will conduct random audits of companies doing business in the EU, or if the authorities will wait for complaints to be filed by individuals who claim their rights have been violated. Enforcement uncertainty and the costs associated with ensuring GDPR compliance are onerous and may adversely affect our business, financial condition, results of operations and prospects.

Additionally, should we elect one or more product candidates to develop and market as non-drug products in foreign countries, such products would also be subject to regulation under various national, local, and international laws that include provision governing, among other things, the formulation, manufacturing, packaging, labeling, and advertising. These regulations may prevent or delay entry into the market or prevent or delay the introduction, or require the reformulation, of certain of our non-drug product candidates.

The regulatory environment outside the United States varies and in general is less developed then in the United States, but some exceptions do exist. The regulatory requirements for nutritional non-drug products and food products outside of the United States varies greatly from jurisdiction to jurisdiction. Each jurisdiction may have its own regulatory framework regarding nutritional non-drug products and food products. The two leading jurisdictions, the United States and the Europe, currently have and may continue to have distinctly different regulatory regimes with different rules and requirements for nutritional non-drug products and food products, with, for example, the European Union having a stronger process for claims review and preapproval for nutritional products. Regulation in Europe is exercised primarily through the European Union, which regulates the combined market of each of its member states. Other European countries, such as Switzerland, have voluntarily adopted laws and regulations that mirror those of the European Union with respect to dietary products.

We cannot predict how the global regulatory landscape regarding our possible nutritional non-drug products or food products, if any, will evolve and we may incur increased regulatory costs as regulations in the jurisdictions in which we operate evolve or change. We cannot predict whether or when any jurisdiction will change its regulations with respect to any of our product candidates.

Should we utilize third part distributors, compliance with such foreign governmental regulations would generally be the responsibility of such distributors, who may be independent contractors over whom we have limited control.

Regulation of Food Products

FDA regulation of dietary supplements

The Dietary Supplement Health and Education Act of 1994 defines dietary supplement products to be "foods" under the FD&C Act, and they are regulated as such by the FDA. The FDA and other regulatory authorities, including the Federal Trade Commission, or FTC, similarly with conventional foods, regulate the manufacturing, preparation, quality control, import, export, packaging, labeling, marketing, advertising, promotion, distribution, safety, and/or adverse event reporting of dietary supplements. Among other things, manufacturers of dietary supplements must meet applicable cGMPs, and certain requirements that govern the manufacturing, packaging, labeling and holding of dietary supplements.

Under federal law, dietary supplements are defined in relevant part as a product (other than tobacco) intended to supplement the diet that bears or contains one or more dietary ingredients, which include any of the following: a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use by humans to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, or extract, or any combination of those substances. Dietary supplements may not include articles that are approved as new drugs or biologics or that have been authorized for investigation as new drugs or biologics for which substantial clinical investigations have been instituted and made public, unless the article was marketed as a dietary supplement or food prior to such approval or authorization.

The manufacturer of a dietary supplement is responsible for ensuring the safety of its product and must demonstrate either that each dietary ingredient was marketed as a dietary supplement in the United States before October 15, 1994, or if the dietary ingredient was not marketed as a dietary supplement in the United States before October 15, 1994, referred to as a "new dietary ingredient," or NDI, then the dietary supplement contains only dietary ingredients that have been present in the food supply as an article used for food in a form in which the food has not been chemically altered. For any supplement containing a new dietary ingredient for which the dietary ingredients have not been present in the food supply as an article used for food in a form in which the food has not been chemically altered, the manufacturer or distributor of the dietary ingredient or the supplement must submit pre-market notification to the FDA at least 75 days before the initial marketing of the dietary ingredient when used under the conditions or suggested in the labeling of the dietary supplement. Even to the extent the NDI was present in the food supply prior to October 15, 1994 or is used in conventional foods, if there are any changes to the ingredient's manufacturing or form as it was present in the food supply at that time or from how it exists in its conventional food form, then the ingredient may also be considered a NDI requiring notification.

Notification of use of a "New Dietary Ingredient" must inform the FDA of the basis on which the manufacturer has concluded that the supplement containing an NDI is reasonably expected to be safe under the recommended conditions of use. The FDA may not respond to such notification, but no response does not mean the FDA has determined that the ingredient is safe or permissible for use in a dietary supplement.

If the FDA determines that a product candidate which has already been brought to market and marketed as a dietary supplement contains a NDI without prior notification or contains some other substance not permitted in supplements, it may determine that the product is adulterated and/or misbranded in violation of federal law. In such a case, the FDA may take enforcement or other legal actions, including, but not limited to, warning or untitled enforcement letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution. Any such enforcement actions or other consequences could have a material adverse effect on the company and its current and future ability to development the product candidates through the selected pathway or other pathways.

In addition, manufacturers of dietary supplements must ensure that ingredients in their products that are not defined as dietary ingredients comply with all the requirements applicable to foods. For example, fillers and other constituents of the product must be approved as food additives or must be deemed GRAS for the conditions of use in order to be sold.

FDA regulation of conventional food

Conventional food products are subject to regulation by the FDA and other regulatory authorities, including the Federal Trade Commission, or FTC, which regulate the manufacturing, preparation, quality control, import, export, packaging, labeling, marketing, advertising, promotion, distribution, safety, and/or adverse event reporting of conventional foods. Among other things, manufacturers of conventional foods must meet applicable current good manufacturing practices, or cGMPs, and certain requirements that govern the manufacturing, packaging, labeling and holding of foods.

The FD&C Act requires that all food products be safe, meaning a reasonably scientific certainty that the substance is not harmful for its intended use. The FD&C Act prohibits the introduction into interstate commerce of a food to which has been added an approved drug or biologic, or a drug or biologic for which substantial clinical investigations have been instituted and made public, unless such a drug was marketed as a food before approval or meets other certain exceptions.

Under sections 201(s) and 409 of the FD&C Act, any substance that is reasonably expected to become a component of food or added to food is considered to be a "food additive", with a few exceptions, and is therefore subject to FDA premarket review and approval, unless the substance is generally recognized among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures or, in the case of a substance used prior to January 1, 1958, through experience based on common use in food, to be safe under the conditions of its intended use, a standard referred to as "generally recognized as safe," or GRAS. A food additive must either already be included within one of the number of FDA regulations authorizing the use of certain food additives under certain conditions of use or be approved for use by the FDA. To obtain approval for use of a food additive, a manufacturer must submit a petition to the FDA with sufficient data to demonstrate reasonable certainty of no harm at the intended levels of use. Any food that contains an unapproved food additive is considered adulterated under section 402(a)(2)(C) of the FD&C Act.

Ingredients that are determined to be GRAS (as described below) do not fall within the definition of a food additive, which, as noted above, requires mandatory premarket approval. Under sections 201(s) of the FD&C Act, and FDA's implementing regulations in 21 CFR § 170.3 and 21 CFR § 170.30, the use of a food substance may be GRAS either through scientific procedures or, for a substance used in food before 1958, through experience based on common use in food.

General recognition of safety through scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the substance as a food additive and must be based upon the application of generally available and accepted scientific data, information, or methods, which are ordinarily published, as well as the application of scientific principles, and may be corroborated by unpublished studies and other data and information. General recognition of safety through experience based on common use in foods requires a substantial history of consumption of a substance for food use by a significant number of consumers. If an ingredient is GRAS for one use or in one form, it is not necessarily GRAS for all uses or forms. Under section 201(s) of the FD&C Act, it is the intended use of a substance, rather than the substance itself, that is eligible for classification as GRAS.

Manufacturers of GRAS substances may notify the FDA of their view that a substance is GRAS and thus not subject to the premarket approval requirements of section 409 of the FD&C Act. The notification must include, among other things, a description of the substance, the applicable conditions of use, the dietary exposure, an explanation of the basis for the determination that the substance was determined to be safe for the intended use and supporting data and information. Upon review of such a notification, the FDA may respond with a "no questions" letter stating that while it has not made its own GRAS determination, it has no questions at the time regarding the applications' own GRAS determination. Alternatively, manufacturers may elect to "self-affirm" a given substance is GRAS without the voluntary FDA notification but should retain all applicable safety data used for the GRAS determination in the case of inquiry by the FDA. However, in neither case does this constitute an approval equivalent to that achieved through the food additive process. A manufacturer's use of such food additive is at its own risk and is dependent upon adequate substantiation and/or scientific support demonstrating safe use.

With certain exceptions, clinical investigations in which an investigational drug is administered to human subjects must be conducted under an IND, as required by FDA regulations. The FDA published a guidance document in September 2013 for clinical investigators, sponsors, and IRBs, "Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted without an IND" that provides the FDA's thinking on when an IND is required for human research studies. Based on this guidance, we understand and believe that the FDA's interpretation of its regulations is that they do not require human testing of food ingredients or dietary supplements to be conducted under an IND unless such testing is intended to evaluate the product's ability to diagnose, cure, mitigate, treat, or prevent a disease or condition. In this guidance, the FDA specifically recognizes an IND will not be required when a study is designed to "evaluate the tolerability of a food in a specific susceptible population, including individuals with a disease in a diseased population," provided the study is not designed to assess the impact of the food or medical food on the disease. There is no assurance that our understanding of the FDA's guidance is accurate or that the FDA's thinking on this matter will not change. If it does, the FDA may decide to take enforcement action to prohibit the Non-IND testing of substances that it believes should be conducted under an IND. For any products that we ultimately develop as drugs, the FDA may delay or deny an IND submitted with supporting data from human studies with such products not conducted under an IND or require alternate or additional data to support the IND before authorizing an applicant to proceed.

Additionally, depending on the circumstances, the use of a substance in certain clinical investigations under an IND may restrict the marketing of such substance in food. Section 301(II) of the FD&C Act prohibits the marketing of any food containing a drug substance that has been approved by FDA or for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, unless the substance was marketed in food before any substantial clinical investigations involving the drug were instituted or one of the other exceptions in section 301(II) applies. Accordingly, we understand and believe that the prior marketing of a substance of interest in food before an IND has been allowed or beginning any clinical investigations preserves the option to continue to market the substance in those forms after substantial clinical investigations have been instituted and their existence has been made public.

The FDA may classify some or all of our potential product candidates as containing a food additive that is not GRAS, or otherwise impermissible substances. Such classification would cause these product candidates to require pre-market approval for a food additive, or else it would need to be subject to an existing food additive regulation authorizing its use, which could substantially delay or prevent the commercialization of these product candidates for non-drug uses. Any delay in the regulatory consultation process or a determination that any of our drug or food product candidates do not meet regulatory requirements of the FDA, including any applicable GRAS requirements, could cause a delay in or prevent the commercialization of our product candidates, which may lead to reduced acceptance by the public or others or an inability to commercialize those candidates at all. Moreover, if the FDA determines that a product candidate marketed as a conventional food contains a non-GRAS additive after the product has already been commercialized, then the FDA may take enforcement or other legal consequences, including, but not limited to, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

Permissible claims for conventional foods and dietary supplements

The FDA and other regulatory authorities, including the FTC, heavily regulate any express or implied claims made about food and dietary supplement products, and/or their ingredients, including, but not limited to, any claims made in product labeling, marketing, promotion, on social media, or on the firm's website. FTC seeks to ensure the truth, accuracy, and substantiation of dietary supplement claims, and the FDA regulates the type and specific content of such claims.

With respect to dietary supplements and conventional foods, products are only allowed to make certain truthful and non-misleading claims without prior FDA-approval, and may not make unapproved health or qualified health claims, or any other claims that expressly or implicitly characterize the relationship between a substance and a disease or health-related condition (e.g., drug claims). Specifically, 21 C.F.R. § 101.93(g) prohibits claims, whether express or implied, that a dietary supplement is intended to "diagnose, mitigate, treat, cure, or prevent disease" and the use of such claims could subject a dietary supplement product to regulation as a drug. The FDA defines "disease" at 21 C.F.R. § 101.93(g)(1) to include any "damage to an organ, part, structure, or system of the body such that it does not function properly . . ., or a state of health leading to such dysfunctioning," though excludes diseases resulting from deficiencies in essential nutrients. For these types of claims, there must be significant scientific support and approval by the FDA prior to marketing the product. Similarly, as in the case for a dietary supplement, a food is considered to be a drug if it is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" under 21 U.S.C. § 321(g)(1)(B), except that a food may bear an authorized health claim about reducing the risk of a disease without becoming a drug. In other words, products marketed as dietary supplements and conventional foods cannot make health claims or drug claims (i.e., that the product is intended to diagnose, prevent, or cure any disease or condition) without prior FDA-approval of such claims. Dietary supplement products are permitted to make
structure/function claims subject to post-market notification to the FDA and inclusion of an FDA required disclaimer. "Structure/function" claims refer to a product's ability to maintain healthy bodily structure or function or claims describing the role of a nutrient or dietary ingredient or characterizing the way in which a nutrient or dietary ingredient supports or maintains such structure or function.

In determining whether or not a particular claim is permissible, the FDA considers the overall context in which that claim is made. As such, the direct recommendation of particular products to users based on deficiencies or other characteristics in their nutritional or health profiles may be viewed by the FDA as an implied disease claim and thus impermissible (except for specific allowed health claims or qualified health claims for supplements or foods or allowed nutrient content claims in foods or structure/function claims for dietary supplements).

The use of product claims on product candidates developed as non-drug products always carries a risk of regulatory enforcement action or other legal consequences, which may include class action litigation. Claims and other marketing or promotional activities also are potentially subject to federal and state consumer protection and unfair competition laws. Any such actions could materially affect us in an adverse way.

FDA regulation of medical food uses

Medical foods are a category of foods distinct from conventional food and dietary supplements. The FDA and other regulatory authorities, including the FTC, also regulate the manufacturing, preparation, quality control, import, export, packaging, labeling, marketing, advertising, promotion, distribution, safety, and/or adverse event reporting of medical foods. Among other things, manufacturers of medical foods must meet relevant cGMPs, and certain requirements that govern the manufacturing, packaging, labeling and holding of foods.

As defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), a medical food is "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." The FDA has established a regulation at 21 C.F.R. 101.9(j)(8) that further defines a medical food as a product that is (1) is specially formulated and processed product (as opposed to a naturally occurring foodstuff used in its natural state) for the partial or exclusive feeding of a patient by means of oral intake or enteral feeding by tube; (2) is intended for the dietary management of a patient who, because of therapeutic or chronic medical needs, has limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone; (3) provides nutritional support specifically modified for the management of the unique nutrient needs that result from the specific disease or condition, as determined by medical evaluation; (4) is intended to be used under medical supervision; and (5) is intended only for a patient receiving active and ongoing medical supervision wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the medical food.

Because the marketing of medical foods generally does not require FDA pre-market approval, the medical food category may offer promising opportunities for our products should we pursue that development path. However, we understand that the FDA considers the statutory definition of medical foods to narrowly constrain the types of products that fit within this category of food. There can be no assurance we will be able to develop the data that are needed to substantiate the positioning of the product as a medical food or that the FDA would concur the product meets the definition of medical food. In such cases, the commercialization of such product candidates may be delayed or prevented. To the extent that any product candidate is marketed as a medical food and subsequently determined to not fall within the proper regulatory category or are considered to be misbranded or adulterated, the company may be subject to enforcement action or other legal consequences, including, but not limited to, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution. Any such actions or other consequences could have a material adverse effect on the firm and its current and future ability to development the product candidates through the selected pathway or other pathways.

Moreover, the ingredients and additives used in medical foods are subject to the same regulations as conventional foods and must be GRAS or otherwise covered by an existing food additive regulation, approved food additive petition, or authorized by a prior sanction. The FDA may determine that some or all of our potential product candidates contain ingredients that are not GRAS and are therefore food additives. Such classification would cause these product candidates to require pre-market approval for a food additive, which could substantially delay or prevent the commercialization of these product candidates for medical food uses. If the FDA determines that a product candidate marketed as a medical food contains a substance that is not GRAS and is therefore a food additive after the product has already been commercialized, and such food additive is not approved or authorized by the FDA pursuant to a food additive regulation, then the firm may face enforcement or other legal consequences including, but not limited to, those mentioned above.

Government regulation of food for special medical purpose in the European Union

The regulatory requirements for foods for special medical purposes, or FSMPs, in the European Union cover FSMP development and commercialization.

In the European Union, FSMPs are designed to feed patients who, because of a particular disease, disorder or medical condition, have nutritional needs that cannot be met by consuming standard foodstuffs. European Union regulation defines food for special medical purposes' as food specially processed or formulated and intended for the dietary management of patients, including infants, to be used under medical supervision; it is intended for the exclusive or partial feeding of patients with a limited, impaired or disturbed capacity to take, digest, absorb, metabolize or excrete ordinary food or certain nutrients contained therein, or metabolites, or with other medically-determined nutrient requirements, whose dietary management cannot be achieved by modification of the normal diet alone.

Businesses intending to commercialize FSMPs in the European Union are required to register their FSMPs by submitting notifications regarding FSMP use, demonstrating compliance with applicable European Union rules, prior to market commercialization. These notifications to competent authority of each European Union Member State include information appearing on the label, and any other information the competent authority may reasonably request to establish compliance with this Regulation.

The European Commission may decide, by means of implementing acts (a) whether a given food falls within the scope of this Regulation; and (b) to which specific category of food a given food belongs. European Food Safety Authority Guidance provides, among other requirements, that the dossier must include an explanation of the scientific and medical basis on which it has been concluded that the use of the specific food product is necessary or is more practical or safer than the exclusive use of non-FSMP foodstuffs.

FSMPs can also fall within the scope of the novel food legislation in the European Union. Where an ingredient used in the FSMP to be marketed in the European Union falls within the definition of a 'novel food ingredient' prior authorization for use of the ingredient needs to be sought. A "novel" food or food ingredients as food that has not been consumed to a significant degree by humans in the European Union before May 15, 1997 and that falls within one of the ten food categories listed. Novel foods and novel food ingredients can only be authorized if they do not pose a safety risk to human health, their intended use does not mislead the consumer and they do not differ from the food they are intended to replace in such a way that its normal consumption would be nutritionally disadvantageous for the consumer. The authorization procedure is likely to take between 12 and 18 months.

In accordance with European Union Clinical Trials directives, before a Clinical Trial site is allowed to start enrolling patients in a Clinical Trial, the IRB/independent ethics committee, or IEC, must provide a positive opinion concerning the study protocol and all study-related materials. The competent authorities of the relevant European Union Member State must also provide their related authorization. Clinical Trials involving the investigation of the action of non-medicinal products (e.g., foods, such as many FSMPs), are not covered and are not required to register the Clinical Trial or to complete a Clinical Trial application (CTA) for approval by a European Union Member State.

Competition

The healthcare industry is characterized by intense competition and rapid innovation. Our potential competitors include major multinational pharmaceutical, nutritional foods companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions.

There are additional companies that are working on modulating specific metabolic pathways involved in various health and disease conditions, although we are not aware of any company creating Axcella product candidate-like products with multifactorial activity for the same indications and targets as Axcella. Entrinsic Biosciences, Inc. is developing amino acid compositions to treat gastrointestinal disorders and other conditions associated with dysfunctional transport membrane proteins. Entrinsic Biosciences has disclosed plans to file an IND for NET Carcinoid Syndrome Diarrhea in 2020 and has a pipeline of product candidates in preclinical and discovery programs. Companies with clinical programs that could compete with our current pipeline of product candidates include Bristol-Myers Squibb Co., Esperion Therapeutics, Inc., Genfit SA, Gilead Sciences, Inc., Intercept Pharmaceuticals, Inc., Kaleido Biosciences, Inc., Madrigal Pharmaceuticals, Inc., NGM Biopharmaceuticals Inc., Novartis AG, Scholar Rock Holding Corporation, and Viking Therapeutics, Inc., among others.

We also anticipate competing with the largest consumer health companies and nutritional and amino acid companies in the world, such as Abbott Laboratories, Ajinomoto Co., Inc., Johnson & Johnson, Nestlé Health Science S.A., and The Procter & Gamble Company, all of which are currently conducting research in competitive indications or may be interested in using amino acids and other EMMs as therapeutics as well as nutritional supplements.

Employees

As of December 31, 2019, we had 64 full-time employees. Of those employees, 32 have Ph.D. or M.D. degrees and 26 were engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

We lease a facility containing 19,200 square feet of laboratory and office space, which is located at 840 Memorial Drive, Cambridge, Massachusetts. The lease expires in April 2021, subject to two options to extend the lease for a total of six years. We believe that our current facilities are sufficient to meet our current and near-term needs.

Legal proceedings

We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report and in other documents that we file with the SEC, in evaluating the Company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks that we face. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

Risks related to our financial position and capital needs

We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.

We are a biotechnology company with a limited operating history. Investment in product development in the healthcare industry, including of biotechnology products, is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and/or become commercially viable. Our product candidates are currently being studied in non-IND, IRB-approved clinical studies as food products, or Clinical Studies, with plans, subject to completion of ongoing Clinical Studies, supportive data and FDA feedback, to have the next clinical trials of AXA1665, AXA1125 and AXA1957 conducted under IND Applications, or Clinical Trials, given our decisions in 2019 to commence development for these product candidates in a drug development path. We have no products approved for commercial sale, have not generated any revenue from product sales to date and continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception in 2008. Our net loss was $59.0 million and $36.1 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $216.1 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of our product candidates in Clinical Studies, Clinical Trials for any product candidate we elect to develop as a drug product candidate under an IND and as we seek regulatory approvals, as necessary, for and commercialize our product candidates, if approved. We anticipate that our expenses will increase substantially if, and as, we:

- conduct preclinical studies, Clinical Studies, and for those product candidates that we elect to develop as therapeutics, Clinical Trials or their equivalent in non-U.S. jurisdictions;
- further develop our proprietary human-focused product development platform, our development platform;
- continue to discover and develop our current product candidates as well as additional product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire or contract additional clinical, scientific, manufacturing, quality and commercial personnel to support our product research, development and commercialization efforts;
- continue to develop, scale and validate a manufacturing process and specifications for our product candidates, including under requirements for drug development;
- continue to establish in-house manufacturing capabilities for our research and product development efforts;
- establish a commercial manufacturing source and secure supply chain capacity sufficient to provide preclinical study material, Clinical Study material, Clinical Trial material for any product candidate we elect to develop as a drug product candidate under an IND, and commercial quantities of any product candidates that we may commercialize as drug or non-drug products, following receipt of any necessary approvals or authorizations;
- acquire or in-license other product candidates and technologies;
- seek various non-drug product marketing pathways and, if applicable, drug regulatory authorizations;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain regulatory approval or identify an alternate regulatory pathway to market; and

- add operational, compliance, financial and management information systems and personnel to support our operations as a public company.

To become and remain profitable, we or any potential future collaborator must develop and eventually commercialize products with significant market potential at an adequate profit margin after cost of goods sold and other expenses. This will require us to be successful in a range of challenging activities, including, but not limited to: completing preclinical studies, Clinical Studies and Clinical Trials for any product candidate we elect to develop as a drug product candidate under an IND; obtaining marketing approval or identifying alternate regulatory pathways for product candidates; manufacturing, marketing and selling products for which we may obtain marketing approval; or successfully satisfying any pre- or post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability. 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 decrease the value of our company, which could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business, which may be significant. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require additional capital to fund our operations and if we fail to obtain necessary financing, we will not be able to complete development and commercialization of our product candidates.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts for our current and future programs: to conduct further research and development, preclinical studies, Clinical Studies and, for any product candidate we elect to develop as a drug product candidate under an IND, Clinical Trials; to validate the manufacturing process and specifications for our product candidates; to seek regulatory approvals for or identify alternate regulatory pathways to market for our product candidates; and to launch and commercialize any products for which we receive regulatory approval or identify an alternate regulatory pathway to market, including potentially building our own commercial organization. As of December 31, 2019, we had $92.1 million of cash and cash equivalents on hand. Based on our current operating plan, we believe that our existing cash and cash equivalents, will enable us to fund our operating expenses, capital expenditure requirements and debt service obligations through at least the next 12 months. However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from our expectations, and we will in any event require additional capital in order to complete clinical development of any of our current product candidates. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- our decisions regarding the development path under which we will develop our product candidates (e.g., either continuing to develop a product candidate as a non-drug product, or initiating development as drug product candidate under an IND or non-U.S. equivalent);
- the initiation, progress, timing, costs and results of preclinical studies, Clinical Studies, planned Clinical Trials, and any need to conduct additional studies as may be required by a regulatory authority, including additional studies that may be required by a regulatory authority in order to allow the initiation of Clinical Trials under an IND or the non-U.S. equivalent for any of our product candidates;
- any clinical development plans we establish for these product candidates;
- further development of our development platform and supporting infrastructure;
- the number and characteristics of product candidates that we develop or may in-license;

- the terms of any partnership or collaboration agreements we may choose to initiate or conclude;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, any other regulatory authorities in the United States, and, when applicable, comparable foreign regulatory authorities, such as the EMA;
- the effect of changes in regulations or policy relating to the development and commercialization of our product candidates by the FDA, any other regulatory authorities in the United States and, when applicable, other comparable foreign regulatory authorities, such as the EMA;
- the cost of establishing, maintaining and overseeing a quality system compliant with GCP, (quality regulations, guidance and standards applicable to oversight of Clinical Trials, if any);
- the costs of establishing, maintaining and overseeing a quality system compliant with current Good Manufacturing Practice, or cGMP, and other quality standards applicable to drug development and a supply chain for the development and manufacture of our product candidates;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us related to our product candidates or our development platform, or other technologies;
- the effect of competing technological and market developments;
- the cost and timing of establishing, expanding and scaling compliance programs related to our activities and product candidate development and commercialization and related legal activities, including defense of any potential litigation against us;
- the cost and timing of establishing, expanding and scaling of manufacturing capabilities, or contracting with third parties for access to such capabilities; and
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval or identify alternate regulatory pathways in regions where we choose to commercialize our products.

We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient product or royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible into or exchangeable for common stock, your ownership interest will be diluted. If we raise additional capital through debt financing, we would be subject to fixed payment obligations and may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends or acquiring or licensing intellectual property rights. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek collaborators for one or more of our current or future product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. 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 the development or commercialization of one or more of our products or product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline, causing you to lose all or part of your investment.

Clinical development is 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 any product candidates, which could impair our ability to fund our operations or obtain financing on acceptable terms, or at all.

To obtain the requisite regulatory approvals to commercialize any of our product candidates that we decide to develop as a drug product candidate, we must demonstrate through extensive preclinical studies and Clinical Trials that our product candidates are safe and effective in humans for their intended use. Clinical Studies to commercialize non-drug products also require a significant financial investment to generate data that supports claims we may make for such products and establish their safety and tolerability. Clinical testing is expensive, difficult to design and implement and can take many years to complete, and its outcome is inherently uncertain. We may be unable to establish, where applicable, endpoints, dose levels and regimens or bioanalytical assay methods that applicable regulatory authorities would consider clinically meaningful or legally permissible. A Clinical Study or Clinical Trial can fail at any stage of testing. Additionally, our Clinical Studies, Clinical Trials or other studies may not result in data that supports intended claims for our product candidates. The outcome of preclinical studies, Clinical Studies and early Clinical Trials may not be predictive of the success of later preclinical studies, Clinical Studies and/or Clinical Trials, and interim results of these studies or trials do not necessarily predict final results. In particular, differences in trial design between Clinical Studies and early-stage Clinical Trials and later-stage Clinical Trials make it difficult to extrapolate from the results of Clinical Studies and earlier Clinical Trials to the results from later Clinical Trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and Clinical Trials have nonetheless failed to obtain marketing approval of their product candidates, or have data that supports desirable marketing claims even where marketing approval is not required.

Successful completion of Clinical Trials is a prerequisite to submitting an NDA to the FDA, or its equivalent in other jurisdictions such as a marketing authorization application to the EMA, for each product candidate targeting therapeutic indication(s) and, consequently, a pre-requisite for the ultimate approval and commercial marketing of any product candidate for therapeutic indication(s). We do not know whether we will be able to initiate or complete Clinical Trials for product candidates we decide to develop as drug product candidates on schedule, if at all. Additionally, we may determine as a result of factors in or out of control to terminate plans or efforts in connection with planned Clinical Studies or Clinical Trials. For example, if we do not have sufficient funds to finance our planned Clinical Studies or Clinical Trials or the FDA or equivalent regulatory authority has requirements we are not able to comply with, or that we decide to not comply with, we may need to delay or cancel one or more of our planned Clinical Studies or Clinical Trials.

We may experience delays in completing our preclinical studies and initiating or completing Clinical Studies and, for those product candidates that we decide to develop as drug product candidates, Clinical Trials. We also may experience numerous unforeseen events during, or as a result of, any future Clinical Studies or Clinical Trials that we may conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including, but not limited to:

- unforeseen events or events over which we have little to no control, such as the COVID-19 pandemic, can cause execution delays for our Clinical Studies or Clinical Trials, such as the temporary suspension of our AXA1957-002 study, and issues related to the quality, completeness and interpretability of our data that could result in significant delays or additional costs and impact development plans for our product candidates;
- we may be unable to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation of Clinical Trials for therapeutic indications for any drug product candidates or the marketing of our products as non-drug products;
- the FDA may not allow us to use data from our Clinical Studies to support a late-phase IND Clinical Trial or an IND Clinical Trial of any phase for AXA1665, AXA1125, AXA1957 or any other product candidate we decide to develop as a drug product candidate instead of a non-drug product candidate;

- the FDA or other regulatory authorities may disagree with the design, implementation or results of our Clinical Studies or Clinical Trials, which may delay or prevent us from pursuing certain regulatory pathways for product developments, or require us to submit additional data such as long-term toxicology studies or impose other requirements before permitting us to initiate or complete a Clinical Trial of any phase. For example, the FDA could require that we terminate a Clinical Study for a product candidate and continue such study only under an IND, and we may not be able to obtain such an IND, if at all, or we may be subject to an enforcement action for conducting a Clinical Study not under an IND. Additionally, although we hope to use data from Clinical Studies that we have completed or are currently conducting for AXA1665, AXA1125, and AXA1957 to support initial Clinical Trials in late phases (Phase 2 or registrational trials), the FDA may not authorize us to pursue a Clinical Trial for one or more of these product candidates in a late phase or at all;
- regulatory authorities, IRBs or ethics committees may not authorize us or our investigators to commence or conduct a Clinical Study or Clinical Trial at a prospective study or trial site or may request early termination of a Clinical Study or Clinical Trial;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective study or trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study or trial sites;
- Clinical Studies or Clinical Trials of any of our product candidates may produce negative or inconclusive results and we may need to conduct additional preclinical studies, Clinical Studies, Clinical Trials or any other studies, or we may decide to abandon product development programs;
- the number of subjects or patients required for Clinical Studies or Clinical Trials of any of our product candidates may be larger than we anticipate, enrollment in these clinical studies or trials may be slower than we anticipate or subjects or patients may withdraw from these clinical studies or trials prior to completion or fail to return for required follow-up post study or trial completion at a higher rate than we anticipate;
- we may need to add new or additional Clinical Study or Clinical Trial sites for various reasons, for example, our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the Clinical Study or Clinical Trial protocol or stop providing services for the study or trial, which may require that we add new clinical study or trial sites or investigators;
- the cost of preclinical studies, Clinical Studies, Clinical Trials or any other studies of any product candidates may be more than we anticipate or more than our available financial resources;
- the supply or quality of our product candidates or other materials necessary to conduct Clinical Studies and Clinical Trials, for which we expect to continue to rely on third party manufacturers and suppliers, may be insufficient or inadequate and may not achieve compliance with applicable cGMP and other quality standards applicable to drug or non-drug product development for various reasons including any potential failure of our oversight of their services or any potential inability of such third parties to successfully execute services in compliance with applicable rules and regulations;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulatory authorities, IRBs or ethics committees to suspend or terminate our Clinical Studies and Clinical Trials, or reports may arise from preclinical or clinical testing of our product candidates that raise safety or other concerns about one or more of our product candidates;
- preclinical studies, Clinical Studies or Clinical Trials of our product candidates may produce negative or inconclusive results, which may result in our deciding, or being required, to conduct additional clinical studies or trials or abandon product development programs; and
- adverse events in a Clinical Study of a product candidate may cause the FDA or comparable foreign regulatory authorities to only allow future studies of such product candidate to proceed under an IND, if at all.

We could also encounter delays if a preclinical study, Clinical Study or Clinical Trial is suspended or terminated for any reason. For example, our AXA1957-002 Clinical Study has been temporarily suspended as a result of COVID-19 impacts on clinical sites, their staff and subjects. This suspension, or other interruptions or suspensions of Clinical Studies related to the COVID-19 outbreak, could result in issues related to the quality, completeness and interpretability of the data from such Clinical Studies or otherwise result in delays or increased costs in our development plans. A suspension or termination may be imposed due to a number of factors, including failure to conduct the Clinical Study or Clinical Trial in accordance with regulatory requirements or our clinical protocols, inspection of the Clinical Study or Clinical Trial operations or trial site by the FDA, comparable foreign regulatory authorities or IRB resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, including death of a study subject, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful or legally permissible endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the Clinical Study or Clinical Trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of Clinical Studies or Clinical Trials may also ultimately lead to the denial of regulatory approval of our product candidates for therapeutic indications, where applicable, or the failure to meet applicable regulatory requirements to support and commercialize non-drug products. Further, the FDA or comparable foreign regulatory authorities may disagree with our Clinical Study or Clinical Trial design and our interpretation of data from these clinical studies or trials, or may change the requirements for regulatory approval of a drug even after they have reviewed and commented on the design for our preclinical studies, Clinical Studies or Clinical Trials.

Our product development costs will increase, or our operations may be hindered or prevented if we experience delays in clinical testing and marketing approvals, if applicable, or otherwise meeting regulatory requirements to commercialize our product candidates. We do not know whether any of our preclinical studies, Clinical Studies or Clinical Trials, if applicable, will begin or be completed as planned, will need to be restructured or will be completed on schedule, or at all. Significant delays in our preclinical studies, Clinical Studies or Clinical Trial also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may 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. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly, and could impair our ability to fund our operations or obtain financing on acceptable terms, or at all.

Risks related to our business, technology and industry

We have a limited operating history, which may make it difficult to evaluate our technology and product development capabilities and predict our future performance.

We are early in our development efforts and we have not initiated Clinical Trials for any of our product candidates to allow for development of such candidates as drug product candidates. In addition, as an organization, we have not yet commenced or completed any Clinical Trials. We are currently conducting Clinical Studies for product candidates AXA1665, AXA1125 and AXA1957 and pending completion of these studies and subject to agreement with the FDA, may conduct Clinical Trials for each of these candidates for OHE and NASH, respectively. AXA4010 is currently being studied as a non-drug product under food regulations in an ongoing Clinical Study, although the ultimate pathway under which we will develop AXA4010, AXA2678 and future other product candidates is subject to change depending on a number of factors. We were formed in 2008, have no products approved for commercial sale as drugs or marketed via other regulatory pathways (e.g., non-drug products such as dietary supplements) and have not generated any revenue from product sales. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend on the successful development and eventual commercialization of our product candidates, which may never occur.

Our limited operating history may make it difficult to evaluate our technology and industry and predict our future performance. Specifically, to date we have conducted Clinical Studies for our product candidates to evaluate safety and tolerability and impact on normal structure and function only in healthy subjects or subjects with certain disease conditions. For product candidates we develop under an IND with patient populations reflecting the desired indication for such product candidate, the physiological structure and function data we observed in our Clinical Studies for such product candidate may not be replicated in or be consistent with results from Clinical Trials and such product candidate may not meet therapeutic efficacy endpoints in Clinical Trials.

Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in evolving fields. If we do not address these or other risks successfully, our business will suffer. Similarly, we expect that our financial condition, expenditures and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our stockholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

In addition, as an early-stage company, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances, which may be significant. To the extent we ultimately pursue a drug development pathway for any product candidates initially studied under Clinical Studies, we will need to transition from a company with a research Clinical Study focus to a company capable of supporting clinical development in Clinical Trials and, if successful, commercial activities. We may not be successful in such transitions.

Any use of our product candidates to support and maintain homeostasis, which helps support normal structures and functions of the body, or to modulate dysregulated metabolism is a novel approach and negative perception of any product candidates that we develop could adversely affect our ability to conduct our business, obtain regulatory approvals or identify alternate regulatory pathways, to the extent required by applicable laws, to market such product candidates.

Using EMMs in the compositions, ratios and formulations we use in our product candidates and the potential drug and non-drug applications of our product candidates represents a novel approach. Our product candidates in general may not be successfully developed or commercialized or gain the acceptance of the public or the medical community. For any product candidate that we choose to develop as a drug product candidate, our success will depend upon physicians who specialize in the treatment of diseases targeted by our product candidates, prescribing potential treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. For any product candidate that we choose to develop as a non-drug product candidate, our success will depend on finding partners in a non-drug market who can help successfully commercialize product candidates as non-drug product candidates, such as dietary supplements. In addition, our success will also depend on consumer acceptance and adoption of our products that we, or a future partner, commercialize, if any. Adverse events, which may include death, in Clinical Studies and Clinical Trials of our product candidates or in studies or Clinical Trials of other parties developing similar products and the resulting publicity, as well as any other adverse events in the field of EMMs and metabolic pathways, could result in a decrease in demand for any product that we may develop. In addition, responses by the U.S. federal, state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval, if applicable, identify alternate regulatory pathways to market or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects, and may delay or impair the development and commercialization of our product candidates or demand for any products we may commercialize.

All of our drug product candidates will require significant additional preclinical and clinical development before we can seek regulatory approval for and launch a drug product commercially.

For any product candidate that we choose to develop as a drug product candidate, which we have done with AXA1665, AXA1125 and AXA1957, our business and future success will depend on our ability to obtain regulatory approval of and then successfully launch and commercialize such product candidate as a drug targeting a disease. Any future Clinical Trials of AXA1665, AXA1125, AXA1957 and any other product candidates that we decide to develop as drug product candidates may experience delays or other complications in Clinical Trial execution, such as complexities surrounding regulatory clearance to initiate Clinical Trials, the need for additional preclinical data to support authorization to proceed with Clinical Trials, modifications in trial design and trial protocols, bioanalytical assay method development, dose level and regimen selection, patient recruitment and enrollment, quality and supply of clinical doses or safety issues. Additionally, even if additional preclinical studies, Clinical Studies or Clinical Trials are successfully executed, there is no guarantee that their results will confirm or be consistent with the results obtained from prior completed preclinical studies, Clinical Studies or Clinical Trials for our product candidates.

The product candidates that we decide to develop as drug product candidates will require significant additional development, including preclinical and clinical development, regulatory review or approval in the jurisdictions that we target for commercialization, substantial investment, access to sufficient validated and cGMP-compliant commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. In addition, if AXA1665, AXA1125, AXA1957 or our other product candidates encounter safety, efficacy, supply or manufacturing problems, developmental delays, regulatory or commercialization issues or other problems, our development plans, including for our other product candidates, and our business would be significantly harmed.

The successful development of our product candidates is highly uncertain.

Successful development of our product candidates is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including, but not limited to:

- results from preclinical or Clinical Studies may demonstrate that our product candidates are not safe, not tolerable or have unanticipated impacts on the normal structure and function of the body and could result in data showing one or more product candidates to have harmful or problematic side effects or toxicities;
- Clinical Trial results may show any drug product candidate to be less effective than expected (e.g., a Clinical Trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to execute the Clinical Studies or Clinical Trials caused by slow enrollment, subjects dropping out of the Clinical Studies or Clinical Trials or other factors, including some which are out of our control, such as COVID-19, length of time to achieve clinical endpoints, additional time requirements for data analysis, or an inability to validate the manufacturing process or to achieve cGMP compliance for our product candidates;
- failure to receive the necessary regulatory approvals or authorizations, where applicable, or to meet and maintain compliance with applicable regulatory requirements, or a delay in such compliance or receiving such approvals or authorizations for, including, but not limited to, an NDA, or delays in NDA preparation, the need to submit a new dietary ingredient, or NDI, notification or other filings with the FDA, discussions with the FDA and comparable foreign regulatory authorities in jurisdictions we target or pursue, responding to an FDA request or other regulatory authority for additional preclinical or clinical data or unexpected safety or manufacturing issues;
- manufacturing costs, formulation issues, manufacturing deficiencies or other factors that could make our product candidates uneconomical;
- proprietary rights of others and their competing products and technologies that may prevent our product candidates from being commercialized; and
- for our EMM drug product candidates, the length of time necessary to complete Clinical Trials and to submit an application for marketing approval for a final decision by a regulatory authority may be difficult to predict, in large part because of the limited regulatory history of EMMs being approved for therapeutic use.

Even if we are successful in obtaining marketing approval for those product candidates that we decide to develop as drugs, commercial success of any approved drugs will also depend in large part on marketing acceptance, the availability of insurance coverage and adequate reimbursement from third-party payors, including government payors, such as the Medicare and Medicaid programs, and managed care organizations, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost-effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide adequate insurance coverage and reimbursement levels for one or any of our drug products once approved, market acceptance and commercial success would be reduced.

In addition, if any drug product candidate is approved for marketing, we will be subject to significant regulatory obligations regarding the submission of safety and other post-marketing information and reports and registration. If approved, our drug products may be subject to restrictions on our products' labels and other conditions of regulatory approval that may limit our ability to market our products for therapeutic indications. We will also need to comply (and ensure that our third-party contractors comply) with cGMP and Good Clinical Practice, or GCP, as we (and our third-party contractors) are and will be required to comply with cGMP for products used in our Clinical Studies and/or Clinical Trials, including for any studies or trials we conduct post-marketing approval for or commercialization of any of our product candidates. In addition, there is always the risk that we or a regulatory authority might identify previously unknown problems with a drug product post-approval or with non-drug products after commercialization, such as adverse events of unanticipated severity or frequency. Compliance with regulatory requirements to address such issues could be costly and any failure to comply or other issues with our drug products, if any, post-approval or non-drug products post-commercialization could have a material adverse effect on our business, financial condition and results of operations.

Similarly, the success of any product candidate we decide to develop as a non-drug product will depend on market acceptance, and even if we succeed in developing a non-drug product, we may still be subject to significant regulatory requirements, including, but not limited to, those with respect to the manufacture, development, processing, handling, labeling, and marketing of our products.

Our planned Clinical Studies or any future Clinical Trials, if applicable, or those of our future collaborators may reveal significant adverse events not seen in our preclinical studies, Clinical Studies or other Clinical Trials and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.

Before obtaining regulatory approvals for the commercial sale of any products for therapeutic indications, we must demonstrate through lengthy, complex and expensive preclinical studies and Clinical Trials that our product candidates are both safe and effective for use in each target indication. Any non-drug products must also be demonstrated to be safe and tolerable. Preclinical and clinical studies or trials and other product candidate testing are expensive and can take many years to complete, and their outcome is inherently uncertain. Failure can occur at any time during the preclinical, Clinical Study or Clinical Trial process. The results of preclinical studies, Clinical Studies as well as early Clinical Trials, as may be conducted, of our product candidates may not be predictive of the results of any later-stage clinical studies or trials. In addition, initial results in Clinical Studies and Clinical Trials, in particular as shown by any interim data, may not be indicative of results obtained when such Clinical Studies and Clinical Trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical studies and trials. Our product candidates have been generally well tolerated in our Clinical Studies to date, but we cannot be certain that we will be able to dose subjects or patients at a high enough dose in any future Clinical Trials of product candidates we may develop as drugs so as to demonstrate efficacy without unacceptable safety risk.

Product candidates in later stages of Clinical Studies may fail to show the desired safety profile despite having progressed through successful preclinical studies and earlier Clinical Studies. Product candidates that we decide to develop as drug product candidates and that progress to Clinical Trials may fail to show the desired safety and efficacy profile despite having progressed successfully through preclinical studies, Clinical Studies and, if applicable, initial Clinical Trials. A number of companies in the healthcare industry have suffered significant setbacks in later development, notwithstanding promising results in earlier trials. Most product candidates that commence Clinical Trials are never approved as products for therapeutic indications, and there can be no assurance that any of our current or future Clinical Studies or Clinical Trials will ultimately be successful or support further clinical development of any of our product candidates.

If significant adverse events, which may include death, or other side effects are observed in any of our current or future Clinical Studies or Clinical Trials, we may have difficulty recruiting subjects or patients for our Clinical Studies or Clinical Trials, subjects or patients may drop out of our Clinical Studies or Clinical Trials or we may be required to significantly redesign or abandon Clinical Studies or Clinical Trials or our development efforts of one or more product candidates altogether. We, the FDA or other applicable regulatory authorities or an IRB may suspend Clinical Studies or Clinical Trials of a product candidate at any time for various reasons, including a belief that subjects or patients in such Clinical Studies or Clinical Trials are being exposed to unacceptable health risks or adverse side effects or FDA or other applicable regulatory authorities could determine that our Clinical Studies need to be stopped and any further research for a product candidate needs to be conducted under a Clinical Trial instead. Some potential non-drug products and drug product candidates that initially showed promise for further development in early-stage testing, including in Clinical Studies or Clinical Trials, have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude a product candidate from obtaining or maintaining marketing approval, if applicable, or being commercialized, undesirable side effects may inhibit market acceptance of the commercialized product due to its tolerability versus other non-drug products or drugs. Any of these developments could materially harm our business, financial condition and prospects.

If we encounter difficulties enrolling subjects or patients in our Clinical Studies or any future Clinical Trials, our development activities could be delayed or otherwise adversely affected.

We may experience difficulties in subject and patient enrollment in our Clinical Studies and Clinical Trials for a variety of reasons. The timely completion of Clinical Studies or Clinical Trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of subjects or patients who remain in the Clinical Study or Clinical Trial until its conclusion. The enrollment of subjects or patients depends on many factors, including, but not limited to:

- the severity of the disease or condition under investigation in the case of a Clinical Trial conducted under an IND for a drug product candidate;
- the subject or patient eligibility and exclusion criteria defined in the protocol;
- the size of the study subject or patient population required for analysis of the primary endpoint(s) of the Clinical Study or Clinical Trial;
- the proximity of subjects or patients to study and trial sites;
- the design of the Clinical Study or Clinical Trial;
- our ability to recruit investigators with the appropriate competencies and experience;
- clinicians', subjects' or patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available drugs or non-drug products, as applicable;
- the efforts to facilitate timely enrollment in Clinical Studies or Clinical Trials;
- the subject or patient referral practices of physicians;
- the ability to monitor subjects or patients adequately during and after study product administration;
- our ability to obtain and maintain subject and patient consents;
- factors we may not be able to control, such as potential pandemics that may limit subject, principal investigator or staff and clinical site availability (e.g. outbreak of COVID-19); and
- the risk that subjects or patients enrolled in Clinical Studies or Clinical Trials will drop out of the Clinical Studies or Clinical Trials before completion.

In addition, our Clinical Studies and Clinical Trials will compete with other clinical studies or trials for product candidates that are in the same target markets as our product candidates, and this competition will reduce the number and types of subjects or patients available to us, because some individuals who might have opted to enroll in our Clinical Studies or Clinical Trials may instead opt to enroll in a study or trial being conducted by one of our competitors. Because the number of qualified clinical investigators is limited, we expect to conduct some of our Clinical Studies or Clinical Trials at the same sites that some of our competitors use, which will reduce the number of subjects or patients who are available for our Clinical Studies and Clinical Trials in such sites. Moreover, because our product candidates represent a departure from more commonly used methods in the non-drug and drug areas we may pursue, potential subjects or patients and their doctors may be inclined to use conventional products or therapies, rather than enroll subjects or patients in any future clinical study or trial.

Delays in subject or patient enrollment or Clinical Study or Clinical Trial delays such as the AXA1957-002 temporary suspension due to COVID-19, may result in increased costs or may affect the timing or outcome of our planned Clinical Studies or future Clinical Trials, which could prevent their completion or otherwise may negatively impact the quality, completeness and interpretability of data that we are able to collect and adversely affect our ability to advance the development of our product candidates.

Interim and preliminary data from our Clinical Studies or future Clinical Trials that we announce or publish from time to time may change as more subject or patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

To date, our Clinical Studies have been exploratory in nature, with a primary focus on the assessment of safety and tolerability and impact on normal structures and functions. Data from larger subsequent studies may not support or may be inconsistent with our observations in our completed Clinical Studies. From time to time, we may conduct Clinical Studies and Clinical Trials that result in interim or preliminary data. For example, in January 2020, we announced an interim analysis of our ongoing Clinical Study of AXA1125/AXA1957 in adult subjects with non-alcoholic fatty liver disease that includes data from approximately half of the study population through the full 16 weeks of administration. These data are subject to the risk that one or more of the outcomes may materially change as subject enrollment continues, more subject data become available and as the study is completed. Preliminary or top-line 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, interim and preliminary data should be viewed with caution until the final data are available. Material inconsistencies between preliminary or interim data and final data could significantly harm our business prospects.

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 have a material adverse effect on the success of 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 research and development activities may involve the use of biological and hazardous materials and may 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, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. 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 negatively impact our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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 biological waste or hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

If product liability claims or lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of testing our product candidates in Clinical Studies and/or Clinical Trials, and will face an even greater risk if we commercialize any products. For example, we may be sued, or claims may be made against us, if our informed consents for subjects or patients in any Clinical Studies or Clinical Trials are or are alleged to be inadequate or inaccurate in any way or fail to fully inform subjects or patients of any potential risks involved with their participation or other material or required information. We may also be sued, or claims may be made against us, if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during Clinical Studies, Clinical Trials, manufacturing, marketing or after sale. Any such product liability claims may include, without limitation, allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, marketing or promotional claims or a breach of warranties. Claims could also be asserted under state consumer protection or other statutes or regulations. If we cannot successfully defend ourselves against product liability claims or any other claims related to our products, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims could have a material adverse effect on our business and operations, and may result in, among other things:

- inability to bring a product candidate to the market;
- decreased demand for and decline in the price charged for our products;
- damage to our reputation;
- withdrawal of Clinical Study or Clinical Trial subjects or patients and inability to enroll future subjects or patients or continue Clinical Studies or Clinical Trials;
- initiation of investigations by regulatory authorities or other regulatory action;

- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to subjects or patients;
- product recalls, withdrawals or labeling, packaging, marketing or promotional modifications or restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidates via any regulatory pathway; and
- decline in our share price.

We maintain Clinical Trial insurance. We review our Clinical Trial insurance policy annually and we believe that our coverage is currently adequate to cover any claims that may arise in connection with our Clinical Studies or Clinical Trials. There is no guarantee that we will be able to obtain additional Clinical Trial insurance at an acceptable cost in the future, which could prevent or inhibit the ongoing development of our products.

Since we have not yet commenced marketing of any products, we do not yet hold product liability insurance for commercialization of our products. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. If and when coverage is secured, our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no or inadequate coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

The market opportunities for our product candidates may be limited and our estimates of the incidence and prevalence of our target populations may be inaccurate.

Our projections of both the non-drug and drug market sizes we may target and the incidence and prevalence of our target populations are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, input from key opinion leaders, patient foundations or secondary market research databases, and other sources and may prove to be incorrect. Further, new studies may change the estimated market sizes or the incidence or prevalence of target diseases we may target with potential drug product candidates. For those product candidates we develop under an IND, regulatory approvals may include limitations for use or contraindications that decrease the addressable patient population. The number of subject individuals may turn out to be lower than expected. Additionally, the potentially addressable patient population for our drug product candidates may be limited or may not be amenable to treatment with such product candidates. For instance, we estimate that (i) there are approximately 633,000 patients currently diagnosed with cirrhosis in the United States, (ii) up to 40% to 60% of cirrhosis subjects have sarcopenia and, separately, 40% have HE symptoms, (iii) approximately 63,000 to 130,000 individuals may be affected at any given time with both cirrhotic sarcopenia and OHE in the United States and (iv) a prevalence of NASH in the U.S. of over 15 million people and a similar prevalence in the five major European countries (France, Germany, Italy, Spain and the United Kingdom). Even if we obtain significant market share for our product candidates, because certain potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications for drugs or expanding the target market size for non-drug products.

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

We are developing our product candidates with our development platform to reprogram metabolism and maintain and restore metabolic health and have decided to pursue development of some of our product candidates as potential therapeutics under IND subject to ongoing Clinical Study completion, supportive data and agreement with the FDA. However, our development platform has not yet led, and may never lead, to marketable drug or non-drug products. We are developing our initial product candidates in liver and blood. We may have problems applying our technologies to these and other future target areas, and our product candidates may not demonstrate a comparable ability in supporting or maintaining health or treating disease, where applicable. Even if we are successful in identifying additional product candidates, they may not be suitable for clinical development as a result of limited efficacy, unacceptable safety profiles or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies, Clinical Studies and/or Clinical Trials with positive results;
- receipt of marketing approvals from applicable regulatory authorities, if necessary;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity, as available, for our product candidates;
- making arrangements with third-party manufacturers for, or establishing our own, commercial manufacturing capabilities;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- entering into new collaborations throughout the development process as appropriate, from preclinical studies through to commercialization;
- acceptance of our products, if and when approved or launched for commercialization under applicable regulations, by patients, consumers, the medical community and third-party payors;
- effectively competing with other drugs and non-drug products, depending on the development pathway that we choose for a product candidate;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our product candidates developed as drug products, if approved by the FDA;
- 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;
- achieving and remaining in compliance with applicable laws and regulations that apply to the research, development and commercialization of our product candidates and having productive interactions and positive regulatory decisions that lead to successful product commercialization;
- maintaining a continued acceptable safety profile of the products following approval or commercialization; 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 using our development platform, we will not be able to obtain product revenue in future periods, which could result in significant harm to our financial position and adversely affect our stock price.

We face significant competition from other healthcare companies, and our operating results will suffer if we fail to compete effectively.

The healthcare industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other drug or non-drug products that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical, nutritional foods companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel drugs or to in-license novel drugs that could make any product candidate that we develop as a drug product candidate obsolete. Mergers and acquisitions in the healthcare industry may result in even more resources being concentrated amongst our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on exclusive basis non-drug products that are safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement, if applicable depending on the development path we choose. We also anticipate that we will face increased competition in the future as additional companies enter our market and scientific developments surrounding other non-drug products and drugs targeted at metabolic pathways continue to accelerate.

In addition, there are additional companies that are working on modulating specific metabolic pathways involved in various health and disease conditions, although we are not aware of any company creating products targeting metabolic multifactorial activity for the same indications and targets as us, Entrinsic Biosciences, Inc. is developing amino acid combinations to treat gastrointestinal disorders and other conditions associated with dysfunctional transport membrane proteins. Entrinsic Biosciences has disclosed plans to file an IND for NET Carcinoid Syndrome Diarrhea in 2020 and has a pipeline of other product candidates in preclinical and discovery programs targeting cystic fibrosis, iron dysregulation, tumor regression, atopic dermatitis and wound healing. Companies with clinical programs that could compete with our current pipeline of product candidates include Bristol-Myers Squibb Co., Esperion Therapeutics, Inc., Genfit SA, Gilead Sciences, Inc., Intercept Pharmaceuticals, Inc., Kaleido Biosciences, Inc., Madrigal Pharmaceuticals, Inc., NGM Biopharmaceuticals Inc., Novartis AG, Scholar Rock Holding Corporation, and Viking Therapeutics, Inc., among others.

We also anticipate competing with the largest consumer health companies and nutritional and amino acid companies in the world, such as Abbott Laboratories, Ajinomoto Co., Inc., Johnson & Johnson, Nestlé Health Science S.A., The Procter & Gamble Company, all of which are currently conducting research in competitive indications or may be interested in using amino acids and other EMMs as therapeutics as well as nutritional supplements.

Even if we obtain regulatory approval to market our product candidates as drugs or are successful in identifying alternate regulatory pathways to market our product candidates under regulations that would apply to non-drug products, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of consumers to accept of our product candidates and choose them over other competitive products on the market or, for product candidates we develop as drugs, of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances.

Even if a drug product candidate or a non-drug product candidate receives marketing approval, or otherwise is commercialized, respectively, such products may fail to achieve the degree of market acceptance by physicians, patients, third-party payors, consumers and others in the medical or healthcare community or other target markets necessary for commercial success.

If any drug product candidate receives marketing approval or otherwise is commercialized under applicable regulations as a non-drug product, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, consumers and others in the medical or health community or other target markets. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including, but not limited to:

- efficacy (for any drug product candidate), safety and potential advantages compared to alternative products;
- the labeled uses or limitations for use, including age limitations or contraindications, for our product candidates compared to alternative products;
- convenience and ease of administration compared to alternative products;
- the willingness of the target patient or consumer population to try new drugs or non-drug products, respectively, and, with respect to any drug product candidates, of physicians to prescribe these therapies or, in the case of non-drug products, the willingness of target consumers in the market of health products to try and healthcare professionals to recommend consumers purchase our products;
- public perception of new drugs and non-drug products, including our product candidates;
- the strength of marketing and distribution support;
- the ability for us to partner in the manufacture and distribution of these products;
- the ability to offer our products, if approved, as applicable, for sale at competitive prices;
- the ability to obtain sufficient third-party insurance coverage and adequate reimbursement, as applicable depending on the development path we pursue; and
- the prevalence and severity of any side effects.

We will need to grow the size of our organization and we may experience difficulties in managing this growth.

As of December 31, 2019, we had 64 full-time employees. As our research, development, manufacturing and commercialization plans and strategies develop, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including, but not limited to:

- identifying, recruiting, compensating, integrating, maintaining and motivating additional employees;
- managing our internal research and development efforts effectively, including identification of clinical candidates, scaling our manufacturing process and navigating product candidate clinical development and the FDA, or other comparable regulatory agency’s, review process for our product candidates; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain organizations, advisors and consultants to provide certain services, including many aspects of legal, intellectual property, regulatory affairs, clinical management and manufacturing. There can be no assurance that the services of these organizations, advisors and consultants will continue to be available to us on a timely basis when needed or that we can find qualified replacements in a timely manner or at all. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical development may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates, if required, or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants, or key employees to provide needed services on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our current operations are located in Massachusetts; and we or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are located in Massachusetts. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, including any potential effects from the current global spread of COVID-19, power shortage, telecommunication failure or other natural or man made accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Natural disasters or pandemics such as the COVID-19 outbreak could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. For example, we have instituted a temporary work from home policy for non-essential office personnel and it is possible that this could have a negative impact on the execution of our business plans and operations. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure our investors that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities or the manufacturing facilities of our third-party contract manufacturers are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

If we lose key management personnel, or if we are unable to recruit additional highly skilled personnel, our ability to identify and develop new or next generation product candidates will be impaired, could result in loss of markets or market share and could make us less competitive.

Our ability to compete in the highly competitive biotechnology industry depends upon our ability to attract and retain highly qualified managerial, scientific, medical and other personnel. We are highly dependent on our management, scientific and medical personnel, including David Epstein, our Chairman of the board of directors, William Hinshaw, our Chief Executive Officer and President, Shreeram Aradhye, M.D., our Executive Vice President and Chief Development Officer, Manu Chakravarthy, M.D., Ph.D., our Chief Medical Officer and Senior Vice President of Clinical Development, Laurent Chardonnet, our Senior Vice President, Chief Financial Officer, Heidy King-Jones, J.D., LLM, our Senior Vice President of Legal, General Counsel, Stephen Mitchener, PharmD, our Chief Business Officer and Senior Vice President, Paul Fehlner, J.D., Ph.D., our Chief Intellectual Property Officer and Senior Vice President, Tony Tramontin, Ph.D., our Chief Scientific Officer and Senior Vice President of Research and Development. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

We conduct our operations in Massachusetts. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Employment of our key employees is at-will, which means that any of our employees could leave our employment at any time, with or without notice. For example, in the fall of 2019, a number of the employees in our finance group left the Company to pursue other employment opportunities and although these positions are currently filled by new full-time employees and consultants, such transitions create operational risks for the Company. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, contract manufacturing organizations, or CMOs, manufacturers of the raw materials used in our product candidates and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, including the current global spread of COVID-19 and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. For our Clinical Studies, we rely on third-party manufacturers to produce our product candidates, on CROs for conducting various portions of such studies and on various consultants throughout the study process. For materials to be used in any future Clinical Trials for drug product candidates, we plan to rely on an external CMO for the entire manufacturing supply chain and plan to continue using CROs and consultants in connection with conducting such trials. Our ability to obtain supplies of our product candidates and services from CROs and consultants could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

COVID-19 may materially and adversely affect our business and our financial results.

The recent outbreak of COVID-19 has spread globally, including to the United States and European countries, which has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns. We have instated some and may take additional temporary precautionary measures intended to help minimize the risk of the virus to our employees, including implementing a work-at-home policy, providing flexibility for working parents and suspending all business-related travel. Additionally, our AXA1957-002 Clinical Study, with sites in the United Kingdom and the United States, has been temporarily suspended due to COVID-19-related impacts. Although we cannot presently predict the scope and severity of COVID-19, these developments and measures could materially and adversely affect our business, our results of operation and financial condition, particularly if the COVID-19 outbreak adversely impacts our ability to conduct and complete our ongoing Clinical Studies and planned Clinical Trials in a timely manner or at all due to patient or principal investigator recruitment or availability challenges, clinical trial site shutdowns or other interruptions and potential limitations on the quality, completeness and interpretability of data we are able to collect; we or our key third-party service providers are not able to complete key program and product development milestones on time or at all; market volatility and conditions limit our ability to raise additional capital to finance our business plans on attractive terms or at all; our business continuity plans are not effective at limiting operational disruptions or delays; we suffer negative impacts to operations that may be vulnerable as a result of government or company measures taken to control the spread of COVID-19; potential shutdowns of government agencies such as the SEC or FDA, which may limit our ability to raise capital and negatively impact our product development timelines; the passage of new legislation that may increase our operating costs or limit our operations, such as the Families First Coronavirus Response Act; we suffer negative consequences due to vulnerabilities that emerge as a result of our limited operations, such as a cybersecurity incident; or one of our key executives, scientists or other personnel becomes incapacitated by COVID-19.

The extent to which COVID-19 impacts our business, operations or financial results will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, new information that may emerge concerning the severity of COVID-19 or the nature or effectiveness of actions to contain COVID-19 or treat its impact, among others. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, results of operation and financial condition.

Our internal computer systems, or those used by our CROs, CMOs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our CROs, CMOs and other contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of data from any 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 currently rely on third parties for the manufacture of our product candidates and to conduct Clinical Studies, 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.

Regulatory authorities globally are also imposing greater monetary fines for privacy violations. For example, in 2016, the European Union adopted a new regulation governing data practices and privacy called the General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR applies to any company that collects and uses personal data in connection with offering goods or services to individuals in the European Union or the monitoring of their behavior. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase the cost of providing our product candidates, if approved, or even prevent us from offering our product candidates, if approved, in certain jurisdictions.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless or negligent conduct that fails to comply with the laws of the FDA and other similar foreign, state or local regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign, state or local regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign, state or local fraudulent misconduct laws or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates, as may be necessary for any product candidates we decide to develop as drugs, or otherwise able to commercialize those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs.

A variety of risks associated with testing and developing our product candidates internationally could materially adversely affect our business.

In addition to researching, developing and commercializing our product candidates in the United States, we also intend to engage in these activities outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries, if our product candidates are approved, including, but not limited to:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act, or FCPA, or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

Additionally, we intend to contract with third parties to conduct some of our Clinical Studies and Clinical Trials outside the United States, which will subject us to additional risks and regulations. These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

We currently have no marketing and sales organization and have no experience in marketing products for therapeutic or non-drug uses. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products for therapeutic uses or other non-drug uses. When appropriate for our product candidates in development, we intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other healthcare companies to recruit, hire, train and retain marketing and sales personnel.

In addition to establishing internal sales, marketing and distribution capabilities, we intend to optimistically pursue collaborative arrangements regarding the sales and marketing of our products, in particular for products we develop as non-drug products; however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas. Even to the extent we are able to develop such capabilities or relationships, the sale, marketing and distribution of our product candidates will be subject to extensive government regulation and if we or related third parties fail to comply with such regulations, we may be subject to regulatory action, third-party claims or other potential liability.

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

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

As of December 31, 2019, we had U.S. federal and state net operating loss, or NOL, carryforwards of $192.1 million and $188.3 million, respectively. These amounts begin to expire in 2030. The federal net operating losses generated in 2018 and 2019 can be carried forward indefinitely. As of December 31, 2019, we also had U.S. federal and state research and development tax credit carryforwards of $6.1 million and $2.3 million, respectively, both of which expire at various dates through 2039. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future taxable income or tax liabilities, respectively. While federal NOLs generated after December 31, 2018 will not be subject to expiration, the deduction for such NOL in any taxable year will be limited to 80% of our taxable income in such year, where taxable income is determined without regard to the NOL deduction itself. In addition, in general, under Sections 382 and 383 of the Code, and corresponding provisions of state law, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOL carryforwards or tax credits, or Credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Our existing NOLs or Credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in connection with or after our initial public offering, or IPO, our ability to utilize NOLs or Credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or Credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or Credits. Furthermore, our ability to utilize our NOLs or Credits is conditioned upon our attaining profitability and generating U. S. federal and state taxable income. We have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; 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 Credits.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that future volatility, disruption or deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets continue to be volatile or are disrupted or deteriorate, including as a result of COVID-19, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

As of December 31, 2019, we had cash and cash equivalents of $92.1 million. While we are not aware of any downgrades, material losses or other significant deterioration in the fair value of our cash equivalents since December 31, 2019, no assurance can be given that further deterioration of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Our loan agreement subjects us to operating restrictions and financial covenants and may restrict our business and financing activities.

On January 9, 2018, we entered into a loan and security agreement with Solar Capital Ltd., or Solar, for term loans in an aggregate principal amount of $26.0 million, which we amended on October 5, 2018 and November 30, 2018. Our obligations under the loan agreement are secured by a first priority security interest in our assets, excluding intellectual property and certain other exceptions. We are subject to a negative pledge covenant with respect to our intellectual property. The loan agreement contains customary representations, as well as customary affirmative and negative covenants. Among other restrictions, the negative covenants, subject to exceptions, prohibit or limit our ability to: declare dividends or redeem or purchase equity interests; incur additional liens; make investments; incur additional indebtedness; engage in mergers, acquisitions and asset sales; transact with affiliates; undergo a change in control; add or change business locations; and engage in businesses that are not related to its existing business. These covenants may restrict our ability to finance our operations and to pursue our business activities and strategies. Our ability to comply with these covenants may be affected by events beyond our control.

Risks related to government regulation

We are very early in our development efforts. Our drug product candidates will require significant additional preclinical and clinical development before we seek regulatory approval. Product candidates that we decide to bring to market as non-drug products may also require additional development, and all of our product candidates may require significant interactions with regulatory authorities and investments before their respective commercial launches. If we are unable to advance our product candidates to final development, meet regulatory requirements, including obtaining regulatory approval, where applicable, or ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have invested substantially all of our efforts and financial resources in the identification and early clinical development of product candidates, including in Clinical Studies and preclinical studies. To date, we have not marketed or commercialized products and have not yet commenced any Clinical Trials with our drug product candidates (i.e. AXA1665, AXA1125 and AXA1957). Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any products, and we may never be able to develop or commercialize a marketable product. The success of our product candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, preclinical studies, Clinical Studies and, if applicable, Clinical Trials;
- clearance of INDs for future Clinical Trials for product candidates that we decide to develop as drug product candidates;
- receipt of regulatory approvals from applicable regulatory authorities for drug product candidates or, alternatively, compliance with regulatory requirements applicable to non-drug products;
- establishing cGMP-compliant supply and commercial manufacturing operations or making arrangements with cGMP-compliant third-party manufacturers for supply and commercial manufacturing;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- launching commercial sales of our product candidates, if and when approved or allowed for marketing, whether alone or in collaboration with others;
- acceptance of our drug product candidates, if and when approved, by patients, the medical community and third-party payors, or acceptance of our non-drug products we may market by consumers;
- effectively competing with other drugs for any product candidate developed and approved as a drug or competing with other non-drug products for any product candidate developed and marketed as such;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement, as applicable;
- enforcing and defending intellectual property rights and claims;
- the marketing of our products; and

- maintaining a continued acceptable safety profile of the product candidates following approval or commercialization.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals or identify and successfully execute on alternate regulatory pathways to market for our product candidates, we may not be able to continue our operations.

Regulatory requirements for development of our product candidates as drugs or as non-drug products are uncertain and evolving. Changes in these laws, including our ability to conduct Clinical Studies or Clinical Trials, or the current interpretation or application of these laws, or conflicts between us and the FDA on the applicability or interpretation of applicable laws, would have a significant adverse impact on our ability to develop and commercialize our products.

In the United States, under Sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act, or the FD&C Act, any substance that is reasonably expected to become a component of food is considered to be a food additive, and therefore subject to FDA premarket review and approval, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use. Moreover, under federal law, dietary supplement products must only contain certain permissible dietary ingredients, and any ingredients considered to be an NDI under the FD&C Act will require pre-market notification to the FDA.

Based on the large body of studies and scientific literature on the human exposure to and safety profiles of certain amino acids, the FDA's promulgation of regulations governing the use of certain amino acids under certain conditions as safe and permissible food additives when used as nutrients, our own data on amino acids used in product candidates and the fact that we use amino acids in our product candidates within amounts previously studied safely in humans, we believe we have designed our product candidates to have acceptable safety profiles, and we further have evaluated or will evaluate the safety and tolerability of these product candidates in Clinical Studies and/or Clinical Trials. Under the FDA's framework governing studies of non-drug products, we believe that use of our product candidates containing amino acids may be studied for safety and tolerability without an IND. However, the FDA or comparable foreign regulatory authorities may disagree with this approach and determine that our studies should be conducted under an IND, which may result in negative consequences.

In prior or future studies or trials of our product candidates, we may have or will expressly or implicitly characterize or classify such candidates as encompassed within a specific regulatory scheme (e.g., as foods or dietary supplements). Regulatory authorities may not agree with the regulatory classification of the product candidates used in our Clinical Studies or any subsequent classification of such candidates prior to commercialization. To date, we have had one pre-IND meeting with FDA regarding our AXA1665 program and have not discussed the development of our other product candidates evaluated in Clinical Studies or our utilization of specific regulatory pathways for our other product candidates with the FDA or comparable foreign regulatory authorities and any such regulator may not agree with our current activities or future approach or plans for further development. The FDA may determine that our product candidates are not safe or appropriate for use in Clinical Studies or are not governed by food regulations and therefore may classify any of our product candidates as being ineligible for investigation in Clinical Studies without an IND. The FDA or other regulatory authorities may also take enforcement action, or otherwise delay or prevent further development or commercialization of our product candidates.

The FDA may determine that our product candidates cannot be marketed as or do not meet the regulatory requirements for marketing or testing as non-drug products. The FDA may take the position that we failed to satisfy the premarket requirements for ingredient compositions, including that the particular product is not generally recognized as safe, or GRAS, is an unapproved food additive, is a NDI requiring premarket review or that our products contain otherwise impermissible ingredients, in which case some or all of our products may be deemed adulterated or misbranded in violation of the FD&C Act. Moreover, if we choose to study a product under an IND before the product candidate has been marketed as a non-drug product, the FD&C Act could prevent us from marketing the product as a non-drug product if we are unable to secure FDA approval as a new drug. Any delay in the regulatory consultation process, or a warning, finding or determination that any of our operations or product candidates do not meet the regulatory requirements of the FDA, including but not limited to any applicable GRAS, food additive or NDI requirements, could subject the company to regulatory enforcement action or other legal action, and/or cause a delay in or prevent the commercialization of one or more of our product candidates, which may lead to reduced acceptance by the public or others for any products we are able to commercialize and could materially adversely affect our business.

The FDA may determine that the only pathway for conducting studies of our product candidates is under an IND or that our Clinical Studies already conducted should have been conducted under an IND. Any such determination could prevent our reliance on existing regulatory frameworks to conduct Clinical Studies for other product candidates or prevent us from relying on or including data from our Clinical Studies in any regulatory submissions to support further clinical development or marketing approval, and could significantly increase the cost of and delay the development or commercialization of our product candidates. If the FDA disagrees with our determination that we may conduct Clinical Studies without filing an IND, they could require that we halt any Clinical Studies we have commenced, or we may be subject to enforcement action. Should we choose to commercialize our product candidates as non-drug products and if the FDA determines our product candidates fall outside the food regulations, we may be subject to regulatory enforcement action and we could be required to stop selling, withdraw, recall, re-label or re-package any products we have commercialized as non-drug products on the market. In addition, if new safety issues are raised by Clinical Studies in advance of deciding whether to file an IND that suggest safety concerns for all of our product candidates, then the FDA could ask us to modify approved labeling for or withdraw from the market any previously approved products for therapeutic uses or products being commercialized for non-drug uses. A decision by the FDA that we cannot conduct Clinical Studies without filing an IND would significantly impact our current business model and we may incur significant expense and operational difficulties.

Changes in the legal and regulatory environment could limit our future business activities, increase our operating or regulatory costs, reduce demand for our product candidates or result in litigation.

The conduct of our current and planned business activities, including, but not limited, to the development, testing, production, storage, distribution, sale, display, advertising, marketing, labeling, packaging, health and safety practices, regulatory classification and approval, where necessary, and use of our product candidates, is subject to various laws and regulations administered by federal, state and local governmental agencies in the United States, as well as to laws and regulations administered by government entities and agencies outside the United States in markets in which we conduct clinical studies or trials under foreign food or drug regulations or in which our product candidates and components thereof (such as packaging) may be manufactured or sold.

These laws and regulations and interpretations thereof may change, sometimes dramatically, as a result of a variety of factors, including political, economic or social events. Such changes may include changes in:

- food and drug laws, including FDA regulations;
- laws related to product labeling;
- advertising and marketing laws and practices;
- laws and programs restricting the sale and advertising of certain product candidates;
- laws and programs aimed at regulating, restricting or eliminating ingredients present in certain of our product candidates;
- increased regulatory scrutiny of, and increased litigation involving, product claims and concerns regarding the actual or possible effects or side effects of ingredients in, or attributes of, certain of our product candidates;

- state and federal consumer protection and disclosure laws;
- changes in law due to unforeseen events such as COVID-19 that may result in additional costs or disruptions in our operations, such as the Families First Coronavirus Response Act, or local government orders or restrictions which could limit our business operations; and
- increased sponsor or company obligations under privacy laws such as the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and GDPR.

New laws, regulations or governmental policy and their related interpretations, or changes in any of the foregoing, may alter the environment in which we do business and, therefore, may impact our operating results or increase our costs or liabilities.

We may rely on academic and private non-academic institutions to conduct investigator-sponsored Clinical Studies or Clinical Trials of our product candidates. Any failure by the investigator-sponsor to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval or otherwise commercialize the applicable product candidates.

We may rely on academic and private non-academic institutions to conduct and sponsor clinical studies or trials relating to our product candidates. We will not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or comparable foreign regulatory authorities will not view these investigator-sponsored studies or trials as providing adequate support to allow for the initiation of future Clinical Trials for those product candidates that we choose to develop as drug product candidates, whether controlled by us or independent investigators, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will likely provide us certain information rights with respect to the investigator-sponsored studies or trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored studies or trials. However, we would not have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored studies or trials. If we are unable to confirm or replicate the results from the investigator-sponsored studies or trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored studies or trials been sponsored and conducted by us, then our ability to design and conduct any future Clinical Trials ourselves may be adversely affected.

Additionally, the FDA or comparable foreign regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored studies or trials or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored studies or trials. If so, the FDA or other comparable foreign regulatory authorities may require us to obtain and submit additional preclinical, manufacturing or clinical data before we may initiate our planned Clinical Trials or may not accept such additional data as adequate to initiate our planned Clinical Trials. In addition, it could limit or prevent our ability to commercialize product candidates for non-drug uses.

Obtaining and maintaining regulatory approval of our drug product candidates or the ability to commercialize our product candidates through a non-drug regulatory pathway in one jurisdiction does not mean that we will be successful in obtaining regulatory approval or identifying a similar alternate regulatory pathway for our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval for drug product candidates or identifying or commercializing our product candidates through non-drug pathways in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval or identify and maintain an alternate regulatory pathway in any other jurisdiction, while a failure or delay in obtaining regulatory approval or an alternate regulatory pathway in one jurisdiction may have a negative effect on the regulatory approval process or path to market in others. For example, even if the FDA grants marketing approval of a drug product candidate for therapeutic indications, comparable foreign regulatory authorities could take opposing positions and decline to approve the manufacturing, marketing and promotion of such product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies, Clinical Studies and Clinical Trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval and the approved price may not lead to profitability or acceptable margins.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States may have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Preclinical and clinical development is uncertain. Our preclinical programs, Clinical Studies and Clinical Trials may experience delays or may never advance to the next stage of development, which would adversely affect our ability to obtain regulatory approvals, where necessary, or identify and execute on alternate regulatory pathways to commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

Our product candidates are in both preclinical and clinical (non-IND) stages of development, and their risk of failure is high. To proceed with our development plans and ultimately commercialization, we may need to conduct and meet regulatory requirements for preclinical, Clinical Studies or, for drug product candidates, Clinical Trials. For therapeutic applications, the FDA may require additional extensive preclinical and other studies. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or comparable foreign regulatory authorities will accept our proposed clinical programs, including our Clinical Studies and future Clinical Trials, if any, including their design, dose level, and dose regimen, or if the outcome of our preclinical testing, Clinical Studies or Clinical Trials, if any, will ultimately support the subsequent development of our clinical programs for therapeutic indications or non-drug applications. As a result, we cannot be sure that we will be able to submit INDs or similar applications in the case of drug product candidates or comply with any other regulatory requirements where necessary for commercialization and marketing of drugs or non-drug products on the timelines we expect, if at all. We cannot be sure that submission of INDs or similar applications, where necessary, or other regulatory required submissions for our product candidates will result in the FDA or comparable foreign regulatory authorities allowing our Clinical Studies or Clinical Trials to begin, be completed or have their data used to support commercialization and required regulatory approvals. We also cannot be certain if our testing and studies will provide support for the further development of product candidates as non-drug products or support for any associated product claims made, and, as a result, we cannot be sure that we will be able to successfully pursue alternative regulatory pathways to commercialization any of our product candidates as non-drug products.

If we are not able to meet certain regulatory requirements for our product candidates or to obtain, or timely obtain, required regulatory approvals for our drug product candidates, we will not be able to commercialize or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization as a drug or non-drug products, including but not limited to their design, testing, manufacture, safety, efficacy, recordkeeping, packaging, labeling, storage, holding, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our product candidates as a drug, we must obtain marketing approval. Before we can commercialize any of our product candidates as a non-drug product, we may be required to follow pre- or post-market notification and other applicable regulatory requirements for ingredients and claims. We have not received approval to market any of our product candidates as drugs from regulatory authorities in any jurisdiction nor executed on requirements for commercialization of non-drug products under applicable regulations, and it is possible that none of our current product candidates, or any product candidates we may seek to develop in the future, will ever obtain regulatory approval, where applicable, or meet other applicable regulatory requirements to reach the market. We, as a company, have no experience in filing and supporting the applications necessary to gain regulatory approvals for drugs or in the submission of other petitions, notifications or registrations in the case of non-drug products, where applicable, and expect to work with or rely on third-party CROs or regulatory consultants to assist us in this process. For example, the FDA and Federal Trade Commission, or FTC, require substantiating data or evidence for marketing claims and may require other regulatory submissions, including, for example, NDI submissions for certain product ingredients in certain non-drug products before they can be sold. With respect to drug product candidates, securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. If we fail to execute competently on these requirements, as applicable, our product candidates may never reach the market.

Securing regulatory approval for therapeutic indications also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug 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 regulatory approvals for therapeutic indications, both in the United States and abroad, is expensive, may take many years if additional Clinical Trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted IND, NDA or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process of our drug product candidates and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our drug product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, including study population, dose level, dose regimen, efficacy endpoints and bioanalytical assay methods, or implementation of our Clinical Trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of our Clinical Trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies, Clinical Studies or Clinical Trials;
- the data collected from our Clinical Studies and Clinical Trials for our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future Clinical Trial results may result in our failing to obtain regulatory approval to market our applicable drug product candidates as drugs, which would significantly harm our business, results of operations and prospects.

If we decide to develop any product candidate in the therapeutic path and submit an NDA, the FDA may also require a panel of experts, or an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval for therapeutic indications. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any drug product candidates based on the completed Clinical Trials.

In addition, even if we were to obtain approval for use of our product candidates as drugs, regulatory authorities may approve any of our product candidates for fewer or more limited therapeutic indications than we request, may include limitations for use or contraindications that limit the suitable patient population, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing Clinical Trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug product candidate. Similarly, regulatory authorities may limit or prohibit label claims that limit the market, price or other factors that are necessary or desirable for the successful commercialization of candidates developed as non-drug products. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays or failures in obtaining regulatory approvals, where applicable, or otherwise experience delays or failures in complying with regulatory requirements for commercialization of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

The FDA and comparable foreign regulatory authorities such as the EMA may implement additional regulations or restrictions on the development and commercialization of products that act on metabolic pathways, which may be difficult to predict.

The FDA and comparable foreign regulatory authorities such as the EMA have expressed interest in further regulating biotechnology products and product candidates such as ours. Agencies at both the federal and state level in the United States, as well as the U.S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Adverse developments in Clinical Studies or Clinical Trials of our product candidates or similar products conducted by others may cause the FDA or comparable foreign regulatory authorities to change the requirements for approval of any of our product candidates. The FDA or comparable foreign regulatory authorities may impose unexpected, onerous requirements on our products because they are composed of multiple amino acids, requiring a clinical demonstration of the functionality and contribution of each component of our EMMs. Such requirements may include additional studies or analyses. Similarly, the EMA and member states govern the development of product candidates as drugs in the European Union and member state regulatory bodies govern the development of product candidates under non-drug regulations and may issue new guidelines concerning the development and marketing authorization for our product candidates and require that we comply with these new guidelines. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may, for our drug product candidates, result in a review and approval process that is longer than we otherwise would have expected and delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete Clinical Trials and commercialize our current and future product candidates in a timely manner, if at all.

We may fail to obtain and maintain orphan drug designations from the FDA or, if applicable, comparable foreign regulatory authorities such as the EMA for our drug product candidates.

Our strategy includes filing for orphan drug designation where available, and applicable, for our drug product candidates. In the United States, under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding toward Clinical Trial costs, tax advantages for clinical drug development and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug or 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 where the original manufacturer is unable to assure sufficient product quantity.

In addition, exclusive marketing rights in the United States may be limited if we seek approval for a product candidate that we decide to develop as a drug an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective, or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity for a given drug product for a given indication. Even with respect to the indications for which we received orphan designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, and thus approval of our product candidates could be blocked for seven years if another company previously obtained approval and orphan drug exclusivity for the same drug and same condition. Moreover, even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our drug product candidates, we may never receive such designations.

In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the European Union, orphan drug designation entitles a party to financial incentives such as reductions of fees, fee waivers and protocol advisory assistance. In addition, ten years of market exclusivity is granted following drug product approval, meaning that another application for marketing authorization of a later similar medicinal product for the same indication will generally not be approved in the European Union. This period may be reduced to six years if the orphan designation criteria are no longer met, including where it is shown that the product is not sufficiently profitable to justify maintenance of market exclusivity.

Even if we receive regulatory approval of any drug product candidates, or commercialize our product candidates as non-drug products, we will be subject to ongoing regulatory compliance obligations or continued regulatory review, which may result in significant additional expense. Additionally, any of our product candidates, if approved or commercialized, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved for therapeutic indications or are commercialized as non-drug products, they will be subject to ongoing regulatory requirements for manufacturing, processing, labeling, packaging, storage, holding, testing, distribution, quality, safety, sale, marketing, advertising, promotion, sampling, record-keeping, export, import, conduct of post-marketing studies and submission of safety, efficacy or other post-market information. Such requirements may be imposed as federal and state requirements in the United States or by comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP requirements as applicable to drug and non-drug products and GCP requirements for any Clinical Trials that we conduct post-approval, if applicable.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority requirements, including ensuring that quality assurance, quality control and manufacturing procedures conform to the respective cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, if applicable, or other marketing application or submission, and previous responses to inspection observations. 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, quality assurance and quality control.

The FDA has significant post-marketing authority, including, for example, the authority to require labeling or packaging changes based on the use of improper product claims or new safety or other information and, where applicable, to require post-marketing studies or Clinical Trials to evaluate serious safety risks related to the use of a drug. With respect to products developed as drugs, any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which a drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 Clinical Trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, program as a condition of approval of drug product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates as drugs for therapeutic uses, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA or comparable foreign regulatory authorities may take regulatory enforcement action or other legal action or, in the case of drugs, impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in potential consequences, including, among other things:

- in the case of drug product candidates, revisions to the approved labeling to add new safety information and required regulatory submissions; imposition of post-market studies or Clinical Trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program;
- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- re-labeling or re-packaging;
- fines, warning or untitled enforcement letters or holds on Clinical Trials;
- in the case of drugs, refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA and FTC strictly regulate marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses for drugs, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Additionally, FDA and other regulatory authorities can take action against a company that makes misleading or inaccurate claims regarding efficacy and safety of an approved product. Non-drug products are prohibited from making any claims, whether express or implied, that the product is intended to "diagnose, mitigate, treat, cure or prevent disease," and doing so may subject a non-drug product to classification as a drug product and regulatory enforcement action. If the FDA or other regulatory agency determines that any of our product candidates make impermissible claims, we may be subject to any of the aforementioned consequences or other legal challenges that may have an adverse effect on the company's business and operations.

The policies of the FDA and of other comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval, where applicable, and commercialization, and continued commercialization, of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained for any drugs, or may no longer be able to market or sell products we develop as non-drug products, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current administration may impact our business and industry. Namely, the current administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities, such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict how these executive actions, including any executive orders, will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, where applicable, our ability to continue to market and sell our products and we may not achieve or sustain profitability.

Non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring or pharmacovigilance requirements, where applicable, can also result in significant financial penalties.

Healthcare insurance coverage and reimbursement may be limited or unavailable in certain market segments for our drug product candidates, if approved, which could make it difficult for us to sell any such drug product profitably.

The success of our product candidates, if approved for therapeutic indications, depends on the availability of adequate coverage and reimbursement from third-party payors, including governmental healthcare programs, such as Medicare and Medicaid, commercial payors and health maintenance organizations. In addition, because our product candidates have the potential to represent a relatively new approach to the treatment of the diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs and commercial payors are critical to new product acceptance. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these other countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. 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 candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Healthcare insurance often does not cover non-drug products administered outside of the hospital setting. This may impact our product candidates if we decide to commercialize them as non-drug products.

For our drug product candidates, our relationships with healthcare providers, 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, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, or FCA, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for Clinical Trials. The applicable federal and state healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- The federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation or arranging of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, 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 FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution.
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false, fictitious or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the federal civil False Claims Act.
- HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The federal Physician Payment Sunshine Act, created under the Patient Protection and Affordable Care Act, or the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.

- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign 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 or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

The failure to comply with any of these laws or regulatory requirements subjects entities to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, reputational harm, exclusion from participation in federal and state funded healthcare programs (such as Medicare and Medicaid), contractual damages and the curtailment or restructuring of our operations, as well as 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. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the company’s business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. For instance, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General will commence enforcement actions against violators beginning July 1, 2020. As currently written, the CCPA may impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. In addition, we may obtain health information from third parties (including research institutions from which we obtain Clinical Trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal and administrative penalties if we knowingly obtain, use or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data or, in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation or adverse publicity and could negatively affect our operating results and business. Moreover, Clinical Study and Clinical Trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

We currently are conducting Clinical Studies and potentially will conduct Clinical Trials in the European Union, which may subject us to additional privacy restrictions. The collection, use, storage, disclosure, transfer, and other processing of personal data, including health data in the European Union is governed by the provisions of the GDPR, which became effective on May 25, 2018. It imposes several requirements relating to the processing health and other sensitive data, the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data, implementation of safeguards to protect the security and confidentiality of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR introduces new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms ensuring compliance with these or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current therapeutic product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, addresses 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, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States Supreme Court and the Trump administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Additionally, Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, two percent per fiscal year through 2029, due to subsequent legislative amendments, unless Congress takes additional action. In January 2013, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget for fiscal year 2019 and 2020 contain further drug price control measures that could be enacted during the 2020 legislative session or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option to use step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2019. This final rule codified CMS’s policy change that was effective January 1, 2019. Although a number of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We may face competition in the United States for our product candidates that we elect to develop as drug product candidates and that are subsequently approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act contains provisions that may change U.S. importation laws and expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. These changes to U.S. importation laws will not take effect unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On December 18, 2019, FDA issued a notice of proposed rulemaking that, if finalized, would allow for the importation of certain prescription drugs from Canada. FDA also issued a draft guidance document outlining a potential pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The regulatory and market implications of the notice of proposed rulemaking and draft guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. 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. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

European Union drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for any drug product candidate in the European member states.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the European Union, the pricing of pharmaceutical products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the European Economic Area, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. 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. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a Clinical Trial or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of any of our product candidates in those countries would be negatively affected.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection Clinical Trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain ex-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our ex-U.S. activities to increase in time. We plan to engage third parties for Clinical Trials or to obtain necessary permits, licenses, patent registrations and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

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

The ability of the FDA to review and approve new products or take action with respect to other regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those 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 to be reviewed or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Similarly, a prolonged government shutdown could prevent the timely review of our patent applications by the United States Patent and Trademark Office, or USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly execute our business plans.

Risks related to our intellectual property

If we are unable to obtain and maintain patent protection for any product candidates we develop or for our development platform or other technologies, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates, development platform and other technologies we may develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad relating to our product candidates and development platform, as well as other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. As of December 31, 2019, we have several issued patents on our product candidates, and we have filed or intend to file patent applications on our product candidates, certain aspects of our development platform and other technology; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that the claims in our pending patent applications covering the composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions of matter relating to our product candidates and proprietary product platform, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use or method of manufacture. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for a use that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their products for our targeted indications of any product candidates we decide to develop as drug products, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our product candidates and development platform could have a material adverse effect on our business, financial condition, results of operations and prospects.

If any of our owned patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned patents. With respect to our patent portfolio, as of December 31, 2019, our product candidate-related patent portfolio consists of 18 patent families, including three granted U.S. patents, 17 U.S. pending patent applications (including provisional applications) and 110 owned pending patent applications in jurisdictions outside of the United States (including Patent Cooperation Treaty applications) that, in many cases, are counterparts to the foregoing U.S. patents and patent applications, which include claims directed to compositions, methods of use, treatment of indications, dosing, formulations and methods of manufacturing. With respect to owned intellectual property, we cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patents and patent applications at a reasonable cost or in a timely manner. Disruptions at the USPTO or other government agencies may also slow the time necessary for patent applications to be reviewed by the USPTO, which could adversely affect our patent portfolio. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, 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 be certain that we were the first to make the inventions claimed in any of our owned or pending patent applications, or that we were the first to file for patent protection of such inventions.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.

The patent position of healthcare companies generally is highly uncertain, involves complex legal and factual questions and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our product candidates, development platform or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

No consistent policy regarding the scope of claims allowable in patents in the biotechnology field has emerged in the United States. The patent situation outside of the United States is similarly uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. With respect to intellectual property that we own, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our products and the methods used to manufacture those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. The area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our patented product candidates and practicing our proprietary technology. Our issued patents and those that may issue in the future may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or limit the length of the term of patent protection that we may have for our product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we may have competition for our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own may be challenged, narrowed, circumvented or invalidated by third parties. Consequently, we do not know whether our product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and patents that we own may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party preissuance submission of prior art to the USPTO or to foreign patent authorities or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review or interference proceedings or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned patent rights, allow third parties to commercialize our product candidates, development platform or other technologies 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. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as *inter partes* reviews, post-grant reviews or derivation proceedings at the USPTO or oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our owned patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates, development platform and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may in the future co-own patent rights relating to future product candidates and our development platform with third parties. We may need the cooperation of any such co-owners of our patent rights in order to enforce such patent rights against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Our rights to develop and commercialize our product candidates and development platform may be subject, in part, to the terms and conditions of future licenses granted to us by others.

We may rely upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our product candidates and development platform. Patent rights that we in-license in the future may be subject to a reservation of rights by one or more third parties. As a result, any such third parties may have certain rights to such intellectual property. In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution and maintenance, and we may not have the right to control the enforcement, and defense of patents and patent applications covering the technology that we license from third parties. We cannot be certain that any in-licensed patent applications (and any patents issuing therefrom) that are controlled by any potential licensors will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce and defend such patent rights, or lose rights to those patent applications (or any patents issuing therefrom), the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our product candidates, development platform technologies and other technologies that are subject of such licensed rights could be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. Moreover, we cannot be certain that such activities by our potential future licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. In addition, even where we may have the right to control patent prosecution of patents and patent applications that we may license to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our potential future licensees, licensors and their counsel that took place prior to the date of assumption of control over patent prosecution.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on our product candidates, development platform technologies and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, 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 have not obtained patent protection to develop their own products and 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. Furthermore, the amino acids that we expect to incorporate into our products are available for purchase separately from a variety of retail outlets, and our intellectual property rights will not prevent these sales from continuing in the future.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural requirements, document submission, fee payment and other requirements imposed by government patent agencies and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned patents and applications. The USPTO and various ex-U.S. government agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first-inventor-to-file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we do could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to file any patent application related to our product candidates, development platform or other technologies.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned patent applications and the enforcement or defense of our owned issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

From time-to-time the U.S. Supreme Court, other federal courts, the U.S. Congress or the USPTO, may change the standards of patentability and any such changes could have a negative impact on our business. For instance, on June 13, 2013, in *Association for Molecular Pathology v. Myriad Genetics*, the Supreme Court held that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated. The Supreme Court did not address the patentability of any innovative method claims involving the manipulation of isolated genes. On January 7, 2019, the USPTO released guidance entitled "2019 Revised Subject Matter Eligibility Guidance." This memorandum provides guidelines for the USPTO's new examination procedure for subject matter eligibility under 35 U.S.C. §101 for claims embracing natural products or natural principles. Although the guidelines do not have the force of law, patent examiners have been instructed to follow them. Some aspects of our technology involve processes or molecules that may be subject to this evolving standard and we cannot guarantee that any of our pending process claims will be patent eligible, or issued claims will remain patent eligible, as a result of such evolving standards. Changes in either the patent laws or in interpretations of patent laws in the United States or other countries could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. We may not develop additional proprietary products, methods and technologies that are patentable.

Issued patents covering our product candidates and any patents that may issue covering our development platform and other technologies, could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we initiated legal proceedings against a third party to enforce a patent covering our product candidates, development platform or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may raise claims challenging the validity or enforceability of our owned patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our product candidates, development platform or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, 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 third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates, development platform or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

If we do not obtain patent term extension and/or data exclusivity for any product candidates we decide to develop as drug product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we decide to develop as drug product candidates, one or more of our owned U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Protection Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. Because many of the components of our product candidates have been approved as active components of drug substances, we may not be eligible for patent term extension, or PTE, as it is only available in the US if any component of a product candidate has never been approved as a drug substance. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our owned patent rights, trade secrets or other intellectual property as an inventor or co-inventor. For example, we may have disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates, development platform or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our owned patent rights, trade secrets or other intellectual property. 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, intellectual property that is important to our product candidates, development platform and other technologies. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

In addition to seeking patents for our product candidates, development platform and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel from academic to industry scientific positions.

We currently, and may in the future continue to, rely on third parties to assist us in developing and manufacturing our product candidates. Accordingly, we must, at times, share know-how and trade secrets, including those related to our development platform, with them. We may in the future also enter into research and development collaborations with third parties that may require us to share know-how and trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our know-how, trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements, and including in our vendor and service agreements terms protecting our confidential information, know-how and trade secrets, with parties who have access to such information, such as our employees, scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and we remind former employees when they leave their employment of their confidentiality obligations. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Despite our efforts, any of the aforementioned parties may breach the agreements and disclose our proprietary information, including our trade secrets, or there may be lapses or failures in our physical and electronic security systems that lead to our proprietary information being disclosed, and we may not be able to obtain adequate remedies in the event of any such breaches. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of our scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. 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. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them 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 or other third party, our competitive position would be materially and adversely harmed.

We rely on our development platform to identify product candidates. Our competitive position could be materially harmed if our competitors develop a similar platform and develop rival product candidates.

We rely on know-how, inventions and other proprietary information to strengthen our competitive position. We consider know-how to be our primary intellectual property with respect to our development platform. Our Clinical Studies allow and future Clinical Trials will allow us to collect clinical data, which we use in a feedback loop to make improvements to our development platform. In particular, we anticipate that, with respect to this platform, this data may over time be disseminated within the industry through independent development, the publication of journal articles describing the method and the movement of skilled personnel.

We cannot rule out that our competitors may have or will obtain the knowledge necessary to analyze and characterize similar data to our known data for the purpose of identifying and developing products that could compete with any of our product candidates. Our competitors may also have significantly greater financial, product development, technical and human resources and access to data. Further, our competitors may have significantly greater experience in using translational science methods to identify and develop product candidates.

We may not be able to prohibit our competitors from using technology or methods that are the same as or similar to our development platform to develop their own product candidates. If our competitors develop associated therapies, our ability to develop and market a promising product or product candidate may diminish substantially, which could have a material adverse effect on our business, financial condition, prospects and results of operations.

We may not be successful in obtaining, through acquisitions, in-licenses or otherwise, necessary rights to our product candidates, development platform technologies or other technologies.

We may need to, or want to for strategic purposes, acquire rights to certain intellectual property, through licenses from third parties, to create new products or advancements to our development platform or further develop our product candidates and development platform technologies. Some healthcare companies and academic institutions are competing with us in the field of EMMs and metabolic pathways and may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. We may also require licenses from third parties for certain technologies that we may evaluate for use with our current or future product candidates. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our current or future product candidates and our development platform at a reasonable cost or on reasonable terms, if at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all.

In the event that we try to obtain rights to required third party intellectual property rights, and are ultimately unsuccessful, we may be required to expend significant time and resources to redesign our technology, product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates or continue to utilize our existing development platform technology, which could harm our business, financial condition, results of operations and prospects significantly.

We may be subject to claims that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants and advisors are currently or were previously employed at universities or other healthcare companies, including our competitors and potential competitors. Although we try to ensure that our employees, consultants and advisors 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 these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in 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 defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violation against us or our collaborators may prevent or delay the development and commercialization of our product candidates, development platform and other technologies.

The field of developing drug or non-drug products that target metabolic pathways is competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property related litigation and proceedings relating to our owned, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our and our collaborators' ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist relating to technologies and fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates, development platform and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our product candidates, proprietary product platform technologies and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, development platform and other technologies might assert are infringed by our current or future product candidates, development platform or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates, development platform or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates, development platform or other technologies, could be found to be infringed by our product candidates, development platform or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates, development platform or other technologies may infringe. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our development platform technologies, manufacturing methods, product candidates or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our product candidates, development platform or other technologies infringes upon these patents. In the event that any third party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our product candidates, development platform or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be non-exclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our product candidates, development platform or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing product candidates, development platform or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our product candidates, development platform or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents, or we may be required to defend against claims of infringement. In addition, our patents also may become involved in inventorship, priority or validity disputes. To counter or defend against such claims can be expensive and time-consuming. In an infringement proceeding, a court may decide that a patent owned by us is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e) or may refuse to stop the other party from using the technology at issue on the grounds that our owned patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned patents at risk of being invalidated or interpreted narrowly. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we may own;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own now or in the future;
- we, or our future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned intellectual property rights;
- it is possible that our current or future pending owned patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks related to our reliance on third parties

Third-party relationships are important to our business. If we are unable to enter into and maintain strategic collaborations or if these relationships are not successful, our business could be adversely affected.

We have limited capabilities for product development and do not yet have any capability for sales, marketing or distribution. Accordingly, we may need to enter into relationships with other companies to provide us with important technologies, services and resources, and we may receive additional technologies and funding under these relationship and other collaborations in the future. Relationships we enter into may pose a number of risks, including the following:

- third parties have, and future third-party collaborators may have, significant discretion in determining the efforts and resources that they will apply;
- third parties may not perform their obligations as expected;
- third parties may not pursue development and commercialization of any product candidates and that achieve regulatory approval, as may be necessary, or may elect not to continue or renew development or commercialization programs based on clinical study or trial results, changes in the third parties' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- third parties may delay Clinical Studies or Clinical Trials, provide insufficient funding for a Clinical Study or Clinical Trial program, terminate a Clinical Study or Clinical Trial or abandon a product candidate, repeat or conduct new Clinical Studies or Clinical Trials or require a new formulation of product candidate for clinical testing;
- third parties could independently develop, or develop with other third parties, products that compete directly or indirectly with our products and product candidates if the third parties believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our current or future third parties as competitive with their own product candidates or products, which may cause such third parties to cease to devote resources to the development or commercialization of our product candidates;
- third parties may fail to comply with applicable regulatory requirements regarding the development, manufacture, processing, packaging, labeling, holding, testing, storage, distribution and/or marketing of a product candidate or product;
- third parties with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with third parties, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- third parties may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- third parties may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if one of our third parties is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- relationships may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our relationships do not result in the successful discovery, development and commercialization of products or if a third-party terminates its agreement with us, or if for any other reason an agreement is terminated or cancelled, we may not receive any future research funding or milestone or royalty payments under such agreement. If we do not receive the funding, we expect under any third-party agreements we enter into, our development of our technology and product candidates could be delayed and we may need additional resources to develop product candidates and our technology. All of the risks relating to product development, regulatory compliance and/or approval and commercialization described herein also apply to the activities of any drug and non-drug collaborators we enter into relationships or agreements in the future. Additionally, if any third party terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

Relationships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable third parties on a timely basis, on acceptable terms, or at all, we may have to curtail the development of product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into relationships or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue or continue to develop our technology, and our business may be materially and adversely affected.

We rely on third parties to conduct our Clinical Studies and will rely on third parties to conduct our Clinical Trials for any product candidate that we decide to develop as a drug product candidate and to assist us in meeting the regulatory requirements applicable to development and marketing of our products. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize any potential product candidates.

We will depend upon third parties, including independent investigators, to conduct preclinical studies, Clinical Studies and plan to do so for any Clinical Trials we conduct in the future under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and study or trial sites, which may result in delays to our development timelines and increased costs.

We have, and will have to, rely heavily on third parties over the course of our Clinical Studies and planned Clinical Trials and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our Clinical Studies and Clinical Trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with, among other things, GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of study or trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our Clinical Studies or Clinical Trials may be deemed insufficient or unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these Clinical Studies or Clinical Trials or perform additional Clinical Studies or Clinical Trials before approving or otherwise permitting our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our Clinical Studies or Clinical Trials comply with applicable regulatory requirements. In addition, our Clinical Trials for therapeutic indications must be conducted with drug products produced under cGMP requirements and may require a large number of patients.

Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of subjects or patients may require us to repeat Clinical Studies or Clinical Trials, which would delay the regulatory approval or commercialization process. Moreover, our business may be implicated if any of these third parties violates federal or state laws or regulations including fraud and abuse or false claims laws and regulations or healthcare privacy and security laws even without our prior knowledge.

Any parties conducting our Clinical Studies or Clinical Trials, if any, generally will not be our employees and, except for remedies that may be available to us under our agreements with the third parties conducting such Clinical Studies or Clinical Trials, if any, we cannot directly control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting Clinical Studies or Clinical Trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our Clinical Studies and Clinical Trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into contractual and other arrangements with alternative CROs or other third parties in a timely manner to meet projected clinical development deadlines or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Further, we expect to work with and/or rely upon third-party CROs and/or regulatory consultants to assist us with meeting regulatory requirements applicable to non-drug products. If we experience delays in meeting or fail to meet the regulatory requirements for commercialization 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 expect to rely on third parties to manufacture our supply of product candidates, and we intend to rely on third parties to produce and process our products, if approved or commercialized.

We currently rely on outside vendors to supply raw materials and other important components, such as the amino acids and excipients that make up our product candidates. We have not yet caused any product candidates to be manufactured or processed on a large clinical or commercial scale and may not be able to do so for any of our product candidates. We will make changes as we work to optimize the manufacturing process for our product candidates, and we cannot be sure that even minor changes in the process will result in products that are safe and, where applicable, effective.

The facilities used to manufacture our drug product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that could be conducted before or will be conducted after we submit a marketing application to the FDA or other foreign regulatory agencies. Additionally, any facilities used for the manufacture of product candidates commercialized for non-drug uses will be subject to registration and inspection by the FDA and comparable foreign regulatory authorities. We do not currently control all aspects of the manufacturing process of, and are currently largely dependent on, our contract manufacturing partners for compliance with regulatory requirements, known as cGMP requirements, for manufacture of our product candidates, but we may be held ultimately responsible for such compliance. If we ever decide to open a manufacturing facility, we will be responsible for our own compliance with cGMP requirements. If we or our contract manufacturers cannot successfully manufacture in conformance with our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we and they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities with respect to the manufacture of our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates, where applicable, or if it withdraws any such approval in the future, or if it otherwise finds that a manufacturing facility is out of regulatory compliance, we may need to find alternative manufacturing facilities, which would significantly impact our ability to research, develop, obtain regulatory approval, where necessary, for and/or market our product candidates. For more information, see "Risk Factors — Risks related to manufacturing and supply" below.

Risks related to manufacturing and supply

Our product candidates rely on the availability of specialty raw materials, including significant quantities of amino acids, which may not be available to us on acceptable terms or at all.

Our product candidates require certain specialty raw materials, including significant quantities of amino acids, some of which we may obtain from third-party small companies with limited resources and experience to support a commercial product. The suppliers may be ill-equipped to support our needs, especially in non-routine circumstances like an FDA or foreign regulatory inspection or medical crisis, such as widespread contamination. Additionally, our suppliers may fail inspections or have other compliance issues with regulatory authorities that, even if unrelated to our supply chain and materials, may impact or cause delays in their ability to deliver agreed upon supplies in a timely manner which can have negative impacts on our business plans, including delays in initiating or continuing Clinical Studies or Clinical Trials. We do not currently have supply contracts in place with all of the suppliers that we may need at any point in time in the future, and if needed, may not be able to contract with them on acceptable terms or at all, in particular for large quantities of pharmaceutical grade raw materials, including amino acids. Accordingly, we may experience delays in receiving key raw materials to support clinical or commercial manufacturing. Additionally, although we are not aware of any impact to date, it is possible that our third party suppliers and manufacturers may be negatively impacted by COVID-19 developments, which could limit our product candidate supply availability, and, depending on extent and scope of impact, could result in delays to our ongoing Clinical Studies or planned Clinical Trials.

Our product candidates require precise, high-quality manufacturing capabilities. If any of our third-party manufacturers encounter difficulties in manufacturing our product candidates, our ability to provide supply of our product candidates for Clinical Studies or Clinical Trials, or for future commercial supply of products we bring to market under applicable regulatory requirements and approvals, could be delayed or terminated, or we may be unable to maintain a commercially viable cost structure.

We do not currently operate manufacturing facilities and rely on third parties under our existing contracts to produce our product candidates. The manufacturing process used to produce our product candidates has not been validated for clinical and commercial production. We combine multiple EMMs in novel combinations and ratios in our manufacturing process for product candidates. These combinations may result in unanticipated manufacturing and product quality issues that we may not be able to resolve without incurring significant expense or delays in our Clinical Studies or Clinical Trials, or at all. Furthermore, our cGMP manufacturing process development and scale-up is at an early stage. The actual cost to manufacture and process our product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates.

Our manufacturing process may be susceptible to manufacturing issues associated with interruptions in the manufacturing process, contamination, equipment or reagent failure, improper installation or operation of equipment, vendor or operator error and variability in product characteristics. Even minor deviations from normal manufacturing processes at our third-party manufacturers could result in reduced production yields, lot failures, product defects, product recalls, product liability claims and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, production at such manufacturing facilities may be interrupted for an extended period of time to investigate and remedy the contamination. Further, as product candidates are developed through preclinical studies, Clinical Studies and/or Clinical Trials toward approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to scale-up and optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of Clinical Studies or Clinical Trials.

Although we continue to optimize our manufacturing process for our product candidates, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced Clinical Studies and Clinical Trials or commercialization, including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency, supplier manufacturing capacity and timely availability of reagents and/or raw materials. We ultimately may not be successful in transferring our production system from our contract manufacturers to any manufacturing facilities we may establish ourselves or other contract manufacturers who can provide cost and process efficiencies, or our contract manufacturer may not have the necessary capabilities to complete the implementation and development process. If we are unable to adequately validate or scale-up the manufacturing process for our product candidates with each of our current manufacturers, we will need to transfer to other manufacturers and complete the manufacturing validation and scale-up processes, which can be lengthy. If we are able to adequately validate and scale-up the manufacturing process for our product candidates with a contract manufacturer, we will still need to negotiate with such contract manufacturer an agreement for commercial supply and it is not certain we will be able to come to agreement on terms acceptable to us. As a result, we may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized.

The manufacturing process for any drug product candidate is subject to the FDA and foreign regulatory authority approval process, and extensive oversight of manufacturing facilities and changes to manufacturing processes. Non-drug products that we may develop will also be subject to extensive legal and regulatory requirements, including those with respect to the manufacturing, packaging, labeling, holding, processing and distribution of such products under appropriate cGMPs, as indicated in other risk factor sections herein. As such, we will need to contract with manufacturers who can meet all applicable FDA, foreign or other regulatory authority requirements on an ongoing basis, including with respect to quality systems and standards. If we or our CMOs are unable to reliably produce products under conditions and to specifications acceptable to the company and/or the FDA or comparable foreign regulatory authorities, we may not obtain or maintain the ability or, in the case of drugs, the requisite approvals to commercialize such products. There is no assurance that our CMOs will be able to manufacture the approved product to specifications acceptable to us, the FDA, comparable foreign regulatory authorities, even if we obtain regulatory approval for any of our product candidates for therapeutic indications, to produce product in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. In the case of product candidates for which a therapeutic pathway is pursued, any of these challenges could delay completion of Clinical Trials, require bridging Clinical Trials or the repetition of one or more Clinical Trials, increase Clinical Trial costs and delay approval of our product candidates. In the case of all product candidates that we choose to commercialize, any of these challenges could delay and/or impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects. Our future success depends on our ability to manufacture our product candidates on a timely basis with acceptable manufacturing costs, while at the same time maintaining good quality control and complying with applicable regulatory requirements, and an inability to do so could have a material adverse effect on our business, financial condition and results of operations. In addition, we could incur higher manufacturing costs if manufacturing processes or standards change, and we could need to replace, modify, design or build and install equipment, all of which would require additional capital expenditures. Specifically, because our product candidates may have a higher cost of goods than other drugs and/or non-drug products, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater.

In addition, we currently handle all batch release for our product candidates for our preclinical studies and Clinical Studies, but in the future may need to transfer such process to a third party, which would substantially increase the cost of this step of the manufacturing process.

In addition to raw materials and CMOs, we depend on third parties for clinical product supplies (e.g., clinical labeling and secondary packaging services) and will likely need to do the same for any future commercial supply, including, in some instances, a single supplier.

In addition to raw materials and CMOs, we depend on third-party suppliers for labeling secondary packaging and other services needed to produce Clinical Study ready supplies of our product candidates and will likely need to do the same for any future supplies for Clinical Trials or commercial supplies. We could be held responsible for the regulatory compliance of such labeling or packaging activities. These supplies may not always be available to us at the standards we require or on terms acceptable to us, or at all, and we may not be able to locate alternative suppliers in a timely manner, or at all. If we are unable to obtain necessary clinical or commercial supplies, our manufacturing operations and Clinical Studies and Clinical Trials and the clinical studies and trials of our collaborators may be delayed or disrupted, and our business and prospects may be materially and adversely affected as a result.

We may rely on a sole supplier for certain of our supplies. If this sole supplier is unable to supply to us in the quantities we require, or at all, or otherwise defaults on its supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all.

We have experience manufacturing our product candidates only for purposes of our ongoing and completed Clinical Studies to date, and have very limited experience manufacturing our product candidates for the purposes of Clinical Trials, or at commercial scale, and if we decide to establish our own manufacturing facility for our product candidates, we cannot assure you that we can manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have experience manufacturing our product candidates only for purposes of our ongoing and completed Clinical Studies, have limited experience manufacturing our product candidates for Clinical Trials and have not yet conducted a Clinical Trial. We similarly have limited experience with the manufacturing requirements for non-drug products at a commercial scale. In the future, we may develop internal manufacturing capacity in part by expanding our own facilities or building additional facilities. This activity will require substantial additional funds and we would need to invest such funds in creating the proper manufacturing infrastructure and to hire and train a significant number of qualified employees to staff these facilities. We may not be able to develop cGMP-compliant manufacturing facilities that are adequate to produce materials for additional later-stage Clinical Studies, Clinical Trials or commercialization, which may materially and adversely affect our business.

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

Risks related to our common stock

An active trading market for our common stock may not be sustainable, and you may not be able to resell your shares at or above the purchase price.

In May 2019, we closed our initial public offering. Prior to that offering, there was no public market for our common stock. Although we have completed our initial public offering and shares of our common stock are listed on The Nasdaq Global Market, an active trading market for our shares may not be sustained. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. As a result of these and other factors, it may be difficult for our stockholders to resell their shares of our common stock at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

The trading price of our stock is highly volatile.

Similar to trading price of stock of other biopharmaceutical companies, the trading price of our common stock is highly volatile and is subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, these factors include:

- any potential impact of COVID-19 on the financial markets generally, the biopharmaceutical industry and our business and operations, including with respect to our ongoing Clinical Studies and planned Clinical Trials;
- the commencement, enrollment or results of our ongoing and planned Clinical Studies, or any future Clinical Studies or Clinical Trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- adverse results from or delays in Clinical Studies or Clinical Trials of our product candidates, including as a result of clinical holds, safety events, enrollment or study or trial protocol amendments;
- our decision to initiate a Clinical Study or Clinical Trial, not to initiate a Clinical Study or Clinical Trial or to terminate an existing Clinical Study or Clinical Trial, or being required to do so by any regulatory authority;

- adverse regulatory decisions, including the FDA's disagreeing with our interpretation and application of applicable rules and regulations and any government actions that may arise from such disagreement and our failure to receive regulatory approval of our product candidates for therapeutic indications or to proceed on alternate regulatory pathways to market for our product candidates;
- changes in laws or regulations applicable to our products, including, but not limited to, Clinical Trial requirements for approvals of drugs or marketing of non-drug products;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services by our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth of our initial target markets;
- actual or anticipated variations in quarterly or annual operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- adoption of new accounting standards;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for healthcare companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock does not increase, you may not realize any return on your investment in us and may lose some or all of your investment. Additionally, your ownership in our stock may be significantly diluted if we raise capital through equity issuances in private or public financings. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, our ability to pay cash dividends is currently restricted by the terms of our loan and security agreement with Solar, and future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited in the foreseeable future to the appreciation of their stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2019, our executive officers, directors and their affiliates and 5% stockholders held, in the aggregate, approximately 66% of our outstanding voting stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that stockholders may feel are otherwise in their best interests.

We are an emerging growth company as well as a small reporting company, and we cannot be certain if the reduced reporting requirements applicable to us will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we completed our IPO, although circumstances could cause us to lose that status earlier. We will 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 our IPO; (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 requires the market value of our common stock that is held by non-affiliates to exceed $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. We cannot predict if investors will find our common stock less attractive because we may 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 more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we may adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. This may make comparison of our financial statements with the financial statements of another public company that is not an emerging growth company, or an emerging growth company that has opted out of using the extended transition period, difficult or impossible because of the potential differences in accounting standards used.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to public company compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, as amended, which requires, among other things, that we file with the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of our IPO. We intend to take advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies will substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. Accordingly, our revenue may depend on development funding and the achievement of development and clinical milestones under current and any potential future license and collaboration agreements and sales of our products, if approved. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees, directors and non-employee consultants based on the fair value of the award on either the grant date or service completion date, and we recognize the cost as an expense over the recipient's service period. Because the variables that we use as a basis for valuing stock-based awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- any potential impact of COVID-19 on our business and operations, including with respect to our ongoing Clinical Studies and planned Clinical Trials;
- the timing and cost of, and level of investment in, research and development activities relating to our current and any future product candidates, which will change from time to time;
- our ability to enroll subjects in Clinical Studies or Clinical Trials and the timing of enrollment;
- the cost of manufacturing our current and any future product candidates, which may vary depending on FDA guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire or develop additional product candidates and technologies;
- the timing and outcomes of Clinical Trials for our current product candidates and any other future product candidates or competing product candidates;
- competition from existing and potential future products that compete with our current product candidates and any other future product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval or commercialization of our current product candidates or any other future product candidates;
- the level of demand for our current product candidates and any other future product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our products, if approved, and existing and potential future products that compete with our current product candidates and any other future product candidates;
- our ability to commercialize our current product candidates and any other future product candidates inside and outside of the United States, either independently or working with third parties;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue and/or earnings guidance we may provide.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock and its development will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

Pursuant to Section 404 of Sarbanes-Oxley, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2020. When we lose our status as an "emerging growth company," our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we may need to implement additional financial and management controls, reporting systems and procedures and may need to hire additional accounting and finance staff.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The Nasdaq Global Market, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including, but not limited to:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Chancery Court does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine. This exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. The forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease a facility containing 19,200 square feet of laboratory and office space, which is located at 840 Memorial Drive, Cambridge, Massachusetts. The lease expires in April 2021, subject to two options to extend the lease for a total of six years.

Item 3. Legal Proceedings

We are not currently party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "AXLA" on the Nasdaq Global Market and has been publicly traded since May 9, 2019. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 1, 2020, there were approximately 40 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2020 Annual Meeting of Stockholders, or the Proxy Statement, and is incorporated herein by reference.

Unregistered Sales of Equity Securities and Use of Proceeds

Recent Sales of Unregistered Equity Securities

The information required by Item 701 of Regulation S-K was previously included in Quarterly Reports on Form 10-Q filed on June 20, 2019, August 12, 2019 and November 12, 2019.

Use of Proceeds from Initial Public Offering

On May 13, 2019, we completed the initial public offering of our common stock, or our IPO, pursuant to which we issued and sold 3,571,428 shares of our common stock at a price to the public of $20.00 per share.

The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File No. 333-230822), which was declared effective by the SEC on May 8, 2019. Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC and SVB Leerink LLC acted as joint book-running managers of our IPO.

We received aggregate gross proceeds from our IPO of $71.4 million, or aggregate net proceeds of $64.5 million after deducting underwriting discounts and commissions and other offering costs. None of the underwriting discounts and commissions or offering expenses were incurred or paid, directly or indirectly, to any of our directors or officers or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

There has been no material change in our planned use of the net proceeds from the IPO as described in our Prospectus dated May 8, 2019.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. Selected Financial Data

Not applicable.

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

The following discussion of the financial condition and results of operations should be read in conjunction with the condensed consolidated financial statements and the related notes thereto included elsewhere in this Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. We caution you that forward-looking statements are not guarantees of future performance, and that our actual results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate, may differ materially from the results discussed or projected in the forward-looking statements contained in this Annual Report. We discuss risks and other factors that we believe could cause or contribute to these potential differences elsewhere in this Annual Report, including under Part I,
Part I, Item 1A. "Risk Factors" and under "Special Note Regarding Forward-Looking Statements." In addition, even if our results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate are consistent with the forward-looking statements contained in this Annual Report, they may not be predictive of results or developments in future periods. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a clinical-stage biotechnology company focused on leveraging endogenous metabolic modulators, or EMMs, to pioneer a new approach for treating complex diseases and improving health. Our product candidates are comprised of multiple EMMs that are engineered in distinct combinations and ratios with the goal of simultaneously impacting multiple biological pathways. Our pipeline includes lead therapeutic candidates for non-alcoholic steatohepatitis, or NASH, and the reduction in risk of overt hepatic encephalopathy, or OHE, recurrence. Additional muscle- and blood-related programs are in earlier-stage development.

Using our development platform, we have efficiently designed a pipeline of product candidates that are comprised of amino acids and their derivatives. These orally administered compositions are designed to have the potential for multifactorial effects, and their constituents have a general history of safe use.

To date, we have funded our operations with proceeds from the sale of preferred stock, the sale of common stock in our initial public offering, or our IPO, and borrowing of debt. Through December 31, 2019, we had received gross proceeds of $197.8 million from the sale of preferred stock, gross proceeds of $71.4 million from the sale of common stock in our IPO and $26.0 million from borrowings under our loan and security agreement. Since our inception, we have incurred significant operating losses. 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 current or future product candidates. Our net losses were $59.0 million and $36.1 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $216.1 million. We expect to continue to incur significant expenses for at least the next several years as we continue to develop our product candidates.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, strategic alliances and marketing and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product 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 product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2019, we had cash and cash equivalents of $92.1 million. We believe that our existing cash and cash equivalents as of December 31, 2019 will enable us to fund our operating expenses, capital expenditure requirements and debt service payments for at least the next 12 months following the filing date of this Annual Report on Form 10-K. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources." To finance our operations significantly beyond that point, we will need to raise additional capital, which cannot be assured.

The recent outbreak of COVID-19 has spread globally, including to the United States and European countries, which has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns. Although we cannot presently predict the scope and severity of COVID-19, these developments and measures could materially and adversely affect our business, our results of operation and financial condition, particularly if the COVID-19 outbreak adversely impacts our ability to conduct and complete our ongoing Clinical Studies and planned Clinical Trials in a timely manner or at all due to patient or principal investigator recruitment or availability challenges, clinical trial site shutdowns or other interruptions and potential limitations on the quality, completeness and interpretability of data we are able to collect; we or our key third-party service providers are not able to complete key program and product development milestones on time or at all; market volatility and conditions limit our ability to raise additional capital to finance our business plans on attractive terms or at all; our business continuity plans are not effective at limiting operational disruptions or delays; we suffer negative impacts to operations that may be vulnerable as a result of government or company measures taken to control the spread of COVID-19; potential shutdowns of government agencies such as the SEC or FDA, which may limit our ability to raise capital and negatively impact our product development timelines; the passage of new legislation that may increase our operating costs or limit our operations, such as the Families First Coronavirus Response Act; we suffer negative consequences due to vulnerabilities that emerge as a result of our limited operations, such as a cybersecurity incident; or one of our key executives, scientists or other personnel becomes incapacitated by COVID-19.

The extent to which COVID-19 impacts our business, operations or financial results will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, new information that may emerge concerning the severity of COVID-19 or the nature or effectiveness of actions to contain COVID-19 or treat its impact, among others. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, results of operation and financial condition.

Components of our Consolidated Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If development efforts for our product candidates are successful and result in regulatory approval or we execute license or collaboration agreements with third parties, we may generate revenue in the future from product sales, payments from collaborations or license agreements that we may enter into with third parties, or any combination thereof.

Operating Expenses

Research and Development Expenses

Our research and development expenses consist primarily of costs incurred in connection with our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- direct external research and development expenses, including fees, reimbursed materials and other costs paid to consultants, contractors, contract manufacturing organizations, or CMOs and clinical research organizations, or CROs in connection with our clinical and preclinical development and manufacturing activities;
- employee-related expenses, including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including any Clinical Studies, planned Clinical Trials and other research programs, including under agreements with third parties, such as consultants, contractors and CROs;
- the cost of developing and scaling our manufacturing process and manufacturing products for use in our preclinical studies, Clinical Studies and Clinical Trials, including under agreements with third parties, such as consultants, contractors and CMOs; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance.

We expense research and development costs as incurred. We often contract with CROs and CMOs to facilitate, coordinate and perform agreed-upon research, design, development, and manufacturing of our product candidates. To ensure that research and development costs are expensed as incurred, we record monthly accruals for clinical studies and manufacturing costs based on the work performed under the contract.

These CRO and CMO contracts typically call for the payment of fees for services at the initiation of the contract and/or upon the achievement of certain clinical or manufacturing milestones. In the event that we prepay CRO or CMO fees, we record the prepayment as a prepaid asset and amortize the asset into research and development expense over the period of time the contracted research and development or manufacturing services are performed. Most professional fees, including project and clinical management, data management, monitoring and manufacturing fees are incurred throughout the contract period. These professional fees are expensed based on their estimated percentage of completion at a particular date. Our CRO and CMO contracts generally include pass through fees. Pass through fees include, but are not limited to, regulatory expenses, investigator fees, travel costs and other miscellaneous costs and raw materials. We expense the costs of pass through fees under our CRO and CMO contracts as they are incurred, based on the best information available to us at the time.

A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform, and, as such, are not separately classified.

Research and development expenses may fluctuate from period to period depending upon the stage of certain projects and the level of clinical and preclinical activities. Many factors can affect the cost and timing of our Clinical Studies and planned Clinical Trials, including slow patient enrollment, the availability of supplies and real or perceived lack of effect on biology or safety of our product candidates. In addition, the development of all of our product candidates may be subject to extensive governmental regulation. These factors make it difficult for us to predict the timing and costs of the further development of our product candidates.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our Clinical Studies and planned Clinical Trials. We may elect to discontinue, delay or modify development of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of Clinical Trials or require us to conduct additional Clinical Studies, Clinical Trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned Clinical Studies or Clinical Trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. Identifying potential product candidates and conducting preclinical testing, Clinical Studies 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. See “Risk Factors” for further discussion of these and additional risks and uncertainties associated with product development and commercialization that may significantly affect the timing and cost of our research and development expenses and our ability to obtain regulatory approval for and successfully commercialize our product candidates. We expect research and development expenses to increase as we advance existing product candidates into additional Clinical Trials and Clinical Studies and develop new product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits, travel and stock-based compensation expense for personnel in executive, finance and administrative functions. General and administrative expenses also include professional fees for legal, consulting, accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development of our product candidates. We also anticipate that we will incur increased finance, accounting, audit, legal, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with operating as a public company. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and expense as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidate.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each year or for our research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss, or NOLs, carryforwards and tax credits will not be realized.

Consolidated Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our consolidated results of operations for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,		
	2019	2018	Change
Operating expenses:			
Research and development	$ 41,658	$ 25,486	$ 16,172
General and administrative	15,781	8,410	7,371
Total operating expenses	57,439	33,896	23,543
Loss from operations	(57,439)	(33,896)	(23,543)
Other income (expense):			
Interest income	1,814	547	1,267
Other income	34	79	(45)
Change in fair value of preferred stock warrant liability	(51)	(14)	(37)
Interest expense	(3,395)	(2,785)	(610)
Total other income (expense), net	(1,598)	(2,173)	575
Net loss	$ (59,037)	$ (36,069)	$ (22,968)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,		
	2019	2018	Change
Salary and benefits-related	$ 12,481	$ 9,265	$ 3,216
Stock-based compensation expense	2,461	1,088	1,373
Clinical research and outside services	21,769	10,106	11,663
Facility related and other	4,947	5,027	(80)
Total research and development expenses	$ 41,658	$ 25,486	$ 16,172

The increase of $3.2 million in salary and benefits-related costs results from our hiring of additional personnel in research and development to support our development programs. Stock-based compensation expense grew by $1.4 million due to an increase in the number of awards and per share fair value of awards granted. Clinical research and outside services costs increased by $11.7 million due to increased product candidate development efforts, including execution of Clinical Studies for AXA1665, AXA1125, AXA1957 and AXA4010.

General and Administrative Expenses

The following table summarizes our general and administrative expenses incurred during the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31, 2019	2018	Change
Salary and benefits-related	$ 5,849	$ 4,462	$ 1,387
Stock-based compensation expense	3,363	1,690	1,673
Other contract services and outside costs	5,888	1,848	4,040
Facility related and other	681	410	271
Total general and administrative expenses	$ 15,781	$ 8,410	$ 7,371

Salary and benefits-related costs grew by $1.4 million due to the hiring of additional personnel in our general and administrative functions to support our operations. The increase in stock-based compensation expense of $1.7 million was driven by an increase in the number of awards and per share fair value of awards granted. Other contract services and outside costs increased by $4.0 million, driven by increases of $2.3 million in professional fees, largely as a result of activities related to becoming a public company, and $1.3 million in consulting expense.

Other Income (Expense), net

Other income (expense), net was a net expense of $1.6 million for the year ended December 31, 2019, compared to a net expense of $2.2 million for the year ended December 31, 2018. The decrease in other expense of $0.6 million was driven by higher interest income of $1.3 million due to our higher cash and cash equivalent position, partially offset by an increase of $0.6 million of interest expense related to increased borrowings under our loan and security agreement.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations to date primarily with proceeds from the sale of preferred stock, the sale of common stock in our IPO and borrowings under our loan and security agreement.

Cash Flows

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

	Year Ended December 31, 2019	2018
Net cash used in operating activities	$ (50,962)	$ (30,712)
Net cash used in investing activities	(117)	(586)
Net cash provided by financing activities	63,666	63,947
Net increase in cash and cash equivalents	$ 12,587	$ 32,649

Operating Activities

During the year ended December 31, 2019, operating activities used $51.0 million of cash and cash equivalents, resulting from our net loss of $59.0 million, partially offset by net non-cash charges of $7.1 million, primarily consisting of stock-based compensation expense, and net cash provided by changes in our operating assets and liabilities of $1.0 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2019 consisted primarily of a $1.6 million increase in accounts payable and accrued expenses and other current liabilities, partially offset by a $0.7 million increase in prepaid expenses and other current assets. The increases in accounts payable and accrued expenses and other current liabilities were primarily due to ongoing research and development work and an increase in incentive bonus accrual as of December 31, 2019. The increase in prepaid expenses and other current assets was primarily due to a $0.7 million increase in prepayments for research and development costs.

During the year ended December 31, 2018, operating activities used $30.7 million of cash and cash equivalents, primarily resulting from our net loss of $36.1 million, partially offset by net non-cash charges of $4.4 million, primarily consisting of stock-based compensation expense, and net cash provided by changes in our operating assets and liabilities of $1.0 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of a $1.6 million increase in accounts payable and accrued expenses, partially offset by a $0.6 million increase in prepaid expenses and other current assets. The increases in accounts payable and accrued expenses were primarily due increases in accrued legal and board fees as of December 31, 2018. The increase in prepaid expenses and other current assets consists of a prepayment to one of our vendors for development work.

Investing Activities

During the years ended December 31, 2019 and 2018, we used $0.1 million and $0.6 million, respectively, of cash and cash equivalents in investing activities primarily consisting of purchases of property and equipment.

Financing Activities

During the year ended December 31, 2019, net cash provided by financing activities was $63.7 million, primarily consisting of net cash proceeds of $64.5 million from our IPO, partially offset by a $1.2 million payment of the success fee payable upon completion of our IPO pursuant to our loan and security agreement.

During the year ended December 31, 2018, net cash provided by financing activities was $63.9 million, primarily consisting of net cash proceeds of $58.9 million from our issuance of Series E preferred stock in November 2018 and borrowings of $6.0 million under our loan and security agreement.

Loan and Security Agreement

At December 31, 2019, we had $26.0 million in outstanding long term debt pursuant to our loan and security agreement. Upon completion of the IPO in May 2019, the interest only period was extended through January 2021 and the maturity date was extended to January 2023. Monthly principal payments of $1.1 million will commence February 2021 for 24 months. The terminal interest fee of 5.35%, or $1.4 million, is due with the final principal payment of the loan. We granted the lender a first priority security interest in all of our assets, excluding intellectual property and granted a negative pledge on such intellectual property. There are no financial covenants under our loan and security agreement.

Funding Requirements

We believe that our existing cash and cash equivalents as of December 31, 2019 will be adequate to satisfy our capital needs for at least the next twelve months from the filing date of this Annual Report with the SEC. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance existing product candidates into additional Clinical Trials and Clinical Studies and develop new product candidates. Our cash requirements depend on numerous factors, including expenditures in connection with our research development programs, including with respect to the timing and progress of Clinical Trials, Clinical Studies and preclinical development activities; payments to CROs, CMOs and other third-party providers; the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; our ability to raise additional equity or debt financing; potential repayments of our long-term debt; and our ability to enter into collaboration or license agreements and our receipt of any upfront, milestone or other payments thereunder. Changes in our research and development plans or other changes affecting our operating expenses may result in changes in the timing and amount of expenditures of our capital resources. See “Risk Factors” for further discussion of these and additional risks and uncertainties that may significantly affect the timing and amount of expenditures of our capital resources.

We will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, strategic alliances and marketing and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all, including as a result of market volatility following the COVID-19 outbreak. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions. We also intend to continue to evaluate options to refinance our outstanding long-term debt. The amounts involved in any such transactions, individually or in the aggregate, may be material.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are 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. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

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 cost incurred for the service when we have not yet been invoiced or otherwise notified of 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 the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to vendors including CROs and CMOs for research and development services.

We base our expenses related to research and development on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct and manage Clinical Trials, Clinical Studies and preclinical development activities 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 expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients or subjects and the completion of clinical milestones. In accruing service fees, we estimate the time period over which services will be performed 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 the estimate, we adjust the accrual or the amount of prepaid expenses 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 reporting amounts that are too high or too low in any particular period. To date, there have not been 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 based on the fair value on the date of the 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. For stock options with service-based vesting conditions, we record the expense for these awards using the straight-line method. For stock options with performance-based vesting conditions, we record the expense for these awards over the requisite service period using an accelerated attribution method to the extent the achievement of the performance condition is probable.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model, which uses as inputs the estimated fair value of our common stock and assumptions we make for 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. In the periods prior to the IPO, the determination of fair value of our common stock required significant judgment. In the periods following the IPO, the fair value of our common stock is determined based on the quoted market price of our common stock.

Prior to our IPO, there was no public market for our common stock, and consequently, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not have, any off-balance sheet arrangements, as defined under applicable SEC rules and regulations.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report.

Emerging Growth Company Status

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

Item 7A. Quantitative and Qualitative Disclosure About Market Risk

Not applicable.

Item 8. Consolidated Financial Statements and Supplementary Data

AXCELLA HEALTH INC.

Index to Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Axcella Health Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Axcella Health Inc. and subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years then ended and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2019, and the results of its operations and its cash flows for each of the years then ended, in conformity with accounting principles generally accepted in the United States of America.

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 regulation 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/ Deloitte & Touche LLP

Boston, Massachusetts

March 23, 2020

We have served as the Company's auditor since 2012.

AXCELLA HEALTH INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31	
	2019	**2018**
Assets		
Current assets:		
Cash and cash equivalents	$ 92,053	$ 79,466
Prepaid expenses and other current assets	1,487	835
Total current assets	93,540	80,301
Property and equipment, net	608	1,076
Security deposits and other assets	211	216
Deferred offering costs	—	251
Total assets	$ 94,359	$ 81,844
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,998	$ 1,612
Accrued expenses and other current liabilities	6,358	5,299
Total current liabilities	8,356	6,911
Long term debt, net of discount	24,897	24,521
Other liabilities	882	1,898
Preferred stock warrant liability	—	425
Total liabilities	34,135	33,755
Commitments and contingencies (Note 9)	—	—
Redeemable convertible preferred stock (Note 7)	—	197,842
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2019; No shares authorized, issued or outstanding at December 31, 2018	—	—
Common stock, $0.001 par value; 150,000,000 and 47,000,000 shares authorized, 23,607,797 and 5,193,915 shares issued and 23,188,816 and 4,774,934 shares outstanding at December 31, 2019 and 2018, respectively	24	6
Additional paid-in capital	276,286	7,290
Treasury stock, 418,981 shares at cost	—	—
Accumulated deficit	(216,086)	(157,049)
Total stockholders' equity (deficit)	60,224	(149,753)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 94,359	$ 81,844

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

AXCELLA HEALTH INC.
Consolidated Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,	
	2019	**2018**
Operating expenses:		
Research and development	$ 41,658	$ 25,486
General and administrative	15,781	8,410
Total operating expenses	57,439	33,896
Loss from operations	(57,439)	(33,896)
Other income (expense):		
Interest income	1,814	547
Other income	34	79
Change in fair value of preferred stock warrant liability	(51)	(14)
Interest expense	(3,395)	(2,785)
Total other income (expense), net	(1,598)	(2,173)
Net loss	$ (59,037)	$ (36,069)
Net loss per share, basic and diluted	$ (3.55)	$ (7.97)
Weighted average common shares outstanding, basic and diluted	16,624,941	4,546,373

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

AXCELLA HEALTH INC.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2019	**2018**
Cash flows from operating activities:		
Net loss	$ (59,037)	$ (36,069)
Adjustment to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	662	1,071
Stock-based compensation expense	5,824	2,778
Change in fair value of preferred stock warrant liability	51	14
Non-cash interest expense	557	529
Gain on sale of property and equipment	(18)	(36)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(652)	(580)
Other long-term assets	5	—
Accounts payable	366	595
Accrued expenses and other current liabilities	1,280	986
Net cash used in operating activities	(50,962)	(30,712)
Cash flows from investing activities:		
Purchases of property and equipment	(136)	(659)
Proceeds from the sale of property and equipment	19	73
Net cash used in investing activities	(117)	(586)
Cash flows from financing activities:		
Payment of deferred offering costs	—	(14)
Proceeds from initial public offering, net of issuance costs	64,546	—
Proceeds from issuance of preferred convertible stock, net of issuance costs	—	58,861
Proceeds from issuance of long term debt	—	6,000
Payment of debt issuance costs	—	(945)
Payment of success fee obligation	(1,220)	—
Proceeds from exercise of common stock options	340	45
Net cash provided by financing activities	63,666	63,947
Net increase in cash and cash equivalents	12,587	32,649
Cash and cash equivalents, beginning of year	79,466	46,817
Cash and cash equivalents, end of year	$ 92,053	$ 79,466
Supplemental cash flow information:		
Cash paid for interest	$ 2,838	$ 2,255
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 237
Purchases of property and equipment included in accounts payable and accrued expenses	$ 59	$ —
Supplemental disclosure of non-cash investing and financing activities:		
Reclassification of warrants to additional paid-in capital	$ 476	$ —
Conversion of preferred stock to common stock upon closing of the initial public offering	$ 197,888	$ —
Accretion of preferred stock to redemption value	$ 46	$ 153

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

AXCELLA HEALTH INC.
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Redeemable convertible preferred stock		Common stock		Additional paid-in capital	Treasury stock		Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Par Value		Shares	Amount		
BALANCE - January 1, 2018	21,549,244	$ 138,828	4,648,078	$ 5	$ 4,621	418,981	$ —	$ (120,980)	$ (116,354)
Issuance of Series E redeemable convertible preferred stock, net of issuance costs of $139	5,282,002	58,861							—
Exercise of common stock options			545,837	1	44				45
Accretion of preferred stock to redemption value		153			(153)				(153)
Stock-based compensation					2,778				2,778
Net loss								(36,069)	(36,069)
BALANCE - December 31, 2018	26,831,246	197,842	5,193,915	6	7,290	418,981	—	(157,049)	(149,753)
Exercise of common stock options			155,043		340				340
Accretion of preferred stock to redemption value		46			(46)				(46)
Conversion of preferred stock to common stock upon closing of the initial public offering	(26,831,246)	(197,888)	14,641,997	15	197,873				197,888
Issuance of common stock, net of issuance costs of $6,896			3,571,428	3	64,529				64,532
Reclassification of warrants to additional paid-in capital					476				476
Exercise of common stock warrant			45,414		—				—
Stock-based compensation					5,824				5,824
Net loss								(59,037)	(59,037)
BALANCE - December 31, 2019	—	$ —	23,607,797	$ 24	$ 276,286	418,981	$ —	$ (216,086)	$ 60,224

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

AXCELLA HEALTH INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. NATURE OF BUSINESS

Axcella Health Inc. and subsidiaries ("Axcella," the "Company" or "we") is a clinical-stage biotechnology company that was incorporated in Delaware on August 27, 2008 and has a principal place of business in Cambridge, Massachusetts. The Company is focused on leveraging endogenous metabolic modulators, or EMMs, to pioneer a new approach for treating complex diseases and improving health. The Company's product candidates are comprised of multiple EMMs that are engineered in distinct combinations and ratios with the goal of simultaneously impacting multiple biological pathways.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, successful development of technology, obtaining additional funding, protection of proprietary technology, compliance with government regulations, risks of failure of preclinical studies, Clinical Studies and Clinical Trials, the need to obtain marketing approval for its product candidates, if required, and successfully market consumer products, fluctuations in operating results, economic pressure impacting therapeutic pricing, dependence on key personnel, risks associated with changes in technologies, development by competitors of technological innovations and the ability to scale manufacturing to large scale production. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and any necessary regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Through December 31, 2019, the Company has funded its operations primarily with proceeds from the sale of preferred stock, borrowings under a loan and security agreement and the sale of common stock in the Company’s initial public offering (“IPO”), which was completed on May 8, 2019. The Company has incurred recurring losses since its inception, including net losses of $59.0 million and $36.1 million for the years ended December 31, 2019 and 2018, respectively. In addition, as of December 31, 2019, the Company had an accumulated deficit of $216.1 million. The Company expects to continue to generate operating losses for the foreseeable future. The future viability of the Company 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 Company believes the cash and cash equivalents on hand as of December 31, 2019 of $92.1 million will be sufficient to fund its operations and capital expenditure requirements through at least the next twelve months following the issuance date of the financial statements.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("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 Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Axcella Health Inc. and its wholly owned subsidiaries. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reporting periods. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but before the final financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

Cash and Cash Equivalents

Cash includes cash in readily available checking accounts. Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. The cash equivalents consisted of money market funds.

Concentrations of Credit Risk

Financial instruments that subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company's cash deposits on hand at one financial institution often exceed federally insured limits. The Company places its cash in a financial institution that management believes to be of high credit quality.

Deferred Offering Costs

The Company capitalized certain legal, professional accounting and other third-party fees that were directly associated with in-process equity financings as deferred issuance costs until such financings were consummated. After consummation of the equity financing, these costs were recorded as a reduction of the proceeds generated as a result of the offering. As of December 31, 2018, the Company recorded deferred issuance costs of $0.3 million related to the IPO within other assets on the consolidated balance sheet. During 2019 and in connection with the IPO, the Company incurred $1.6 million of additional deferred offering costs. All deferred offering costs were reclassified into equity at the closing of the offering.

Property and Equipment

Property and equipment are recorded at cost. Depreciation and amortization is calculated using the straight-line method over the following estimated useful lives of the assets:

	Estimated useful life
Laboratory equipment	3 - 5 years
Furniture and fixtures	3 - 5 years
Office and computer equipment	3 - 5 years
Leasehold improvements	Shorter of the asset's estimated useful life or the remaining lease term

Upon disposal, retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Expenditures for repairs and maintenance that do not improve or extend the lives of the respective assets are charged to expense as incurred.

Impairment of Long-Lived Assets

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

Fair Value Measurements

Certain assets and liabilities of the Company were carried at fair value under GAAP (see Note 4). Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

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

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company operates in 1 segment.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities, Clinical Studies and Clinical Trials as well as to manufacture research and development materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and are recognized as an expense as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered or the services rendered.

The Company has entered into various research and development related contracts with parties both inside and outside of the United States. The payments to these agreements are recorded as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the Clinical Studies or Clinical Trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

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

Income Taxes

Deferred tax assets and liabilities are recognized for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on the difference between the consolidated financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax asset to an amount, which, more likely than not, will be realized.

The Company recognizes the tax benefit from any uncertain tax positions only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position are measured based on the largest benefit that has a greater than fifty percent likelihood of being realized upon ultimate settlement. Interest and penalties associated with uncertain tax positions are recorded as a component of income tax expense. As of December 31, 2019 and 2018, the Company has not identified any uncertain tax positions for which reserves would be required.

Redeemable Convertible Preferred Stock

The Company classified stock that was redeemable in circumstances outside of the Company's control outside of permanent equity. The Company recorded redeemable convertible preferred stock at fair value upon issuance, net of any issuance costs, and the carrying value was increased by periodic accretion to its redemption value at the earliest redemption date, when the events that give rise to redemption are deemed probable of occurrence. These increases were charged to the accumulated deficit. Upon the closing of the IPO, the outstanding shares of redeemable convertible preferred stock were converted to common stock.

Stock-Based Compensation

For stock-based awards, the Company measures the estimated fair value of the stock-based award on the date of grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards with service-based vesting conditions, the Company records the expense for these awards using the straight-line method. For stock options with performance-based vesting conditions, the Company records the expense for these awards over the requisite service period using an accelerated attribution method to the extent the achievement of the performance condition is probable. The Company accounts for forfeitures as they occur.

The Company classifies stock-based compensation expense in its consolidated statements of operations in the same manner in which the award recipient’s cash compensation costs are classified.

Warrant to Purchase Preferred Stock

The Company classified the warrant for the purchase of shares of its redeemable convertible preferred stock as a liability on its consolidated balance sheet as the warrant was a free-standing financial instrument that may have required the Company to transfer assets upon exercise. The preferred stock warrant liability was initially recorded at fair value upon the date of issuance and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant to purchase preferred stock were recognized as a component of other income (expense), net in the consolidated statements of operations.

Upon the completion of the IPO, the warrant to purchase preferred stock was converted to a warrant to purchase common stock. The carrying amount of the warrant to purchase preferred stock as of the date of IPO was transferred to additional paid in capital. No further revaluation was needed for the warrant to purchase common stock. The warrant was subsequently net settled in June 2019.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders’ equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2019 and 2018, there was no difference between net loss and comprehensive loss in the accompanying consolidated financial statements.

Net Income (Loss) Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period. The Company allocated no loss to the redeemable convertible preferred stock because those shares had no contractual obligation to share in the losses of the Company. Diluted net income (loss) per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. All common stock equivalents have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Recently Adopted Accounting Pronouncements

Accounting Pronouncements Issued and Not Adopted

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less may be accounted for similar to existing guidance for operating leases today. ASU 2016-02 supersedes the previous leases standard, ASC 840, *Leases*. This standard is effective for the Company beginning January 1, 2021. The Company is evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements and expects to recognize a lease liability and right-of-use asset related to the Company's leased facilities. See further discussion of the Company's lease obligations in Note 9.

3. PROPERTY AND EQUIPMENT

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

	December 31,	
	2019	2018
Laboratory equipment	$ 3,511	$ 3,489
Leasehold improvements	597	564
Office and computer equipment	111	294
Furniture and fixtures	122	122
Property and equipment, gross	4,341	4,469
Less: accumulated depreciation and amortization	(3,733)	(3,393)
Property and equipment, net	$ 608	$ 1,076

Depreciation and amortization expense for the years ended December 31, 2019 and 2018 was $0.7 million and $1.1 million, respectively.

4. FAIR VALUE MEASUREMENTS

The following table sets forth by level, within the fair value hierarchy, the assets and liabilities carried at fair value on a recurring basis (in thousands):

	Fair value measurements at December 31, 2019 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 91,803	$ —	$ —	$ 91,803
Total	$ 91,803	$ —	$ —	$ 91,803

	Fair value measurements at December 31, 2018 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 79,216	$ —	$ —	$ 79,216
Total	$ 79,216	$ —	$ —	$ 79,216
Liabilities:				
Success fee liability	$ —	$ —	$ 1,220	$ 1,220
Preferred stock warrant liability	—	—	425	425
Total	$ —	$ —	$ 1,645	$ 1,645

Cash equivalents are comprised of funds held in an exchange traded money market fund and the fair value of the cash equivalents is determined based upon quoted market price for that fund.

The fair value of the preferred stock warrant was determined using the Black-Scholes option-pricing model with the following assumptions: expected volatility of 65%; risk-free interest rate of 2.49%; weighted-average remaining contractual term of 1.28 years; and expected dividend yield of 0%.

The fair value of the success fee liability was determined using a probability weighted present value of cash flows. The Company has projected that 100% of the liability would be paid and that the time value of discounting those cash flows did not have a material impact on the fair value measurement due to the expected term.

As a result of the IPO, the preferred stock warrants were converted to warrants to purchase common stock and the fair value of the warrant liability was reclassified to stockholders' equity and subsequently net settled in June 2019. The success fee liability was also paid.

A roll forward of the fair value of the success fee liability and preferred stock warrant liability categorized with Level 3 inputs for the years ended December 31, 2019 and 2018 is as follows (in thousands):

	Success fee	Preferred stock warrant liability
Balance — January 1, 2018	$ 700	$ 411
Increase in success fee included in other liabilities	520	—
Increase in warrant fair value included in other expense	—	14
Balance — January 1, 2019	1,220	425
Increase in warrant fair value included in other expense	—	51
Reclassification to additional paid-in capital in connection with IPO	—	(476)
Payment of success fee	(1,220)	—
Balance — December 31, 2019	$ —	$ —

There were no transfers among Level 1, Level 2, or Level 3 categories in the periods presented.

The carrying value of accounts payable and accrued expenses that are reported on the consolidated balance sheets approximate fair value due to the short-term nature of these assets and liabilities. The carrying value of the long term debt approximates fair value as evidenced by the variable rate and short contractual maturity.

5. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other liabilities consisted of the following (in thousands):

	December 31,	
	2019	2018
Accrued employee compensation and benefits	$ 3,109	$ 1,957
Accrued external research and development expenses	1,799	1,679
Accrued professional fees	985	678
Other	465	985
Total accrued expenses and other current liabilities	$ 6,358	$ 5,299

6. DEBT FINANCING

Long term debt consisted of the following (in thousands):

	December 31,	
	2019	2018
Principal amount of long term debt	$ 26,000	$ 26,000
Debt discount	(456)	(612)
Deferred financing fees	(647)	(867)
Long term debt, net of discount	$ 24,897	$ 24,521

In January 2018, the Company entered into a secured debt facility (the "2018 Facility") with the existing lender that replaced a prior debt facility. The 2018 Facility increased the funding up to $21.0 million. The Company paid a transaction fee of $0.9 million to the lender in connection with the 2018 Facility, and that fee was recognized as debt discount. The 2018 Facility has an interest rate equal to the LIBOR plus 8.50% per annum (10.20% as of December 31, 2019) payable monthly and a $1.1 million success fee which was payable upon the occurrence of certain events, including an IPO. The Company granted the lender a first priority security interest in all assets of the Company, excluding intellectual property and granted a negative pledge on such intellectual property.

In October 2018, the Company amended the 2018 Facility (the "Amended 2018 Facility") to extend the interest only period through July 2020 or January 2021 and the maturity date to July 2022 or January 2023 if certain conditions were met. The Amended 2018 Facility provides additional funding in the amounts of $5.0 million ("Term B Loan") and $4.0 million ("Term C Loan") if certain conditions are met. The Term B Loan of $5.0 million was drawn in December 2018. The success fee increased to $1.2 million. Deferred financing costs of $0.1 million were incurred related to the amendment. The interest rate was not changed through the amendment.

Upon completion of the IPO in May 2019, the interest only period was extended through January 2021 and the maturity date was extended to January 2023. Monthly principal payments of $1.1 million are to commence February 2021 for 24 months. The $1.2 million success fee was also paid upon completion of the IPO.

Terminal Interest Fee

The Company's debt facility includes a terminal interest fee obligation totaling $1.4 million, which is due with the final principal payment of the loan and has been modified from time to time as the facilities were amended. The Company is accruing the terminal fee obligation over the term of the facility. The carrying value of the terminal interest fee was $0.9 million and $0.7 million at December 31, 2019 and 2018, respectively.

The scheduled principal maturity of the long term debt as of December 31, 2019 is as follows (in thousands):

Year Ending December 31,	
2020	$ —
2021	11,917
2022	13,000
2023	1,083
	$ 26,000

7. STOCKHOLDERS' EQUITY

Redeemable Convertible Preferred Stock

As of December 31, 2018, the Company's redeemable convertible preferred stock (the "Preferred Stock") consisted of the following (in thousands, except for share data):

	December 31, 2018				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Common stock issuable upon conversion
Series A preferred stock	5,874,334	5,761,539	$ 11,235	$ 11,235	3,127,870
Series B preferred stock	4,737,041	4,737,041	12,250	12,250	2,571,679
Series B-1 preferred stock	1,084,441	1,084,441	2,998	3,000	588,730
Series C preferred stock	6,969,044	6,969,044	70,062	70,248	3,783,401
Series D preferred stock	2,997,179	2,997,179	42,434	42,500	1,702,785
Series E preferred stock	6,266,786	5,282,002	58,863	59,000	2,867,532
	27,928,825	26,831,246	$ 197,842	$ 198,233	14,641,997

Upon closing of the IPO, all outstanding Preferred Stock converted into an aggregate of 14,641,997 shares of common stock. The holders of the Company's Preferred Stock had certain voting, dividend, and redemption rights, as well as liquidation preferences and conversion privileges. All rights, preferences, and privileges associated with the preferred stock were terminated at the time of the Company's IPO in conjunction with the conversion of all outstanding shares of Preferred Stock into shares of common stock.

Common Stock

As of December 31, 2018, the Company had authorized 47,000,000 shares of common stock, $0.001 par value.

In May 2019, the Company restated its certificate of incorporation, which, among other things: (i) authorized 160,000,000 shares, consisting of (i) 150,000,000 shares of common stock, $0.001 par value per share, and (ii) 10,000,000 shares of undesignated preferred stock, $0.001 par value per share. As of December 31, 2019, no preferred stock was outstanding.

Initial Public Offering

In May 2019, the Company issued 3,571,428 common shares at a public offering price of $20.00 per share for net proceeds of $64.5 million, after deducting underwriting discounts and commissions and other offering expenses.

2010 Stock Option and Incentive Plan

The Company's 2010 Stock Incentive Plan (the "2010 Plan") provided for the Company to issue incentive stock options or nonqualified stock options, restricted stock, and other equity awards to employees, directors and consultants of the Company.

Upon effectiveness of the 2019 Plan, no future issuances will be made under the 2010 Plan. The awards granted under the 2010 Plan have terms that are the same as those of the 2019 Plan.

2019 Stock Option and Incentive Plan

The 2019 Stock Option and Incentive Plan (the "2019 Plan") was approved by our board of directors on April 29, 2019 and became effective upon the IPO. The 2019 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards and cash-based awards to the Company's officers, employees, directors and consultants. The number of shares initially reserved for issuance under the 2019 Plan is 905,000, which shall be cumulatively increased on January 1, 2020 and each January 1 thereafter by 4% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31, or such lesser number of shares determined by the Company's board of directors or compensation committee of the board of directors.

The number of options available for future grant under the 2019 Plan was 36,466 as of December 31, 2019.

2019 Employee Stock Purchase Plan

The 2019 Employee Stock Purchase Plan (the "2019 ESPP") was approved by our board of directors on April 29, 2019 and became effective upon the IPO. A total of 237,181 shares of common stock were initially reserved for issuance under this plan, which shall be cumulatively increased on January 1, 2020 and each January 1 thereafter by 1% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31, or such lesser number of shares determined by the Company's board of directors or compensation committee of the board of directors.

The total number of common shares that may be issued under the ESPP is 237,181 shares. As of December 31, 2019, the initial purchase period under the ESPP has not yet commenced.

Stock Option Valuation

Given the absence of an active market for the Company’s common stock prior to the IPO, the Company and its board of directors (the “Board”), the members of which the Company believes have extensive business, finance, and venture capital experience, were required to estimate the fair value of the Company’s common stock at the time of each grant of a stock-based award. The Company and the Board determined the estimated fair value of the Company’s equity instruments based on a number of factors, including external market conditions affecting the biotechnology industry sector. These estimates and assumptions include a number of objective and subjective factors in determining the value of the Company’s common stock at each grant date, including: (1) prices paid for the Company’s redeemable convertible preferred stock, which the Company had sold to outside investors in arm’s-length transactions, and the rights, preferences, and privileges of the Company’s redeemable convertible preferred stock and common stock; (2) valuations performed by an independent valuation specialist; (3) the Company’s stage of development; (4) the fact that the grants of stock-based awards involved illiquid securities in a private company; and (5) the likelihood of achieving a liquidity event for the common stock underlying the stock-based awards, such as an IPO or sale of the Company, given prevailing market conditions.

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option pricing model. As there was no public market for its common stock prior to May 9, 2019, which was the first day of trading, and as the trading history of the Company’s common stock was limited through December 31, 2019, the Company determined the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company’s stock options has been determined utilizing the “simplified” method for awards that qualify as “plain-vanilla” options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The Company has not paid, and does not anticipate paying, cash dividends on its common stock; therefore, the expected dividend yield is assumed to be zero.

The assumptions that the Company used to determine the grant-date fair value of stock options granted were as follows:

	Year Ending December 31,	
	2019	2018
Risk-free interest rate	2.09 %	1.93% - 3.02%
Expected option life (in years)	6.16	0.25 - 6.25
Expected dividend yield	0 %	0 %
Expected volatility	71 %	65 %

The following table summarizes the Company's stock option activity for the year ended December 31, 2019:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Life (in Years)	Intrinsic Value (in thousands)
Outstanding as of January 1, 2019	4,039,464	$ 5.67		
Granted	1,620,351	11.07		
Exercised	(155,043)	2.19		
Canceled	(327,828)	7.66		
Outstanding as of December 31, 2019	5,176,944	$ 7.35	7.9	$ 1,490
Exercisable as of December 31, 2019	2,202,669	$ 5.57	6.7	$ 1,268
Vested or expected to vest as of December 31, 2019	5,176,944	$ 7.35	7.9	$ 1,490

The intrinsic value of options exercised during the years ended December 31, 2019 and 2018 was $0.4 million and $0, respectively.

The weighted-average grant date fair value of the options granted during the years ended December 31, 2019 and 2018, was $7.21 and $3.63 per share, respectively.

Stock-based compensation related to stock options and unvested stock awards are classified as follows (in thousands):

	December 31,	
	2019	2018
Research and development	$ 2,461	$ 1,088
General and administrative	3,363	1,690
	$ 5,824	$ 2,778

As of December 31, 2019, there was $14.4 million of unrecognized compensation expense that is expected to be recognized over a weighted-average period of approximately 2.7 years.

8. INCOME TAXES

There is no provision for income taxes because the Company has historically incurred operating losses and maintains a full valuation allowance against its deferred tax assets. A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations as of December 31, 2019 and 2018 are as follows:

	December 31,	
	2019	2018
Tax at U.S. statutory rate	21.0 %	21.0 %
State taxes, net of federal benefit	6.0 %	6.2 %
Permanent differences	(1.9)%	(1.5)%
Tax credits	4.1 %	3.8 %
Change in valuation allowance	(29.2)%	(29.5)%
Effective income tax rate	0.0 %	0.0 %

Significant components of the Company's deferred tax asset at December 31, 2019 and 2018 are as follows (in thousands):

	December 31,	
	2019	2018
Net operating loss carryforwards	$ 52,242	$ 38,337
Research and development tax credit carryforwards	7,917	5,470
Start-up costs	35	43
Capitalized research and development costs	169	277
Depreciation	413	479
Accrued expenses	1,102	811
Stock-based compensation	1,087	600
Other items	971	710
Total deferred tax assets	63,936	46,727
Valuation allowance	(63,936)	(46,727)
Net deferred tax asset	$ —	$ —

As of December 31, 2019, the Company had federal and state net operating loss carryforwards of $192.1 million and $188.3 million, respectively, which may be used to offset future taxable income, if any. These amounts begin to expire in 2030. The federal net operating losses generated in 2018 and 2019 can be carried forward indefinitely. As of December 31, 2019, the Company had federal and state research and development tax credit carryforwards of $6.1 million and $2.3 million, respectively. These amounts expire at various dates through 2039. Due to the degree of uncertainty related to the ultimate use of the deferred tax assets, the Company has fully reserved these tax benefits, as the determination of the realization of the deferred tax benefits was not determined to be more likely than not. The valuation allowance increased in 2019 and 2018 by $17.2 million and $10.6 million, respectively, due to the increase in deferred tax assets by the same amount (primarily due to net operating loss carryforwards) and the Company's recording of a full valuation allowance.

Utilization of the net operating loss and research and development credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. As of December 31, 2019, the Company had not yet completed an analysis of whether its net operating loss and research and development credit carryforwards may be limited.

The Company files income tax returns in the U.S. federal, Massachusetts and New Jersey jurisdictions. The statute of limitations for assessment by the Internal Revenue Service, or IRS, and state tax authorities is closed for tax years prior to 2016, although carryforward attributes that were generated prior to tax year 2016 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a future period. There are currently no federal or state audits in progress.

9. COMMITMENTS AND CONTINGENCIES

Leases

The Company leases laboratory and office space under a lease agreement that expires on April 1, 2021. The lease agreement and most recent amendment contained escalating rent payments. Rent expense is recorded on a straight-line basis. The Company is obligated to make minimum lease payments under the facility lease as follows (in thousands):

Years Ending December 31,		
2020	$	1,226
2021		415
2022		—
Total	$	1,641

Rent expense in each of the years ended December 31, 2019 and 2018 was $1.2 million.

We enter into contracts in the normal course of business with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs") and other third parties for preclinical research studies, Clinical Studies, Clinical Trials and testing and manufacturing services. These contracts do not contain minimum purchase commitments and are cancelable by upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of service providers, up to the date of cancellation.

Legal Proceedings

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

10. RETIREMENT PLAN

The Company has a 401(k) retirement and savings plan (the "Plan") covering all qualified employees. The Plan allows each participant to contribute a portion of his or her base wages up to an amount not to exceed an annual statutory maximum. The Company is permitted to make discretionary matching contributions to the Plan. As of December 31, 2019, the Company had not made any discretionary contributions.

11. NET LOSS PER SHARE

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	December 31,	
	2019	2018
Numerator:		
Net loss	$ (59,037)	$ (36,069)
Accretion of redeemable convertible preferred stock	(46)	(153)
Net loss attributable to common stockholders	$ (59,083)	$ (36,222)
Denominator:		
Weighted average common shares outstanding, basic and diluted	16,624,941	4,546,373
Net loss per share, basic and diluted	$ (3.55)	$ (7.97)

The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	December 31,	
	2019	2018
Redeemable convertible preferred stock (as converted to common stock)	—	14,641,997
Warrants to purchase redeemable convertible preferred stock (as converted to common stock)	—	61,235
Outstanding stock options	5,176,944	4,039,464
	5,176,944	18,742,696

12. RELATED-PARTY TRANSACTIONS

In April 2013, the Company entered into a services agreement with Flagship Pioneering, Inc. (“Flagship”), an affiliate of one of the Company’s principal stockholders, to provide various strategic consulting services to the Company. The total expense which includes services and reimbursement for travel and entertainment under the agreement for the years ended December 31, 2019 and 2018 was $18,000 and $0, respectively. As of December 31, 2019 and 2018, there was $1,000 and $0, respectively, payable to Flagship for costs related to the services agreement.

In August 2019, the Company entered into a consulting agreement with the Chairman of the Company's Board of Directors, to provide various consulting services to the Company. The total expense under the agreement for the year ended December 31, 2019 was $0.3 million. As of December 31, 2019, there were no amounts payable to the Chairman for costs related to the consulting agreement.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this report. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures as of the end of the period covered by this report were effective at a reasonable assurance level in ensuring that information required to be disclosed by us in reports that we file or submit under the Exchange Act (i) is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms; and (ii) accumulated and communicated to management, including our Chief Executive Officer and Principal Accounting Officer, as appropriate, to allow timely discussions regarding required disclosure. We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

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

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the three months ended December 31, 2019 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

Incorporated by reference from the information in our Proxy Statement, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

Item 11. Executive Compensation

Incorporated by reference from the information in our Proxy Statement, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

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

Incorporated by reference from the information in our Proxy Statement, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

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

Incorporated by reference from the information in our Proxy Statement, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

Item 14. Principal Accounting Fees and Services

Incorporated by reference from the information in our Proxy Statement, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

Part IV

Item 15. Exhibits and Financial Statement Schedules

(a) Documents Filed as Part of this Annual Report

1. *Financial Statements*

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page 76 of this Annual Report, incorporated into this Item by reference.

2. *Financial Statement Schedules*

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

3. *Exhibits*

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report are listed in the Exhibit Index below. The exhibits listed in the Exhibit Index are incorporated by reference herein.

(b) Exhibit Index

Exhibit No.	Exhibit Index
3.1	Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on May 13, 2019).
3.2	Amended and Restated Bylaws of Registrant (Incorporated by reference to Exhibit 3.4 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on May 13, 2019).
4.1	Specimen Stock Certificate evidencing shares of common stock (Incorporated by reference to Exhibit 4.1 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1/A (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
4.2	Fifth Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated November 30, 2018 (Incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 12, 2019).
4.3*	Description of the Registrant's Securities
10.1#	2010 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.2#	2019 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Amendment No. 2 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on May 6, 2019).
10.3#	2019 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.4#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.5#	Amended and Restated Employment Agreement between the Registrant and William Hinshaw, dated December 20, 2018 (incorporated by reference to Exhibit 10.5 to the Registrant's Amendment No. 2 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on May 6, 2019).

10.6#	Employment Agreement between the Registrant and Shreeram Aradhye, dated January 1, 2019 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019).
10.7#	Amended and Restated Employment Agreement between the Registrant and Stephen Mitchener, dated December 29, 2018 (incorporated by reference to Exhibit 10.7 to the Registrant's Amendment No. 2 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on May 6, 2019).
10.8#	Employment Agreement between the Registrant and Laurent Chardonnet, dated November 11, 2019. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on November 25, 2019).
10.9#	Chairman and Consulting Agreement between the Registrant and the Chairman of the Board of Directors, dated August 22, 2019 (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 12, 2019).
10.10#	Form of Indemnification Agreement between the Registrant and each of its directors (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 12, 2019).
10.11#	Form of Indemnification Agreement between the Registrant and each of its executive officers (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 12, 2019).
10.12	Riverside Technology Center Commercial Lease Agreement between Rivertech Associates II, LLC and the Registrant, dated as of December 28, 2010 (incorporated by reference to Exhibit 10.10 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.13	Fifth Lease Extension and Modification Agreement to the Lease Agreement between Rivertech Associates II, LLC and the Registrant, dated as of April 28, 2017 (incorporated by reference to Exhibit 10.11 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.14	Loan and Security Agreement among Solar Capital Ltd. and the Lenders thereto and the Registrant, dated as of January 9, 2018 (incorporated by reference to Exhibit 10.12 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
10.15	Second Amendment to Loan and Security Agreement, dated November 30, 2018 (incorporated by reference to Exhibit 10.13 to the Registrant's Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-230822) filed with the Securities and Exchange Commission on April 30, 2019).
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Deloitte and Touche LLP, Independent Registered Public Accounting Firm
24.1*	Power of Attorney (included on signature page to this Annual Report on Form 10-K)
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of 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 Rule 13a-14(a) or Rule 15d-14(a) of 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 and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101INS*	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.
101SCH*	Inline XBRL Taxonomy Extension Schema Document.Inline XBRL Taxonomy Extension Schema Document.
101CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document.
101PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
101DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.

104* Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)

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* Filed herewith.

\# Indicates a management contract or any compensatory plan, contract or arrangement.

† The certification furnished in Exhibit 32.1 hereto is deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

Item 16. Form 10-K Summary

The company has elected not to include summary information.

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.

AXCELLA HEALTH INC.

Date :March 23, 2020 By: /s/ William R. Hinshaw, Jr.

William R. Hinshaw, Jr.
President, Chief Executive Officer and Director

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints William R. Hinshaw, Jr. and Laurent Chardonnet, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ William R. Hinshaw, Jr. William R. Hinshaw, Jr.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 23, 2020
/s/ David R. Epstein David R. Epstein	Chairman, Director	March 23, 2020
/s/ Laurent Chardonnet Laurent Chardonnet	Senior Vice President and Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 23, 2020
/s/ William D. Baird III William D. Baird III	Director	March 23, 2020
/s/ Grégory Behar Grégory Behar	Director	March 23, 2020
/s/ David A. Berry, M.D., Ph.D. David A. Berry, M.D., Ph.D.	Director	March 23, 2020
/s/ Stephen Hoge, M.D. Stephen Hoge, M.D.	Director	March 23, 2020
/s/ Gary Pisano, Ph.D. Gary Pisano, Ph.D.	Director	March 23, 2020
/s/ Cristina M. Rondinone, Ph.D. Cristina M. Rondinone, Ph.D.	Director	March 23, 2020
/s/ Catherine A. Sohn, PharmD. Catherine A. Sohn, PharmD.	Director	March 23, 2020

Description of the Registrant's Securities
Registered Pursuant to Section 12 of the
Securities Exchange Act of 1934

The summary of the general terms and provisions of the registered securities of Axcella Health Inc. (the "Company," "we," "us," and "our") set forth below does not purport to be complete. It is subject to and qualified in its entirety by reference to our Restated Certificate of Incorporation ("Certificate of Incorporation") and our Amended and Restated Bylaws ("Bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and by applicable law. We encourage you to read our Certificate of Incorporation, our Bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

Authorized Capital Stock

Our authorized capital stock consists of 150,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of preferred stock, $0.001 par value per share, all of which are undesignated preferred stock.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights, or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. All outstanding shares are fully paid and nonassessable.

Listing

Our common stock is listed and traded on The NASDAQ Stock Market LLC under the symbol "AXLA."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. Our board of directors may also designate the rights, preferences and privileges of the holders of each such series of preferred stock, any or all of which may be greater than or senior to those granted to the holders of common stock. While, the issuance of preferred stock provides flexibility in connection with possible future financings and acquisitions and other corporate purposes, the rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Though the actual effect of any such issuance on the rights of the holders of common stock will not be known until such time as our board of directors determines the specific rights of the holders of preferred stock, the issuance of preferred stock could have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock.

No shares of preferred stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.3 is filed as an exhibit.

Anti-Takeover Effects of Delaware Law and Provisions of our Charter Documents

Certain provisions of the Delaware General Corporation Law and of our Charter Documents could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Charter Documents

Our Charter Documents include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies. In accordance with our Certificate of Incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our Certificate of Incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds (2/3) or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No Written Consent of Stockholders. Our Certificate of Incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders. Our by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements. Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also 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 our company.

Amendment to By-laws and Certificate of Incorporation. As required by the Delaware General Corporation Law, any amendment of our Certificate of Incorporation must first be approved by a majority of our board of directors and, if required by law or our Certificate of Incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our by-laws and Certificate of Incorporation must be approved by not less than two-thirds (2/3) of the outstanding shares entitled to vote on the amendment, and not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class. Our by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the by-laws; and may also be amended by the affirmative vote of at least two-thirds (2/3) of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank Check Preferred Stock. Our Certificate of Incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our Certificate of Incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum. Our Bylaws provide 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 any state law claim for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our Certificate of Incorporation or Bylaws; (4) any action to interpret, apply, enforce or determine the validity of our Certificate of Incorporation or Bylaws or (5) any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision does not apply to any actions arising under the Securities Act or the Exchange Act.

List of Subsidiaries

Subsidiary	**Jurisdiction of incorporation or organization**
Acora Nutrition LLC	Delaware
Axcella Health Securities Corporation	Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-231570 on Form S-8 of our report dated March 23, 2020, relating to the financial statements of Axcella Health Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 23, 2020

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULE 13a-14(a) OR 15d-14(a)
OF THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, William R. Hinshaw, Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K of Axcella Health Inc.;

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

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

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

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2020

By: /s/ William R. Hinshaw, Jr.

William R. Hinshaw, Jr. President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO RULE 13a-14(a) OR 15d-14(a)
OF THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Laurent Chardonnet, certify that:

1. I have reviewed this Annual Report on Form 10-K of Axcella Health Inc.;

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

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

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

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2020

By: /s/ Laurent Chardonnet

Laurent Chardonnet
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Annual Report of Axcella Health Inc. (the "Company") on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to the best of his knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and

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

Date: March 23, 2020

By: /s/ William R. Hinshaw, Jr.

William R. Hinshaw, Jr. President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 23, 2020

By: /s/ Laurent Chardonnet

Laurent Chardonnet
Chief Financial Officer
(Principal Financial Officer)