2022 Annual Report

[THIS PAGE INTENTIONALLY LEFT BLANK]

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, 2022
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.)**
P.O. Box 1270 Littleton, Massachusetts **(Address of principal executive offices)**	01460 **(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, $0.001 par value per share	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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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 $67,802,542 as of June 30, 2022 (based on a closing price of $2.03 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 28, 2023, the registrant had 73,683,027 shares of common stock, $0.001 par value per share, outstanding.

AXCELLA HEALTH INC.
TABLE OF CONTENTS

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 Studies or Clinical Trials.

"non-drug" to refer to a non-therapeutic use of a product candidate. Such use may be as a medical food, 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:

- our plans and expectations regarding our strategic alternative review process and the timing and success of such process regarding a potential transaction;
- success in retaining our officers, key employees or directors;
- our ability to fund our planned operations for the next twelve months and our ability to continue to operate as a going concern;
- expectations that our cash will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2023, particularly in light of our recent payoff with SLR;
- expectations that we will be able to obtain funding for our operations, including funding necessary to complete further development, any future clinical trials we may conduct and, if approved, commercialization of any product candidates we may develop;
- the benefits of our product candidates to health and/or disease and their commercial potential;
- the success, cost and timing of our product development activities, 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, including our IND submissions and Clinical Trials for AXA1125 and AXA1665;

- our ability to use our research platform to design new product candidates with desirable biological activity;
- 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;
- impairment charges for long-lived assets;
- 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 pandemic on any of the foregoing; and
- other risks and uncertainties, including those discussed in Part II, 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.

SUMMARY OF MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- We do not currently have sufficient working capital to fund our planned operations for the next 12 months and may not be able to continue as a going concern, and our cash has been depleted by our recent payoff of the SLR loan. Further, we have recently announced a strategic plan, which significantly reduced our operations to focus on our pursuit of strategic alternatives;
- We have significantly reduced our employee base;
- We will require additional capital to fund our operations and if we fail to obtain necessary financing (which will be challenging if not impossible to obtain), we will not be able to complete development and commercialization of our product candidates.
- 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 have identified material weaknesses in our internal control over financial reporting. Failure to achieve and maintain effective internal control over financial reporting could harm our business and negatively impact the value of our common stock.
- 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.
- 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.
- We face significant competition from other healthcare companies, and our operating results will suffer if we fail to compete effectively.
- 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.
- COVID-19 may materially and adversely affect our business and our financial results.

- Regulatory requirements for development of our product candidates as drugs or as non-drug products are uncertain and evolving. Should we choose to develop any product candidate in parallel for more than one indication, the results from a Clinical Study or Clinical Trial in one indication, particularly any observation of a serious adverse event, may impact the Clinical Study or Clinical Studies or Clinical Trial or Clinical Trials in another indication. 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.

- 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.

- We rely on third parties to conduct our Clinical Studies and Clinical Trials, and to assist us in meeting the regulatory requirements applicable to the 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.

- 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.

- The trading price of our stock is highly volatile.

The summary risk factors described above should be read together with the text of the full risk factors below and in the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. If any such risks and uncertainties actually occur, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, prospects, financial condition and results of operations.

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 pioneering a new approach to treat complex diseases using compositions of endogenous metabolic modulators, or EMMs. 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 the treatment of Long COVID (also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19, or "PASC") associated fatigue, and the treatment of non-alcoholic steatohepatitis, or NASH.

Using our discovery platform, we have efficiently designed product candidates that are comprised of amino acids and their derivatives, which have a general history of safe use. The orally administered EMM compositions that we have tested clinically to date in our development model have shown the potential to generate multifactorial effects in our initial Clinical Studies.

In December 2022, we announced that we discontinued our EMMPACT Phase 2b clinical trial of AXA1125 for the treatment of NASH to focus on AXA1125 for the treatment of Long COVID associated fatigue. We also announced a corporate restructuring and that we have initiated a process to explore a range of strategic alternatives to maximize shareholder value and we have engaged an investment bank to act as a strategic advisor for this process. We expect to devote substantial time and resources to exploring strategic alternatives that our board of directors believes will maximize shareholder value. Despite devoting significant efforts to identify and evaluate potential strategic alternatives, there can be no assurance that this strategic review process will result in us pursuing any transaction or that any transaction, if pursued, will be completed on attractive terms or at all. We have not set a timetable for completion of this strategic review process, and our board of directors has not approved a definitive course of action. Additionally, there can be no assurances that any particular course of action, business arrangement or transaction, or series of transactions, will be pursued, successfully consummated or lead to increased stockholder value or that we will make any additional cash distributions to our stockholders.

As of December 31, 2022, we had cash and cash equivalents of $17.1 million. Based on our current financial resources and forecasted operating plan, we believe that we will be able to operate into the second quarter of 2023.

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, including mitochondrial function and cellular bioenergetics, nutrient sensing and handling, 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. More recently, the role of various EMMs, including amino acids, in nutrient sensing and cellular signaling have been elucidated.

The loss of homeostasis can be manifested in many conditions and complex diseases, including Type 2 diabetes, or T2D, NASH and non-alcoholic fatty liver disease, or NAFLD, Long COVID, OHE, 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 and insulin resistance, key features of NASH. Similarly, a complex cascade of substrate 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 linked to clinical outcomes and overall survival, such as in end-stage liver disease (cirrhotic sarcopenia).

We believe that our EMM compositions have the potential to address system-wide metabolic dysregulation to restore, improve, support and/or maintain homeostasis in complex diseases where more than one pathway may be dysregulated. For example, in NASH, there are disordered pathways causing dysregulated metabolism, inflammation and fibrosis. We believe these biologies can be regulated via multiple pathways using AXA1125, a proprietary combination of six amino acids and derivatives.

In addition to their known biological impacts, amino acids also have a long history of general safe use across a wide spectrum of ages and underlying medical conditions. As a result, we believe our EMM compositions will have limited off-target effects in humans as compared to traditional pharmaceutical agents and will have limited potential to cause drug-drug interactions. All the above factors taken together provide the potential to bring about a transformation in treating complex diseases and/or supporting health.

Our EMM Composition Design Approach

Our systems biology and discovery platform allow us to efficiently design and test multi-targeted EMM compositions with the aim of restoring and maintaining cellular and system-wide homeostasis in multiple biologies and pathways. This platform integrates advanced data science, cell biology capability, and expertise, leveraging artificial intelligence, machine learning and big data sets that are available both publicly and through institutional human data registries. This data-rich environment, combined with our internal discovery and data science tools, provides for the rapid identification of potential new biological applications and the design of EMM compositions to target specific biologies.

Our platform integrates digital knowledge of amino acid and related molecules and the ecosystem of internal and external data on disease, pathways, genes, and our existing and in-development EMM compositions. As part of our cell biology capability, our human primary cell systems directly inform multiple biological mechanisms implicated in disease and metabolic dysregulations. All of this is supported by a comprehensive EMM safety database derived from the literature and our previous Clinical Studies and ongoing Clinical Trials. The data and learnings generated through this process further enrich and anchor our design process against clinically relevant biologies.

Through a combination of biological and data science capability, program and disease-specific data can subsequently be utilized to elucidate the stoichiometric ratios for EMM compositions, more accurately characterize their pharmacokinetics and pharmacodynamics, and develop a biomarker strategy. The data is also utilized to build a variety of translational models to facilitate the pharmacologic and treatment response characterization, paving the way for translation into the clinic.

Rapid Advancement into Human Clinical Trials

Nonclinical Research

Upon prioritization of an area of interest for clinical development, we leverage internal data and external human data registries to elucidate biological and phenotypic features to design multi-targeted EMM compositions against relevant canonical and non-canonical pathways. This allows us to leverage the appropriate primary human cell models and in vitro assays to provide data that can be assessed in a translationally relevant way. We conduct our model systems in environments that aim to simulate physiological levels of biofluids and nutrients. These models include multiple cell types to deconstruct dysregulated metabolism or disease conditions and isolate effects of EMM compositions on subsets of metabolic pathways. The throughput of these models enables us to test individual EMMs, simple combinations of EMMs as well as complete EMM compositions to identify and understand interactions and characterize the function of each of the utilized constituents.

Preclinical pharmacology, biology experiments, and advanced modeling capabilities inform the design of our EMM compositions (i.e., amounts and ratios), the development of a biomarker strategy, and translation into the clinic. We also evaluate whether existing in-vivo models can inform our design and translation process, de-risking our translation into the clinic. Animal models are commonly used in drug development with the primary goal of investigating safety. Given the generally regarded as safe (GRAS) status of the EMMs utilized in our compositions, we are able to avoid many of these costly and time-intensive models, which we believe provides us with additional development efficiencies.

Clinical Development Approach

Once a product candidate is designed, we then decide whether to evaluate the candidate in a Clinical Study or under a Clinical Trial. We conduct our Clinical Studies under the FDA's September 2013 Guidance for Clinical Investigators, Sponsors, and Institutional Review Boards (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 Clinical Studies include a substantial number of biomarkers that may improve our understanding of biologies relevant to the healthy structures and functions of the body as well as the safety, tolerability and dose-response relationship on relevant biologies. The ability to interrogate the effect of an EMM composition directly in human biologies makes the process of candidate selection both time and resource efficient. These Clinical Studies 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.

To date, we have completed clinical investigations of our product candidates in Clinical Studies. Based on initial Clinical Study results, we decided to pursue further development of AXA1125 and AXA1665 as therapeutics via Clinical Trials under INDs and a CTA. These Clinical Trials, which have been initiated, are, therefore, evaluating each product candidate's ability to treat targeted diseases.

On average, it has been estimated that it takes seven or more years for a therapeutic to progress from product candidate design to Phase 2 development. Our approach has enabled us to rapidly design and investigate our product candidates, providing meaningful insights into their safety, tolerability, and biological activity in diseased human subjects. As a result of our approach, we were able to initiate our Phase 2 trials approximately four years after finalizing the design of our lead product candidates, which we believe validates the speed and efficiency of our approach.

Our Pipeline

The following chart summarizes our current pipeline:

PRODUCT CANDIDATE	POTENTIAL INDICATION	INITIAL CLINICAL STUDIES[1]		THERAPEUTIC DEVELOPMENT
AXA1125	Long COVID			Phase 2a Clinical Trial N=41, 2 arms, 1 dose
AXA1125	Adult NASH	AXA1125-002 N=32, 1 arm, 1 dose	AXA1125-003 N=102, 4 arms, 1 dose	EMMPACT℠ Phase 2b Clinical Trial N=~300, 3 arms, 2 doses
AXA1125	Pediatric NASH			
AXA1665	Overt Hepatic Encephalopathy	AXA1665-001 N=16, 2 periods, 2 doses	AXA1665-002 N=60, 3 arms, 2 doses	EMMPOWER℠ Phase 2 Clinical Trial N=~150, 2 arms, 1 dose

Completed Terminated

1. Initial Clinical Studies refers to Non-IND Clinical Studies initiated prior to a development path decision.

AXA1125 for the Treatment of Long COVID

AXA1125 is also currently being developed as a product candidate for the treatment of Long COVID. In October 2021, we announced that our Clinical Trial Authorisation application, or CTA, for this candidate was cleared by the Medicines and Healthcare products Regulatory Agency, or MHRA, in the United Kingdom, enabling us to proceed directly into a Phase 2a Clinical Trial, which was initiated in the fourth quarter of 2021. Based on AXA1125's differentiated, multi-targeted design and data from our earlier Clinical Studies, we believe this candidate holds the potential, if approved, to serve as a first-line Long COVID therapy for patients.

About Long COVID

Long-term effects, particularly fatigue, have been reported with a variety of viral infections, including West Nile, Zika, Dengue, Zika, seasonal flu as well as the other corona-related viruses such as MERS and SARS-1. Long COVID, also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19, or PASC, has generally been defined as a condition, experienced by patients at least 12 weeks after COVID-19 infection, in which they experience a range of symptoms that cannot be explained by an alternative diagnosis. Emerging research indicates that Long COVID can be experienced by anyone who has contracted COVID-19, regardless of the variant with which they were infected, whether their illness was mild or severe, or whether the individual was vaccinated or unvaccinated.

It is generally estimated that between 20-30% of all people who are infected by COVID-19 will experience Long COVID. While this condition encompasses dozens of symptoms, fatigue is the most predominant of them, impacting a majority of Long COVID patients.

Mitochondrial dysfunction is increasingly being implicated in published studies as an overarching mechanism of Long COVID fatigue and muscle weakness. In this setting, mitochondrial dysfunction includes dysregulated energetics, increased inflammation and oxidative stress, as well dysregulated lipid and amino acid metabolism. It is hypothesized that the COVID-19 virus can trigger a cascade within cells that may include a fuel switch to inefficient glycolysis, compromises cellular bioenergetics and respiration, an increase in oxidative stress, causing compounding inflammation, and an impairment in immune response. Ultimately, this virally mediated cellular reprogramming is believed to contribute to the symptoms of exertional fatigue and muscle weakness that can be persistent, severe, and debilitating. The sheer number of COVID-19 infected patients throughout the world, occurring contemporaneously, may enable better mechanistic insights into mitochondrial dysfunction not only in Long COVID, but also across a range of post-viral syndromes.

AXA1125 in Long COVID

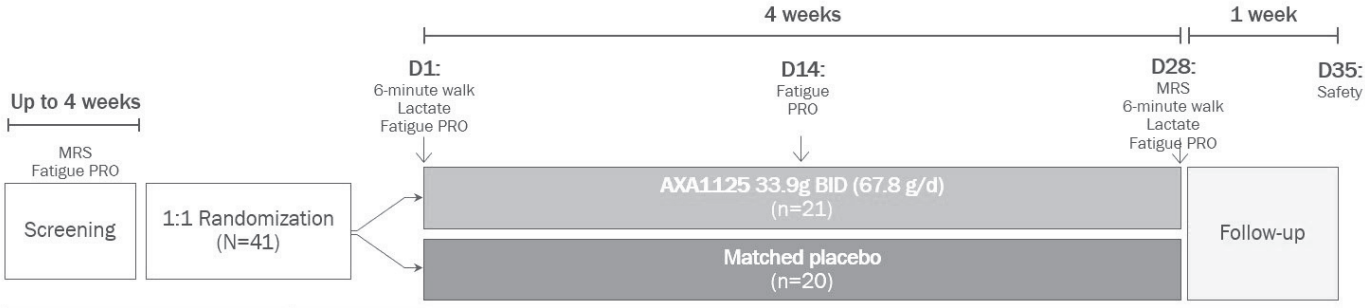
In two prior successful Clinical Studies and in preclinical models, we believe AXA1125 has demonstrated an ability to restore mitochondrial function, providing the potential to treat patients with Long COVID.

Underlying Biology	**Potential Benefits of AXA1125 Treatment**
Dysregulated energetics, with a switch to inefficient glycolysis	Increased fatty acid oxidation and reduced glycolysis
Increased oxidative stress and inflammation	Reduced inflammation, restoration of reactive oxygen species, improved vascular perfusion
Dysregulated fatty acid and lipid metabolism	Restored fatty acid and lipid metabolism, upregulated beta-oxidation

Completed Phase 2a Long COVID Clinical Trial

Phase 2a Long COVID Clinical Trial Design (AXA1125-201)

A 4-week study in participants with Long COVID fatigue



Core elements	Description
Design	• Randomized double blind, placebo-controlled study over 28 days
Study population	• Including Long COVID patients (>12 wks post PCr+) with fatigue-predominant symptoms/abnormalities: – PCr recovery time of ≥50 sec – Chalder Fatigue score of ≥8 (indicates severe fatigue) • Excluding patients with other potential drivers of fatigue and MRS abnormalities (vascular disease, diabetes, etc.)
Endpoints include	• PCr recovery time • Lactate levels • 6-minute walk test • CFQ-11 (Fatigue PRO) scores • Safety and tolerability

Following clearance of the CTA, we initiated a Phase 2a Clinical Trial of AXA1125. The Phase 2a trial is a randomized, double-blind, placebo-controlled investigation to evaluate the efficacy and safety of AXA1125 in patients with exertional fatigue related to Long COVID. 41 patients were enrolled and randomized to receive either 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 28 days, with a one-week safety follow-up period. This same daily dose of AXA1125 has already been investigated in a 12-week Clinical Study in subjects with presumed NASH and was generally well tolerated.

The Phase 2a trial's primary endpoint was change in phosphocreatine (PCr) recovery time, as measured by 31-phosphorus magnetic resonance spectroscopy (MRS), from baseline to Day 28 as an assessment of improvement of mitochondrial function within the skeletal muscle. PCr recovery time is a well-established and highly sensitive measure that has been strongly correlated with the 6-minute walk test (6MWT), a functional measure that has been used as a registrational endpoint in several other diseases in which fatigue and muscle weakness play a central role. Key secondary endpoints include lactate levels, a 6MWT, patient reported fatigue scores assessed by the Chalder Fatigue Questionnaire (CFQ-11), and safety and tolerability. The CFQ-11 is a validated patient reported outcome measure of fatigue that has been used in measuring patient impact in fatigue states such as chronic fatigue syndrome. The Clinical Trial was conducted with researchers at Oxford University's Radcliffe Department of Medicine in the United Kingdom.

In May 2022, we completed patient enrollment in our Phase 2a Clinical Trial and on August 2, 2022, and we reported topline results. Subjects who received AXA1125 had improvements in measures of mental and physical fatigue that were both highly statistically significant and clinically relevant compared to those who received placebo. Mean changes in total, physical and mental scores in the CFQ-11 versus placebo were -4.30 ($p=0.0039$), -2.94 ($p=0.0097$) and -1.32 ($p=0.0097$), respectively. Clinically meaningful shifts in the severity of physical and mental fatigue were also noted in subjects who received AXA1125 compared to those who received placebo. There was a statistically significant correlation of improvement in fatigue score and greater distance achieved in the 6MWT ($p=0.0027$), an objective measure of physical ability, only observed in subjects who received AXA1125 when compared to those receiving placebo. There was a notable trend toward significant improvement in serum lactate levels after a 6MWT in AXA1125 subjects ($p=0.0730$). AXA1125 was well tolerated with no significant emergent adverse events or serious adverse events reported by study subjects.

Baseline PCr among all subjects was significantly higher and had a higher degree of inter-subject variability (92.46 seconds + 35.3 seconds) than previously reported in the literature. These findings support the hypothesis that there is significant mitochondrial dysfunction in these patients but limits the utility of this parameter in a clinical trial. The trial did not meet this exploratory primary endpoint of showing a change from baseline to week four in the PCr recovery rate following moderate exercise between subjects receiving AXA1125 and placebo.

In January 2023, we received regulatory guidance from the MHRA supporting a single trial that could serve as the registration trial for patients with Long COVID associated fatigue. In February 2023, we announced our Investigational New Drug (IND) application to initiate a phase 2b/3 trial in the U.S. for AXA1125 in the treatment of Long COVID associated fatigue had been cleared by the U.S. Food and Drug Administration (FDA). The study design now has acceptance from both the U.S. and U.K. regulatory authorities.

AXA1125 for Nonalcoholic Steatohepatitis (NASH)

AXA1125 is an oral product candidate for the treatment of NASH. In 2021, our IND for this candidate was cleared by the FDA, enabling us to proceed directly into a global Phase 2b Clinical Trial that was initiated in the second quarter of 2021. We branded this global trial EMMPACT based on the potential for AXA1125, an EMM composition, to deliver meaningful, multifactorial clinical benefits to patients with NASH. Based on AXA1125's differentiated, multi-targeted design and data from our earlier Clinical Studies, we believe this candidate holds the potential, if approved, to serve as a first-line NASH monotherapy for both adult and pediatric patients and be used in combination with other agents if required.

About NAFLD and 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. In addition, in association with the rise of childhood obesity, NAFLD emerging as a significant medical need in children.

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. According to the Global Liver Institute's U.S. NASH Action Plan published in December 2020, up to 40 million people in the U.S. alone are living with NASH and approximately 10% of U.S. children are afflicted with this disease. Incidence is expected to continue increasing in parallel with the obesity and type 2 diabetes epidemics. This same report estimates that the lifetime costs for all U.S. NASH patients now exceeds $300 billion, reflecting the severity of this public health issue and its substantial burden on the overall healthcare system.

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 in the United States.

To date, most compounds in development have focused on single key targets within metabolic, inflammation or fibrosis pathways. Few, however, have demonstrated therapeutic benefit, which by current regulatory standards is defined as steatohepatitis resolution with no worsening of fibrosis or improvement in liver fibrosis with no worsening of steatohepatitis. Moreover, safety and tolerability are paramount in this chronic condition and in this patient population, which suffers from a range of comorbidities such as diabetes and cardiovascular disease. Significant challenges to this approach include the potential for compounding of overlapping side effect profiles, drug-drug interactions and high development and treatment costs.

We believe a multitargeted agent that impacts metabolism/liver fat, inflammation and fibrosis, is orally administered, and that is safe, well tolerated and without drug-drug interactions would be well positioned for first-line use in both pediatric and adult NASH.

AXA1125 in NASH

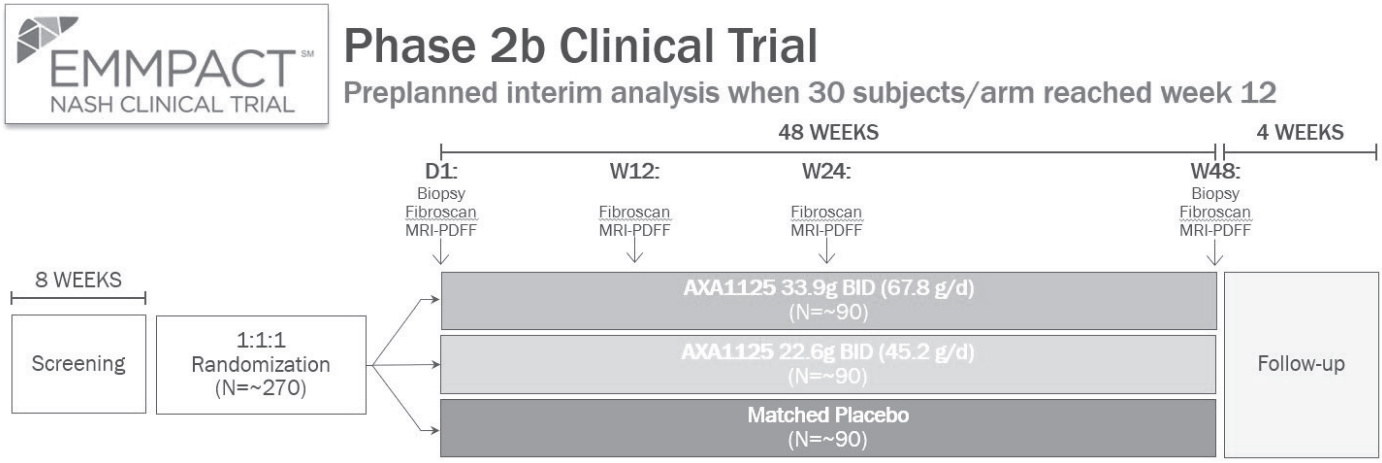
AXA1125 is an oral product candidate that contains six amino acids and derivatives. This product candidate, which has been granted a Fast Track Designation for the treatment of NASH with liver fibrosis, targets multiple pathways that affect metabolism, inflammation and fibrogenesis, providing the potential to treat patients with NASH.

Underlying Biology	Potential Benefits of AXA1125 Treatment
Metabolism	Lower lipotoxicity, improve insulin sensitivity and mitochondrial function by enhancing fatty acid beta-oxidation via activation of pathways such as peroxisome proliferator-activated receptor alpha (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

Most Recent Completed Clinical Study: AXA1125-003

We have conducted two prior Clinical Studies of AXA1125 in subjects with presumed NASH. AXA1125 was generally well tolerated in both of these studies with meaningful and sustained reductions shown in key measures of hepatic fat, insulin resistance, inflammation and fibrosis. In 2020, Axcella completed its most recent Clinical Study of AXA1125, AXA1125-003. This was a 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 two distinct EMM compositions, AXA1125 and AXA1957, in 102 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. Subjects were stratified by the presence or absence of T2D. In this study, subjects received either AXA1125, two different doses of AXA1957 or a calorie-matched placebo control twice a day, or BID. Results from the study showed that AXA1125 and AXA1957 were generally well-tolerated, with sustained reductions noted for both product candidates versus placebo in key biomarkers of metabolism, inflammation and fibrosis over 16 weeks. Notably, the forementioned results were seen without an impact on mean body weight or serum lipids.

Terminated Phase 2b EMMPACT Clinical Trial



Core elements	Description
Design	• Randomized, double-blind, placebo-controlled, dose-ranging study over 48 weeks
Study population	• Biopsy-proven F2/F3 NASH with NAS≥4 • Stratification by type 2 diabetes status
Preplanned IA on secondary endpoints	• Improvement in non-invasive markers, including MRI-PDFF, ALT and Fibroscan

Following FDA clearance of an IND application for AXA1125, we initiated our EMMPACT Phase 2b Clinical Trial for this candidate in the second quarter of 2021. This global randomized, double-blind, placebo-controlled, multi-center Clinical Trial was evaluating the efficacy, safety and tolerability of AXA1125 in adult patients with biopsy-confirmed F2/F3 NASH. Following a protocol amendment, approximately 300 subjects (an increase of 30 subjects over the original design to ensure sufficient liver biopsy data) were to be enrolled and randomized 1:1:1 to receive either 45.2 or 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 48 weeks, with a four-week safety follow-up period. Patients were to be stratified based on the presence or absence of type 2 diabetes.

The Clinical Trial's primary endpoint was to assess the proportion of subjects with a biopsy-confirmed ≥2-point improvement in their NAFLD Activity Score (NAS) after the 48-week treatment period. Secondary endpoints were to include the proportion of patients achieving biopsy-confirmed resolution of NASH without worsening of fibrosis and the proportion of patients achieving a ≥1 stage improvement in fibrosis without worsening of NASH, as well as a range of non-invasive markers, such as MRI-PDFF, vibration controlled transient elastography (Fibroscan®), liver enzymes and measures of insulin resistance.

In September 2022, we reported interim results from our EMMPACT Phase 2b Clinical Trial. These interim results report findings regarding the effects of AXA1125 administration on selected outcome measures after 12 and 24 weeks of treatment. This interim analysis was preplanned to be conducted when enrollment reached 30% of the original target population of 270 subjects with biopsy confirmed stage 2 or 3 NASH across all trial arms. Data from this ongoing blinded study included 82 subjects at week 12 and 58 subjects at week 24; approximately half of the subjects have type 2 diabetes mellitus (T2DM). In addition to effects on hepatic fat and alanine aminotransferase (ALT), previously reported in 2 other studies, this study also included vibration controlled transient elastography (FibroScan®), a widely accepted and accessible non-invasive test (NIT) that assesses both liver fat and stiffness. Specifically, the study examines liver stiffness, changes of which have been correlated with improvements in liver fibrosis and outcomes in clinical studies. Study participants were randomized 1:1:1 to receive either a placebo or 22.6g or 33.9g of AXA1125 twice daily.

At 24-weeks there were statistically significant improvements in the liver stiffness measurement (LSM) compared to placebo in the high dose arm for all subjects. Absolute changes in LSM were 0.13, -2.01, and -4.07 kilopascals (kPa) in the placebo, low dose and high dose arms, respectively (p= 0.0992 and 0.0096 for the low and high dose, respectively, compared to placebo). These results were supported by statistically significant improvements in other NITs of liver fibrosis: ELF and FIB-4. Statistically significant improvements in ALT were seen at both weeks 12 and 24 in all subjects (placebo-adjusted difference of -28.61% (p=0.0183) and -36.3% (p=0.0017) for the low and high doses, respectively). All subjects experienced significantly greater changes from baseline in MRI-PDFF at 12-weeks compared to the change from baseline in the placebo group (placebo adjusted difference of -18.98% (p=0.0082) and -21.24% (p=0.0014) for the low and high doses, respectively). Numerical trends of improvement relative to placebo in PDFF were seen at week 24 but these were not statistically significant in the small number of subjects. Overall, these positive results confirm AXA1125's multi-targeted impact, a differentiated approach to directly and simultaneously targeting multiple pathways that are dysregulated in NASH. Consistent with previous results, AXA1125 was found to be well-tolerated in this study. Both dose levels are active and will be continued. Consistent with prior clinical trials, T2DM showed results comparable to non-diabetics.

In December 2022, we terminated our EMMPACT Phase 2b Clinical Trial of AXA1125 for NASH. The Company will consider options for pursuing AXA1125 in NASH should resource availability change.

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

AXA1665 is a product candidate for the reduction in risk of OHE recurrence in adult patients with liver cirrhosis. In 2021, we announced that our IND for this candidate was cleared by the FDA, enabling us to proceed directly into a Phase 2 Clinical Trial, which was initiated in the second quarter of 2021. We have branded the Phase 2 trial EMMPOWER based on the potential for AXA1665, an EMM composition, to help patients, physicians and other caregivers overcome significant challenges associated with cirrhosis and OHE. Based on AXA1665's differentiated, multi-targeted design and data gathered to date, we believe this candidate holds the potential to reduce OHE events and improve the quality of life for cirrhotic patients.

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. It has been reported that prevalence of cirrhosis in the United States is approximately 0.27%, corresponding to nearly 700,000 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 reportedly 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 overt HE, or OHE. It is estimated that up 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 OHE 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 OHE, each focuses primarily on ammonia reduction, and despite their use, many patients continue to experience OHE breakthrough events. We believe there is a strong need for additional OHE treatment options, particularly those that have the potential to address the systemic complications of cirrhosis, including frailty.

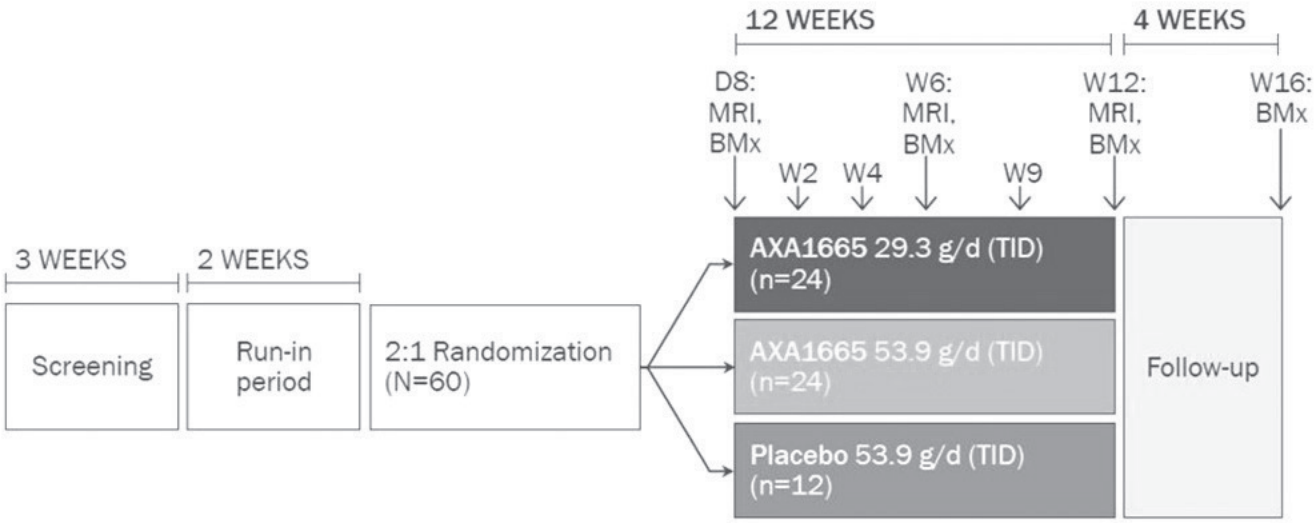
AXA1665

AXA1665 is a composition of eight amino acids and derivatives that is administered orally and holds the potential to influence multiple metabolic pathways intersecting key organ systems (liver, muscle and gut) to treat patients with OHE.

Underlying Biology	Potential Benefits of AXA1665 Treatment
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
Neurocognitive impairment	Improve neurocognition and reduce OHE events

Most Recently Completed Clinical Study: AXA1665-002

We have conducted two prior Clinical Studies of AXA1665 in subjects with mild (Child Pugh A) and moderate (Child Pugh B) hepatic insufficiency. AXA1665 was generally well tolerated in both studies, with multifactorial effects seen in subjects. In 2020, Axcella completed its most recent Clinical Study of AXA1665, AXA1665-002. This was a 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.

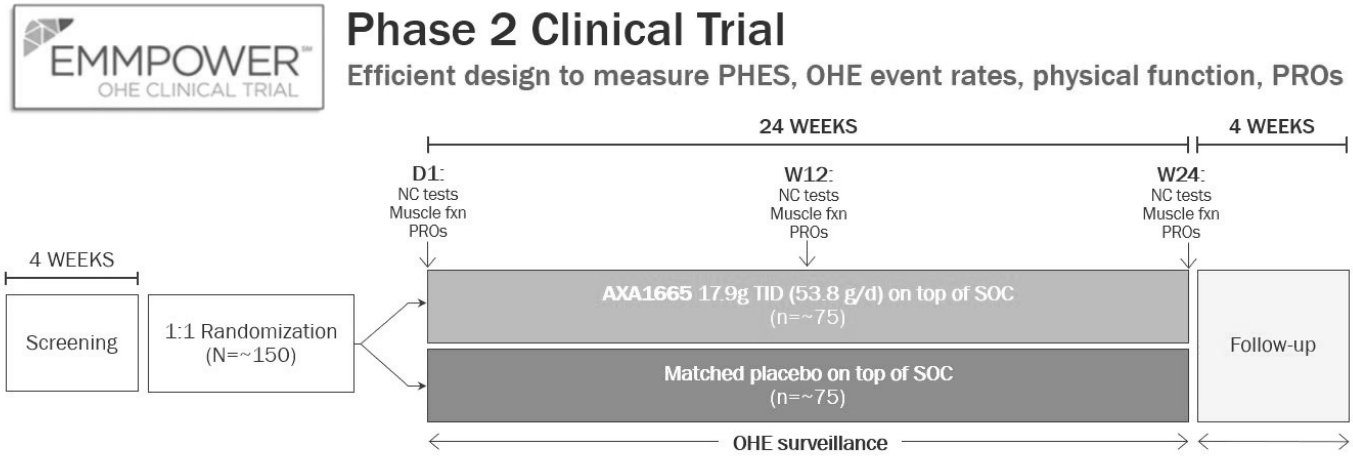


1. Study design for AXA1665-002. This Clinical Study was initiated prior to determination of AXA1665 as a therapeutic product candidate.

Results from the study showed that AXA1665 demonstrated dose dependent improvements across all three psychometric tests that were utilized. These included a statistically significant ($p < 0.05$) improvement for the high dose arm vs. placebo in the psychometric hepatic encephalopathy score (PHES), which is a highly specific assessment to diagnose minimal hepatic encephalopathy (MHE). A higher proportion of subjects in the AXA1665 arms also achieved a ≥0.3 absolute reduction in liver frailty index, or LFI, versus placebo. Previous studies suggest that a ≥0.3 reduction in the LFI score may correlate with an improved ability to conduct activities of daily living in subjects with end-stage liver disease. Additionally, a dose dependent and statistically significant ($p < 0.05$) increase from baseline in Fischer Ratio (FR; a measure of branched chain amino acids ÷ aromatic amino acids) was seen in the AXA1665 arms relative to placebo, which was sustained over 12 weeks. Despite the increased nitrogen load delivered via the amino acids in AXA1665, fasted plasma ammonia levels remained stable in the active arms over the 12-week dosing duration. In a subset of subjects with evidence of MHE at baseline as assessed by PHES, a mean reduction from baseline in fasted plasma ammonia levels was observed in subjects receiving both doses of AXA1665 at week 12.

Both doses of AXA1665 were generally well tolerated. Rates of adverse events (AEs) were low, mostly unrelated to study product and generally mild or moderate. There were five serious adverse events reported in the study and two deaths (one due to complications of COVID-19; one due to a myocardial infarction during the study run-in period prior to dosing), none of which were determined to be related to AXA1665.

Terminated Phase 2 EMMPOWER Clinical Trial



Core elements	Description
Design	• Randomized double blind, placebo-controlled study over 24 weeks
Study population	• Cirrhotic patients with at least 1 prior OHE event and with PHES ≤ −4 at screening with no active OHE at baseline • Stable OHE background therapy and stratified on rifaximin use
Primary endpoint	• Proportion of patients with ≥2 improvement in PHES from baseline to 24 weeks
Secondary and other endpoints	• Proportion of patients experiencing an OHE breakthrough event; time to first OHE breakthrough event, including time to hospitalization; changes in physical function; patient reported outcomes; ammonia, amino acid and inflammatory biomarkers

NC: neurocognitive; fxn: function; PROs: patient reported outcomes; SOC: standard of care (lactulose ± rifaximin)

Following FDA clearance of an IND application for AXA1665, we initiated our EMMPOWER Phase 2 Clinical Trial for this candidate in the second quarter of 2021. This global randomized, double-blind, placebo-controlled, multi-center investigation was evaluating the efficacy and safety of AXA1665 in patients who have experienced at least one prior OHE event and have neurocognitive dysfunction at screening. Approximately 150 patients on lactulose ± rifaximin (stratified by rifaximin use) were to be randomized 1:1 to receive either 53.8 grams per day of AXA1665 or a matched placebo in three divided doses for 24 weeks, with a four-week safety follow-up period.

The Clinical Trial's primary endpoint was to assess the proportion of patients with a ≥2-point increase in the psychometric hepatic encephalopathy score (PHES) after the 24-week treatment period. Key secondary endpoints were to focus on the proportion of patients experiencing an OHE breakthrough event and time to first OHE breakthrough event, including time to hospitalization. Other secondary endpoints were to include changes in physical function and patient-reported outcomes.

In May 2022, we terminated our EMMPOWER Phase 2 Clinical Trial of AXA1665 for reduction in risk of recurrent OHE. The Company will consider options for pursuing AXA1665 should resource availability change.

Future Pipeline Opportunities

Many EMMs, including amino acids, are well established agents used to support health. Single EMMs and simple EMM combinations 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 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.

Intellectual Property

We are establishing a broad, global intellectual property portfolio for our technology and have already received 12 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 (177 patents pending worldwide as of March 13, 2023). 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 March 13, 2023, our patent portfolio consisted of 19 patent families, 12 granted U.S. patents and 200 worldwide patents granted or pending (including U.S.). 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 12 granted U.S. patents and 3 pending U.S. patent applications, and 11 granted foreign patents and 6 pending foreign patent applications.

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 Treatment of Long COVID (Post-Acute Sequelae of COVID-19)

Our patents on compositions of matter covering AXA1125 include its use in a Long COVID indication. Currently, patent rights relating specifically to Long COVID and related conditions include 1 U.S. patent application and 1 corresponding International (PCT) patent application. We would expect any granted patent based on this portfolio to expire in 2042, excluding any patent term adjustments or extensions.

Compositions and Methods for NAFLD/NASH

Our patent applications cover a class of compositions for fatty liver disease, including our drug product candidate AXA1125. Currently, patent rights relating to AXA1125 and related compositions and their uses in fatty liver disease include 5 granted U.S. patents, 1 U.S. patent application, and over 30 foreign national patent applications and patents. 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 related compositions and uses currently includes 1 U.S. patent application. 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 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 3 granted U.S. patents, 1 pending U.S. patent application, and over 30 foreign national patent applications and patents. We expect any granted patent based on this family to expire in 2038, excluding any patent term adjustments or extensions.

Compositions and Methods for Blood and Sickle Cell Disease

Our patent applications cover a class of compositions for blood health and sickle cell disease. Currently, this family of applications includes 1 granted U.S. patent, 1 U.S. patent application and over 15 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 more specifically to related compositions and uses currently includes 1 U.S. 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. Currently, patent rights relating to muscle atrophy include 1 U.S. patent application and over 25 foreign national patent applications and patents. 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 related compositions currently includes 2 granted U.S. patents, 1 U.S. patent application, and 5 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 2 U.S. patent application and 8 foreign national patent applications. We expect any granted patent based on this portfolio to expire in 2038, excluding any patent term adjustments or extensions.

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 1 allowed U.S. patent application and 14 foreign national patent applications);
- taste formulations (currently 1 granted U.S. patent, 1 pending U.S. patent application and 13 foreign national patent applications and patents); and
- unique formulations of candidate compositions (1 U.S. patent application and 9 foreign national patent 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. 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 the EU, 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 which prevent generic applicants from referencing the innovator's data when applying for market authorization and two additional years of market exclusivity where the generic product (even if approved) 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 if, 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 the EU. 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 an application for 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, 2022, our trademark portfolio contains more than 50 registrations and pending applications. We have trademarks in over 18 countries, including the European Union. For the marks AXCELLA and the Axcella LOGO, we also have registrations in countries, including China, India, Japan and the UK. In the United States, we have registrations for the Axcella LOGO, AXCELLA HEALTH, and AXCELLA 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. We continue to make enhancements to our product candidates to make them even more patient-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 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. 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.

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);
- 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.

Regulation of Drug Product Candidates and Drugs

Preclinical and Clinical Trials

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(s) 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.

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.

Fast Track Designation and Accelerated Approval

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. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to 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 compliant 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 to secure final approval of the NDA and may require additional clinical or preclinical testing 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.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including Phase IV clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs, and those supplying products, ingredients, and components of them, 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. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. 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 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. Factors that payors consider in determining reimbursement are based on whether the 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.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.

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.

We expect that healthcare reform measures that 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals or clearances of our product candidates, if any, may be.

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), certain other licensed health care practitioners and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers
- 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).

Current and Future Healthcare Reform Legislation

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system. In particular, in 2010 the ACA was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed 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; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% 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; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted:

- The U.S. Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. Subsequent legislation extended the 2% reduction which remains in effect through 2030. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.
- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

The Inflation Reduction Act of 2022, or IRA, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $2,000 starting in 2025; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

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.

Foreign Regulations

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. For example, we were subject to MHRA regulations for approval of our clinical trial of AXA1125 in Long COVID. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the 27-Member States of the EU, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under EU regulatory systems, a company may submit marketing authorization applications either under a centralized procedure or one of the procedures administered by the competent authorities in the EU Member States (e.g. the decentralized or mutual recognition procedures). The centralized procedure, which is compulsory for medicinal products produced by biotechnology processes, advanced-therapy medicinal products (i.e. gene-therapy, somatic cell-therapy or tissue-engineered medicines); designated orphan medicinal products or those medicinal products containing new active substances for specific indications, namely for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases or auto-immune and other immune dysfunctions. The centralized procedure is optional for products that contain a new active substance for any other indications, or which are of a significant therapeutic, scientific or technical innovation and whose authorization would be in the interest of public health in the EU. Under the centralized procedure, a marketing authorization application is submitted to the EMA where it will be evaluated by the Committee for Medicinal Products for Human Use (CHMP). A favorable opinion by the EMA typically results in the grant by the European Commission of a single marketing authorization that is valid across all EU Member States, and the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway) (EEA), within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed it is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "Concerned" Member States based on an assessment of an application performed by one Member State, known as the "Reference" Member State. Under the decentralized procedure, an applicant submits an application, or dossier, and related materials to the Reference Member State and Concerned Member States. The Reference Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the Reference Member State's assessment report, each Concerned Member State must decide whether to approve the assessment report and related materials. If a Member State does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all Member States involved. Where a product has already received a marketing authorization in one Member State, another Member State can recognize that marketing authorization under the mutual recognition procedure.

When conducting clinical trials in the EU, we must adhere to the provisions of the EU Clinical Trials Regulation (EU) No 536/2014. This requires among other things, that the prior authorization of an independent ethics committee and the submission and approval of a clinical trial authorization application be obtained in each Member State before commencing a clinical trial in that Member State. The new Clinical Trials Regulation replaced the Clinical Trials Directive 2001/20/EC on 31 January 2022 and overhauled the system of approvals for clinical trials in the EU. Specifically, the new Regulation, which is directly applicable in all Member States (meaning that no national implementing legislation in each EU Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU. The main characteristics of the new Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System (CTIS); 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 contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Concerned Member State. Strict deadlines have also been established for the assessment of clinical trial applications.

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic or biosimilar product. For example, in the EU, if any of our products receive a marketing authorization, we expect that we will benefit from eight years of data exclusivity and an additional two years of marketing exclusivity. An additional one-year extension of marketing exclusivity is possible if, during the data exclusivity period, we obtain an authorization for one or more new therapeutic indications that is deemed to bring a significant clinical benefit compared to existing therapies. The data exclusivity period begins on the date of the product's first marketing authorization in the EU and prevents generic or biosimilar applicants from referencing the innovator's pharmacological, toxicological and clinical data for a period of eight years in order to apply for a generic or biosimilar marketing authorization. After eight years, a generic or biosimilar marketing authorization application may be submitted and the sponsoring companies may rely on the marketing authorization holder's data for the reference product, but the generic or biosimilar product cannot be marketed until the expiry of the two-year market exclusivity period. There is no guarantee that a product will be considered by the EU's regulatory authorities to be an innovative medicinal product and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on a marketing authorization application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

As in the United States, a sponsor may apply for designation of a product as an orphan medicinal product for the treatment of a specific indication in the EU before the application for a marketing authorization is made. A product can be designated as an orphan medicinal product in the EU if its sponsor can establish: (1) that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (i) the prevalence of the condition is not more than five in ten thousand persons in the EU when the application is made, or (ii) without incentives, it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product has to be of a significant benefit compared to products available for that condition. Orphan medicinal products in the EU enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication, except for in the following limited circumstances:

- a second applicant can establish that its product, although similar to the authorized orphan product, is safer, more effective or otherwise clinically superior;
- the marketing authorization holder of the authorized orphan product consents to a second orphan medicinal product application; or
- the marketing authorization holder of the authorized orphan product cannot supply enough orphan medicinal product.

A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The aforementioned EU rules are generally applicable in the EEA.

The UK formally left the EU on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of Good Manufacturing Practice, or GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently largely aligns with EU regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. For example, the UK clinical trials legislation is currently based on the now repealed EU Clinical Trials Directive. The extent to which the regulation of clinical trials in the United Kingdom will mirror the new EU Clinical Trials Regulation that has come into effect is not yet known, however the MHRA has opened a consultation on a set of proposals designed to improve and strengthen the United Kingdom clinical trials legislation. Such consultation took place from January 17, 2022 until March 14, 2022, and the MHRA is currently analyzing feedback. Currently, in order to conduct a clinical trial of a medicinal product in the UK, a clinical trial authorization application must be submitted to and approved by the MHRA. The application must also be approved by an independent ethics committee. The sponsor of a clinical trial in the UK must be established in the UK or the EEA or, if this is not the case, the sponsor must have a legal representative who is so established.

As a result of the Northern Ireland Protocol, centralized EU marketing authorizations continue to be recognized in Northern Ireland. A separate marketing authorization is, however, required in order to place medicinal products on the market in Great Britain. On January 1, 2021, all medicinal products with an existing centralized marketing authorization were automatically converted to Great Britain marketing authorizations. For a period of three years from January 1, 2021, the MHRA may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. This is known as the EC Decision Reliance Procedure, or ECDRP. Under the ECDRP, a marketing authorization application can be submitted to the MHRA at any time after the approval of an EU marketing authorization, however a delay in submission may affect the delivery of a decision within the specified timelines. Where a submission is made within five days of a positive opinion issued by the CHMP, the MHRA will aim to determine the Great Britain marketing authorization as soon as possible after European Commission approval, and by day 67 at the latest provided that the European Commission decision has been received. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when determining an application for a new Great Britain marketing authorization.

The MHRA also offers a 150-day assessment timeline for all high-quality applications for a UK, Great Britain or Northern Ireland marketing authorization. The 150-day timeline does not include a "clock-off" period which may occur if issues arise or points require clarification following an initial assessment of the application. Such issues should be addressed within a 60-day period, although extensions may be granted in exceptional cases.

Competition

The healthcare industry is characterized by intense competition and rapid innovation. Our potential competitors include major multinational pharmaceutical, 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 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. Companies with clinical programs that could compete with our current pipeline of product candidates include 89bio, Inc., AgelessRx, AIM ImmunoTech, Akero Therapeutics, Inc., Bausch Health, Bristol-Myers Squibb Co., Esperion Therapeutics, Inc., Genfit SA, Gilead Sciences, Inc., Intercept Pharmaceuticals, Inc., Madrigal Pharmaceuticals, Inc., Mallinckrodt plc, Novartis AG, OrganiCell, Resolve Therapeutics, Scholar Rock Holding Corporation, and Viking Therapeutics, Inc., among others.

Human Capital

In December 2022, we announced a reduction-in-force of approximately 85%. Following the reduction-in-force, as of December 31, 2022, we had 11 full-time U.S.-based employees engaged to facilitate exploration and consummation of a strategic transaction. None of our employees were represented by labor unions or subject to collective bargaining agreements.

Inclusion & Diversity

We are committed to developing policies that promote awareness and behaviors to ensure fair treatment and equality of opportunity, building a culture of diversity and inclusion, and proactively addressing inequality. In line with our core value of collaboration as noted above, we strive to foster an inclusive culture and actively seek diverse perspectives as we believe diverse experiences and expertise enriches our way of thinking and is essential to achieving our goals. This includes policies and practices that uphold these principles throughout the sourcing, hiring, compensation and assessment of candidates and the retention of our employees. As an example of this commitment, we have joined the MassBio Open Letter 2.0 CEO Pledge for a More Equitable and Inclusive Life Sciences Industry.

Addressing pay equity is important to us. In making compensation decisions, our policy is to not consider race; color; creed; religion; national origin; age; ancestry; nationality; marital, domestic partnership or civil union status; sex, gender, gender identity or expression; affectional or sexual orientation; disability; veteran or military status or liability for military status. We include pay equity as a component during our bi-annual review of all employee compensation plans.

Compensation & Benefits

Our compensation philosophy is to pay at the fiftieth percentile for most roles. Our compensation package is comprised of three components: base pay, incentive pay and equity awards. For the base pay cash components, we review all salaries twice annually and make adjustments as needed to maintain our position against the market by role. In addition to base pay, all employees are eligible for an annual bonus with amounts determined by a bonus target defined by the level of the role. The third pay component is equity, which is generally granted in the form of stock options that vest over time and is used to incrementally incentivize our employees. Additionally, we offer a competitive benefits package to all of our full-time and part-time (20+ hours/week) employees.

COVID Response

In response to the COVID-19 pandemic and as part of our commitment to ensure the safety and well-being of our employees, we activated our applicable business continuity plans, including creating an employee committee under our human resources function to recommend and implement policies consistent with U.S. Government, Massachusetts, City of Cambridge, and industry standard regulations and guidance. In addition, our management, human resource, and legal professionals participated in function networks around the COVID-19 response.

From mid-March 2020 until early 2022, the vast majority of our employees were working exclusively from home. We recently reopened our office in a hybrid working environment in which employees are able to work in the office and from home. We have put appropriate safety measures in place, including implementing occupancy limits, restricting business travel, providing and requiring the use of personal protective equipment, daily health screening, cleaning and visitor protocols, and easy access to COVID-19 testing. Our measures have been effective to date, and we have had no known infections from exposure at our workplace.

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 2024, subject to an option to extend the lease for an additional three years.

Our Corporate Information

We were incorporated under the laws of the state of Delaware in August 2008 under the name Newco LS16, Inc. Our principal executive offices are located at 840 Memorial Drive, Cambridge, Massachusetts. Our telephone number is 857 320-2200, and our website is located at www.axcellatx.com. References to our website are inactive textual references only and the content of our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, are available free of charge on our website located at www.axcellatx.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission (the "SEC").

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC's Internet website address is http://www.sec.gov.

A copy of our Corporate Governance Guidelines, Code of Conduct and Business Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.axcellatx.com, under "Investors and News".

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 occur, 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 are exploring strategic alternatives for the Company that could significantly impact our future operations and financial position.

In December 2022, we announced that we are exploring strategic alternatives with the goal of enhancing stakeholder value and we have engaged an investment bank to act as a strategic advisor for this process. Potential strategic alternatives that may be considered as part of this process include an acquisition, merger, reverse merger, other business combination, sales of assets, licensing or other strategic transactions involving the Company. There can be no assurance that the exploration of strategic alternatives will result in any agreements or transactions, or that, if completed, any agreements or transactions will be successful or on attractive terms. No timetable has been established for the completion of this process, and we do not expect to disclose developments unless and until our board of directors has concluded that disclosure is appropriate or required. If we determine to change our business strategy or to seek to engage in a strategic transaction, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management. Because of the significant uncertainty regarding our future plans, we are not able to accurately predict the impact of a potential change in our business strategy and future funding requirements.

Until the review process is concluded, perceived uncertainties related to our future may result in the loss of potential business opportunities and volatility in the market price of our common stock and may make it more difficult for us to attract and retain qualified personnel and business partners.

If we do not successfully consummate a strategic transaction, our board of directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that the process to identify a strategic transaction will result in a successfully consummated transaction. If no transaction is completed, our board of directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, ultimately, such liquidation, since the amount of cash available for distribution continues to decrease as we fund our operations while we evaluate our strategic alternatives. In addition, if our board of directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation of our company, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. Our commitments and contingent liabilities may include (i) obligations under our employment and related agreements with certain employees that provide for severance and other payments following a termination of employment occurring for various reasons, including a change in control of our company; (ii) potential litigation against us, and other various claims and legal actions arising in the ordinary course of business; and (iii) non-cancelable contractual obligations. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation of our company. If a dissolution and liquidation were pursued, our board of directors, in consultation with its advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up of our company.

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 an adequate effect or an acceptable safety profile, gain regulatory approval and/or become commercially viable. In December 2022 our capital balance required us to lay off fifty-two (52) employees constituting approximately 85% of our workforce and terminate a Clinical Trial under an IND of AXA1125 for the treatment of NASH, for which we had reported an interim analysis on September 29, 2022. We sold our laboratory equipment in January 2023. As of January 31, 2023, we no longer occupied our offices and laboratories at 840 Memorial Drive in Cambridge. 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 $81.2 million for the year ended December 31, 2022. As of December 31, 2022, we had an accumulated deficit of $418.4 million. If we are able to obtain sufficient capital to initiate a potential registration trial of AXA1125 in Long COVID and continue other operations, 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 or non-U.S. equivalent and as we seek regulatory approvals, as necessary, for and commercialize our product candidates, if approved. In addition, inflationary pressure could adversely impact our financial results. 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;
- incur setbacks or delays to the initiation or completion of preclinical studies, product development, Clinical Studies and/or Clinical Trials due to the COVID-19 pandemic or any other international crisis;
- further develop our proprietary human-focused product development platform;

- continue to 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;
- incur any disruption or delays to the supply of our product candidates due to the COVID-19 pandemic or any other international crisis;
- 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 or non-U.S. equivalent, 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 or non-U.S. equivalent; 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.

Substantial doubt exists as to our ability to continue as a going concern.

As of December 31, 2022, we had cash and cash equivalents of $17.1 million, and an accumulated deficit of $418.4 million. We believe that we will require additional working capital to fund our planned operations through a full 12 months from the issuance date of this Annual Report on Form 10-K. In March 2022, we sold common stock through a registered direct offering for net proceeds of approximately $24.8 million after deducting estimated offering expenses payable by us. In September 2022, we made a $6.4 million prepayment under our $26.0 million loan and security agreement with SLR Investment Corp. On October 13, 2022 we sold common stock through a registered direct offering for net proceeds of approximately $28.1 million after deducting estimated offering expenses payable by us, including $6.0 million received as cancellation of indebtedness upon the conversion of convertible notes that we issued on September 20, 2022. On December 15, 2022 we paid $21.0 million to SLR Investment Corp. to fully pay off our loan and security agreement with them. Additional funding will be necessary beyond this point to continue to fund our research and development activities. Our plans to alleviate our financing requirements include, among other things, pursuing the sale of our common stock, a transaction of the Company or our AXA1125 product candidate for Long COVID, and funding through the establishment of a collaboration(s) with a potential partner(s) to further advance our product pipeline, none of which can be guaranteed or are entirely within our control. As of December 15, 2022, we were forced to discontinue some of our operations and develop and implement a plan to further extend payables, reduce overhead and scale back our current operating plan until sufficient additional capital is raised to support further operations. These factors individually and collectively raise substantial doubt about our ability to continue as a going concern, and; therefore, it may be more difficult for us to attract investors. Unless we are able to raise additional capital to finance our operations, our long-term business plan may not be accomplished, and we may be forced to cease, further reduce, or further delay operations.

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 if we are able to execute our current and future programs: to conduct further research and development, preclinical studies, Clinical Studies and/or Clinical Trials for any product candidates we elect to develop as a drug product candidate under an IND or non-U.S. equivalent; 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, 2022, we had $17.1 million of cash and cash equivalents. Based on our current operating plan, we believe that our existing cash and cash equivalents balance is not sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months following the filing date of this Annual Report on Form 10-K. 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, 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;
- any setbacks or delays to the initiation or completion of preclinical studies, Clinical Studies and/or Clinical Trials due to the COVID-19 pandemic;
- 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 MHRA and 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 MHRA and the EMA;
- the cost of establishing, maintaining and overseeing a system to ensure our ongoing and planned Clinical Trials are compliant with Good Clinical Practice, or GCP;
- the costs of establishing, maintaining and overseeing a quality system compliant with current Good Manufacturing Practice, or cGMP, and other quality standards applicable to non-drug and drug product development and a supply chain for the development and manufacture of our product candidates;
- any disruption or delays to the supply of our product candidates due to the COVID-19 pandemic or any other international crisis;
- the cost of prosecuting or defending intellectual property disputes, including patent infringement actions we bring against third parties for infringement of our patents or 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 revenue or, if we were to enter into third-party agreements, sufficient 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. We may sell or merge the company or sell substantially all the assets of the Company. 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 be forced to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives, significantly reduce our operating expenses, including by reductions in staff, complete a strategic transaction, and/or limit or cease and wind-down operations. 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.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non-performance by financial institutions or transactional counterparties, could adversely affect the Company's current and projected business operations and its financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. Although we are not a borrower or party to any such instruments with SVB, Signature or any other financial institution currently in receivership, if any of our lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. In addition, if any of our suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected. In this regard, counterparties to SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the Company, the financial institutions with which the Company has credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which the Company has financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Delayed or lost access to, or reductions in borrowings available under revolving existing credit facilities or other working capital sources and/or delays, inability or reductions in the company’s ability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- Potential or actual breach of contractual obligations that require the Company to maintain letters of credit or other credit support arrangements;
- Potential or actual breach of financial covenants in our credit agreements or credit arrangements;
- Potential or actual cross-defaults in other credit agreements, credit arrangements or operating or financing agreements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, impact the available strategic alternatives we are exploring to maximize shareholder value, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our suppliers, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a supplier may determine that it will no longer deal with us as a customer. In addition, a supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on the Company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any supplier bankruptcy or insolvency, or the loss of any significant supplier relationships, could result in material losses to the Company and may have a material adverse impact on our business.

Clinical development is a lengthy and expensive process, with a highly 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, such as AXA1125, 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 about effects on normal structure and function of the body 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. Results from preclinical studies, Clinical Studies, or Clinical Trials 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. Should we choose to develop any product candidate in parallel for more than one indication, the results from a Clinical Study or Clinical Trial in one indication, particularly any observation of a serious adverse event, may impact the Clinical Study or Clinical Studies or Clinical Trial or Clinical Trials in another indication. A Clinical Study or Clinical Trial can fail at any stage of testing. Additionally, our Clinical Studies, Clinical Trials or other preclinical studies may not result in data that supports intended claims for our product candidates. For example, 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 have unacceptable side effects or toxicities. 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. Interim and preliminary 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. Further, 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 a new drug application, or 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 Clinical Studies or Clinical Trials. If we do not have sufficient funds to finance our 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 Clinical Studies or Clinical Trials. For instance, in May 2022, we had announced the termination of our Clinical Trial of AXA1665 for the reduction in risk of recurrent OHE, which is a rare disease of very ill patients with enrollment challenges and long timelines for approval, to focus our resources on our Long COVID and NASH programs. In December 2022, we announced the termination of our Clinical Trial of AXA1125 for NASH.

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, including AXA1125, 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 or any other international crisis, can cause execution delays for our Clinical Studies or Clinical Trials;
- 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;
- results from one Clinical Study or Clinical Trial, particularly observation of a serious adverse event, may impact the other Clinical Study or Clinical Studies or Clinical Trial or Clinical Trials of the same product candidate;
- 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 a 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, or we may be subject to an enforcement action for conducting a Clinical Study not under an IND;
- 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;
- preclinical studies, 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, or we may fail to execute the Clinical Studies or Clinical Trials as a result of 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;
- 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; and
- 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.

We could also encounter delays if a preclinical study, Clinical Study or Clinical Trial is suspended or terminated for any reason. 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 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, including, but not limited to, 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. 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

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.

The development of EMM compositions with defined ratios and formulations, and the potential drug and non-drug applications of these 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 and medical foods. 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.

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, established biotechnology companies, specialty pharmaceutical companies and universities, nutritional foods companies, 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 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. Companies with clinical programs that could compete with our current pipeline of product candidates include 89bio, Inc., AIM ImmunoTech, Akero Therapeutics, Inc., AstraZeneca plc, Bristol-Myers Squibb Co., Direct Biologics LLC, Genentech, Inc., Genfit SA, GeNeuro SA, Gilead Sciences, Inc., Intercept Pharmaceuticals, Inc., Inventiva S.A., Madrigal Pharmaceuticals, Inc., Novartis AG, Novo Nordisk A/S, OrganiCell, Resolve Therapeutics, Todos Medical Ltd., Tonix Pharmaceuticals, Inc., and Viking Therapeutics, Inc., among others.

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.

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, and laid off about 85% of our personnel across functions in December 2022. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and our inability to hire 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. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees.

We are in non-compliance with Nasdaq's continued listing standards, and if we do not regain compliance we will be delisted from Nasdaq.

On December 30, 2022, we received a deficiency letter from the Listing Qualifications Department, or the Staff, of The Nasdaq Stock Market LLC, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the $1.00 per share minimum bid price requirement for continued inclusion on the Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(a)(1) (which we refer to as the "Minimum Bid Price Requirement"). The Nasdaq deficiency letter has no immediate effect on the listing of our common stock, and our common stock will continue to trade on the Nasdaq Global Market under the symbol "AXLA" at this time. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), or the Compliance Period Rule, we have been provided a period of 180 calendar days, or until June 28, 2023 (which we refer to as the "Compliance Date"), to regain compliance with the Minimum Bid Price Requirement. If, at any time ending June 28, 2023, the bid price for our common stock closes at $1.00 or more for a minimum of ten consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that we have regained compliance with the Minimum Bid Price Requirement and our common stock will continue to be eligible for listing on the Nasdaq Global Market, unless the Staff exercises its discretion to extend this ten-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H). If we do not regain compliance with the Minimum Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our common stock to The Nasdaq Capital Market, provided that we meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, with the exception of the Minimum Bid Price Requirement, and would need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period. To effect such a transfer, we would also need to pay an application fee to Nasdaq and provide written notice to the Staff of our intention to cure the deficiency during the second compliance period by effecting a reverse stock split if necessary. As part of its review process, the Staff will make a determination of whether it believes we will be able to cure the deficiency. Should the Staff conclude that we will not be able to cure the deficiency, the Staff will provide written notification to us that our common stock will be subject to delisting. At that time, we may appeal the Staff's delisting determination to a Nasdaq Listing and Hearing Review Panel. However, there can be no assurance that, if we receive a delisting notice and appeal the delisting determination by the Staff to the panel, such appeal would be successful. We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Minimum Bid Price Requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain, or even pursue, compliance with the Minimum Bid Price Requirement, secure a second period of 180 days to regain compliance, or maintain compliance with any of the other Nasdaq continued listing requirements.

A future pandemic like COVID-19 may materially and adversely affect our business and our financial results.

The COVID-19 pandemic resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions, supply chain disruptions, business shutdowns and clinical site closures to non-essential care and clinical trials. Although we cannot presently predict the full scope and severity of a future pandemic such as COVID-19, including a resurgence of COVID-19 or a new variant of the SARS-CoV02 virus or should the H5N1 avian influenza virus jump species into humans, these developments and measures could materially and adversely affect our business, our results of operation and financial condition. Furthermore, a future pandemic such as the COVID-19 pandemic may adversely impact our ability to complete our ongoing and planned Clinical Trials of AXA1125 in a timely manner or at all due to patient or principal investigator recruitment or availability challenges, Clinical Trial site shutdowns or other interruptions. Additionally, we may also experience potential limitations on the quality, completeness and interpretability of data we are able to collect. For instance, on May 7, 2020, a subject death was reported as a result of COVID-19 by one of our principal investigators in our AXA1665-002 Clinical Study. This serious adverse event and any others that may result from a future pandemic such as COVID-19 may impact the quality, completeness and interpretability of the data that we were able to collect. The supply chain disruptions that resulted from COVID-19-related manufacturing shutdowns, global transportation changes, and loss of workers in key industries show that a future pandemic could affect access to raw materials and operations for manufacturing our product candidates, and distribution of product candidates to clinical sites or for commercialization. In addition, as a result of the a future pandemic such as COVID-19 pandemic, we or our key third-party service providers may be not able to complete key program and product development milestones on time or at all; quarantines, shelter-in-place and similar government orders may impact personnel at third-party manufacturing facilities that negatively impact the availability or cost of materials used in our product candidates; market volatility and conditions may limit our ability to raise additional capital to finance our business plans on attractive terms or at all; our business continuity plans may not be effective at limiting operational disruptions or delays; we may suffer negative impacts to operations that may be vulnerable as a result of government or company measures taken to control the spread of a pandemic infection such as COVID-19; potential shutdowns of government agencies such as the SEC or FDA may limit our ability to raise capital and negatively impact our product development timelines; the passage of new legislation may increase our operating costs or limit our operations, such as the Families First Coronavirus Response Act; we may 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 may become incapacitated by a future pandemic.

The extent to which a future pandemic such as 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 pandemic, new information that may emerge concerning the severity of the pandemic or the nature or effectiveness of actions to contain the pandemic or treat its impact, among others. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. However, if we or any of the third parties with whom we engage 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.

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

As an organization, we have completed a limited number of Clinical Trials and Clinical Studies, and we have terminated an ongoing study early due to resource constraints in December 2022.

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 or non-U.S. equivalent 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. For instance, while we previously announced positive top-line data in our AXA1125-003 Clinical Study, including reductions in liver fat content and markers of fibroinflammation, such results may not be replicated 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. Given our completed and potential future Clinical Trial for the treatment of Long COVID, we will need to transition from a company that has undertaken relatively small, early-stage Clinical Studies to a company capable of completing larger scale, global, late-stage Clinical Trials and, if successful, commercial activities. We may not be successful in such transitions.

Our planned, ongoing, and future Clinical Studies and Clinical Trials, 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, Clinical 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. 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 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 or non-U.S. equivalent 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. the COVID-19 pandemic); 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 may result in increased costs or may affect the timing or outcome of our planned and ongoing Clinical Studies or 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.

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 were 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 conducted previously may involve the use of biological and hazardous materials and may produce hazardous waste products. We generally contracted with third parties for the disposal of these materials and wastes.

We cannot be sure that in our prior R&D operations that we eliminated the risk of contamination or injury from these materials, and materialization of such past risk 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 complied with the standards prescribed by these laws and regulations, we cannot guarantee that this has been 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 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 if we restart laboratory research operations. In addition, if we restart our laboratory research operations, 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 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 or non-U.S. equivalent, 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 up to 40 million people in the U.S. alone are living with NASH. 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 INDs or non-U.S. equivalents. 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 for liver conditions and Long COVID. 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:

- successful enrollment in, and completion of, preclinical studies, Clinical Studies and Clinical Trials with positive results;
- clearance of INDs or non-U.S. equivalents for 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;
- overcoming any delays or interruptions to our supply chain, Clinical Studies or Clinical Trials as a result of the COVID-19 pandemic;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity, as available, for our product candidates;

- establishing cGMP-compliant supply and commercial manufacturing operations or making arrangements with cGMP-compliant third-party manufacturers for supply and commercial manufacturing;
- 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 businesspeople 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.

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 drug product candidates or non-drug products, respectively;

- the willingness of physicians to prescribe our drug product candidates to patients;
- the willingness of healthcare professionals to recommend our non-drug products to consumers;
- public perception of new drugs and non-drug products, including our product candidates;
- the strength of marketing and distribution support;
- any impacts to market health as a result of COVID-19;
- the ability for us to partner in the manufacturing 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 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's, 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 for 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 on may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

While we have reorganized as a virtual company with no set location, our current operations are centered in Massachusetts. In addition, we have created a United Kingdom limited company, which is a wholly-owned subsidiary of Axcella Health Inc. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, including any potential effects from 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 distributed locations, 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 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 pandemic could further disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that damaged critical infrastructure, such as 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, we cannot assure our investors that the amounts of insurance will be sufficient to satisfy any damages and losses. If 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 programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

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, derechos, 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, 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.

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 liabilities and the 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 EU GDPR, which became effective on May 25, 2018. In addition, following withdrawal of the UK from the EU (Brexit), as of January 2021, the UK incorporated the EU GDPR into United Kingdom law along with the UK Data Protection Act 2018 (referred to as the "UK GDPR" and together with the EU GDPR, referred to as the "GDPR"). 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/£17.5 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 developing and commercializing our product candidates in the United States and the United Kingdom, we also intend to engage in these activities outside of the United States and United Kingdom 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 geopolitical 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.

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. The United Kingdom and other countries outside of the United States where the Company may do business may undertake review of its tax laws. 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.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses, or NOLs, or research and development tax credit carryforwards. As of December 31, 2022, we had U.S. federal and state net operating loss, or NOL, carryforwards of $329.2 million and $318.3 million, respectively. These amounts begin to expire in 2029. The federal net operating losses generated since 2018 can be carried forward indefinitely. As of December 31, 2022, we also had U.S. federal and state research and development tax credit carryforwards of $10.6 million and $3.2 million, respectively, both of which expire at various dates through 2042. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future taxable income or tax liabilities, respectively.

In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future through subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. The CARES Act includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Unstable market and economic and political 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. In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions that may be initiated by nations including the U.S., the United Kingdom, the European Union or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. 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 or the military conflict between Russia and Ukraine, 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, 2022, we had cash and cash equivalents of $17.1 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, 2022, 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 restructuring of the Company, the volatility of the stock market and the general economic downturn.

Our loan agreement subjected us to operating restrictions and financial covenants and restricted our business and financing activities.

On September 2, 2021, we entered into a Loan and Security agreement with SLR Investment Corp., formerly known as Solar Capital Ltd., for term loans in an aggregate principal amount of $26.0 million. The Loan and Security Agreement replaced the Prior Loan and Security Agreement between us and SLR Investment Corp., dated as of January 9, 2018 and further amended on October 5, 2018, November 30, 2018 and August 28, 2020. On September 8, 2022, the Company made a $6.4 million repayment to SLR under the Loan and Security Agreement, and on December 15, 2022, the Company paid $21.0 million to SLR, fully paying off the Loan and Security agreement, resulting in release of all liens against Company assets.

Our obligations under the Loan and Security agreement were secured by a first priority perfected security interest in our assets, including intellectual property. The Loan and Security Agreement also contained customary representations and warranties, as well as customary affirmative and negative covenants. Among other restrictions, the negative covenants, subject to exceptions, prohibit or limit our ability to: maintain collateral accounts; 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. The Loan and Security Agreement also contained certain financial covenants, including an unrestricted minimum cash level of $20.0 million until certain study data conditions were met.

Risks Related to Government Regulation

Regulatory requirements for development of our product candidates as drugs or as non-drug products are uncertain and evolving. Should we choose to develop any product candidate in parallel for more than one indication, the results from a Clinical Study or Clinical Trial in one indication, particularly any observation of a serious adverse event, may impact the Clinical Study or Clinical Studies or Clinical Trial or Clinical Trials in another indication. 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.

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 have further 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 in human food studies. However, the FDA or comparable foreign regulatory authorities may disagree with this approach and determine that our studies should be conducted under an IND or non-U.S. equivalent, 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 submitted and the FDA has cleared an IND for our Phase 2 Clinical Trial of AXA1665, which we initiated in the second quarter of 2021 and terminated in the second quarter of 2022. Additionally, we have submitted and the FDA has cleared an IND for our Phase 2b Clinical Trial of AXA1125 for the treatment of NASH, which we initiated in the second quarter of 2021 and terminated in December 2022. We have also submitted and the United Kingdom's MHRA has accepted a CTA for our Phase 2a Clinical Trial of AXA1125 for the treatment of Long COVID, which we initiated in December 2021 and reported top line results in August 2022. In November 2022, we conducted a Scientific Meeting with the MHRA, and in January 2023 the MHRA agreed with the Company's plan for a registrational Phase 2b/3 Clinical Trial of AXA1125 for the treatment of Long COVID. In January 2023 we submitted an Investigation New Drug application to the FDA for a Phase 2b/3 Clinical Trial of AXA1125 for the treatment of Long COVID, and the FDA cleared that application in February 2023. We 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.

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 Clinical 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, EMA or MHRA 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;
- laws related to the approval framework for generic drugs; 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.

Obtaining and maintaining regulatory approval of our drug product candidates 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 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 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. Similarly, even if a foreign regulatory authority grants marketing approval of a drug product candidate for a therapeutic indication, the FDA could take opposing positions and decline to approve such product in the U.S. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States. 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 such as the United Kingdom. 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.

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 product, 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. We have not received approval to market any of our product candidates as drugs from regulatory authorities in any jurisdiction, and it is possible that none of our product candidates 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 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 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. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. 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 product candidates. Such requirements may include additional studies or analyses. Similarly, the EMA and competent authorities of the European Union Member States govern the development of product candidates as drugs in the European Union 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 Clinical 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.

The regulatory pathway for AXA1125 for treatment of patients with Long COVID is still evolving, and may result in unexpected or unforeseen challenges.

The speed at which parties are acting to create and test therapeutics and vaccines for COVID-19 is unusual. Evolving or changing plans or priorities within the FDA and comparable regulatory authorities, including those based on new knowledge of COVID-19, Long COVID and how these conditions affect the human body, may significantly affect the clinical and regulatory timelines for our product candidates. Results from ongoing clinical trials and discussions with regulatory authorities may raise new questions and require us to redesign proposed clinical trials, including revising proposed endpoints or adding new clinical trial sites or cohorts of subjects. Any such developments could delay the development timeline for our product candidates and materially increase the cost of the development for such candidates.

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

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation for a particular indication. We have been granted Fast Track designation for AXA1125 for the treatment of NASH with liver fibrosis. We may seek Fast Track designation in the U.S. or comparable designation in other countries, such as Innovative Licensing and Access Pathway (ILAP) in the United Kingdom, for other indications or for certain of our future product candidates, but there is no assurance that the FDA will grant this status to any of our other proposed product candidates. Marketing applications filed by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

Even if we receive regulatory approval of any drug product candidates, 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, 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 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 and applicable product tracking and tracing requirements. 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;
- 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 our 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. It is difficult to predict how any 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 any 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.

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. 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. See section entitled "*Business – Regulation of Drug Product Candidates and Drugs – Coverage and Reimbursement*" in Part I Item 1, Business of this Annual Report.

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.

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.

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as those we are developing.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. Among policy-makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. See section entitled "*Business – Regulation of Drug Product Candidates and Drugs – Current and Future Healthcare Reform Legislation*" in Part I Item 1, Business of this Annual Report.

For example, in August 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. The effect of IRA on our business and the healthcare industry in general is not yet known. There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;

- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. 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 and enacted 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.

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 payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our 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.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our future, potential customers and third-party payors, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act ("FCA"), and data privacy and physician sunshine laws and regulations. These laws or their relevant foreign counterparts may impact, among other things, our proposed sales, marketing, and education programs and our relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient privacy regulation by the federal government and the states in the U.S. as well as other jurisdictions. See section entitled "*Business – Regulation of Drug Product Candidates and Drugs – Other Healthcare and Privacy Laws*" in Part I Item 1, Business of this Annual Report.

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. 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, costly, and can divert a company's attention from the business.

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, 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 U.S. 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 requires 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 commenced enforcement actions against violators beginning July 1, 2020. As currently written, the CCPA may impact our business activities; however, there continues to be uncertainty about how the law will be interpreted and enforced. 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. HIPAA requires covered entities and business associates to develop and maintain policies and procedures with respect to PHI that is used or disclosed, including the adoption of administrative, physical and technical safeguards to protect such information and ensure the confidentiality, integrity and availability of electronic PHI. HIPAA also implemented the use of standard transaction code sets and standard identifiers that covered entities must use when submitting or receiving certain electronic healthcare transactions, including activities associated with the billing and collection of healthcare claims. The United States Office of Civil Rights may impose penalties on a covered entity for a failure to comply with a requirement of HIPAA. Penalties will vary significantly depending on factors such as the date of the violation, whether the covered entity knew or should have known of the failure to comply, or whether the covered entity's failure to comply was due to willful neglect. These penalties include significant civil monetary penalties, criminal penalties and, in certain instances, imprisonment. HIPAA also authorizes state attorneys general to file suit on behalf of their residents. Courts may award damages, costs and attorneys' fees related to violations of HIPAA in such cases. While HIPAA does not create a private right of action allowing individuals to sue us in civil court for violations of HIPAA, its standards have been used as the basis for duty of care in state civil suits such as those for negligence or recklessness in the misuse or breach of PHI. Furthermore, in the event of a breach as defined by HIPAA, the covered entity has specific reporting requirements under HIPAA regulations. In the event of a significant breach, the reporting requirements could include notification to the general public. Enforcement activity can result in reputational harm, and responses to such enforcement activity can consume significant internal resources. Additionally, if we are unable to properly protect the privacy and security of PHI, we could be found to have breached our contracts. Determining whether PHI has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and we cannot be sure how these regulations will be interpreted, enforced or applied to our operations.

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 plan to conduct Clinical Trials in the European Union or the United Kingdom, which may subject us to additional privacy restrictions. We will be subject to the data protection laws of the European Union ("EU") and United Kingdom ("UK") in relation to personal data we collect from these territories. These laws impose additional obligations and risk upon our business, including substantial expenses and changes to business operations that are required to comply with these laws. The withdrawal of the UK from the EU (Brexit) and the subsequent separation of the data protection regimes of these territories mean we are required to comply with separate data protection laws in the EU and UK which may lead to additional compliance costs and could increase our overall risk. The collection, use, storage, disclosure, transfer, and other processing of personal data in the European Union is governed by the provisions of the General Data Protection Regulation ("EU GDPR"), which became effective on May 25, 2018. Further to Brexit, the EU GDPR ceased to apply in the United Kingdom at the end of the transition period on December 31, 2020. As of January 1, 2021, the United Kingdom's European Union (Withdrawal) Act 2018 incorporated the EU GDPR into United Kingdom law along with the UK Data Protection Act 2018 (referred to as the "UK GDPR" and together with the EU GDPR, referred to as the "GDPR"). Failure to comply with the GDPR, and any supplemental European Economic Area ("EEA") country's national data protection laws which may apply by virtue of the location of the individuals whose personal data we collect, may result in fines and other administrative penalties, including monetary penalties of up to €20/£17.5 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.

The GDPR imposes several requirements relating to the processing personal data, including the requirement to provide a notice to individuals about personal data processing activities, the lawful basis for processing personal data, having data processing agreements with third parties who process personal data, appointing data protection officers, conducting data protection impact assessments, record-keeping, responding to individuals' requests to exercise their rights in respect of their personal data, notification of data breaches to the competent national data protection authority, and the implementation of safeguards to protect the security and confidentiality of personal data. The GDPR also imposes several additional requirements relating to the processing of health and other sensitive data which may require us to obtain consent from the individual to whom the personal data relates.

The GDPR imposes strict rules on the transfer of personal data out of the EEA and UK to countries not regarded by European Commission and the United Kingdom government as providing adequate protection ("third countries"), including the United States. These transfers are prohibited unless an appropriate safeguard specified by data protection laws is implemented (such as the Standard Contractual Clauses ("SCCs") approved by the European Commission and the UK International Data Transfer Agreement/Addendum ("UK IDTA")) or a derogation applies. When relying on the SCCs and the UK IDTA for data transfers, we may also be required to carry out transfer impact assessments, on a case-by-case basis, taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred personal data, to ensure an "essentially equivalent" level of protection to that guaranteed in the EEA and UK, in the jurisdiction where the data importer is based. The international transfer obligations under the EEA and UK data protection regimes will require significant effort and cost, and may result in us needing to make strategic considerations around where EEA and UK personal data is transferred and which service providers we can utilize for the processing of EEA and UK personal data.

Although the United Kingdom is regarded as a third country under the EU GDPR, the European Commission has issued a decision recognizing the United Kingdom as providing adequate protection under the EU GDPR ("Adequacy Decision") and, therefore, transfers of personal data originating in the EEA to the United Kingdom remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the United Kingdom to countries not regarded by the United Kingdom as providing adequate protection. The United Kingdom government has confirmed that personal data transfers from the United Kingdom to the European Economic Area remain free flowing.

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.

The UK Government has also now introduced a Data Protection and Digital Information Bill ("UK Bill") into the UK legislative process with the intention for this bill to reform the UK's data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EU data protection regime and threaten the UK Adequacy Decision from the EU Commission. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

European Union drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for any 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 product candidates. The requirements governing product pricing vary widely from country to country. For example, Member States in the European Union are able 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. 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 product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

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 induce improper performance is typically governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the European Union.

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.

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 and 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 to 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, 2022, we have 12 granted U.S. patents covering certain of our product candidates and other technologies, 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.

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. Thus, a third party that files a patent application before we do in the USPTO after March 2013 could 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.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time

Patents have a limited lifespan. In most countries, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest national filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, it is possible that patents protecting our product candidates might expire before or shortly after we commercialize those candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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 to compensate 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 to compensate 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. 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 agreement breaches or are in violation of 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 and Clinical Trials 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, or that while we suspend our research and development operations as a result of our reorganization that competitors may not catch up to our level of knowledge and understanding. 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 technologies 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 they have been infringed upon 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

We rely on third parties to conduct our Clinical Studies and Clinical Trials, and to assist us in meeting the regulatory requirements applicable to the development and marketing of our products. If we are unable to meet our obligations to these third parties in a timely fashion and as a result these third parties discontinue or delay services or 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 depend upon third parties to conduct preclinical studies, Clinical Studies and Clinical Trials. We expect to have to negotiate budgets and contracts with CROs, which may result in delays to our development timelines and increased costs.

We have heavily relied upon, and will continue to heavily rely upon, third parties over the course of our planned and ongoing Clinical Studies and Clinical Trials. As a result, we will have limited control over 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 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 planned and ongoing 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, such as due to the impacts of the COVID-19 pandemic, 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 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 Clinical 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 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 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 Clinical Trials or may not accept such additional data as adequate to initiate our Clinical Trials. In addition, it could limit or prevent our ability to commercialize product candidates for non-drug uses.

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 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, including as a result of impacts due to the COVID-19 pandemic;
- 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 Clinical 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, manufacturing, 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 de-emphasize 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.

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 a 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 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. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

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.

Risks Related to Manufacturing and Supply

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.

In reliance on third parties, we have limited experience manufacturing our product candidates for Clinical Trials. We similarly have limited experience with the manufacturing requirements for non-drug products at a commercial scale. 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. 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.

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 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. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

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 and Clinical Trial ready supplies of our product candidates and will likely need to do the same for any future 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.

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.

Risks Related to Our Common Stock

The trading price of our stock is highly volatile.

Similar to the 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:

- the impact of the Company's restructuring in December 2022;
- any potential impact of COVID-19 on the financial markets generally, the biopharmaceutical industry and our business and operations, including with respect to our planned and ongoing Clinical Studies and Clinical Trials;
- the commencement, enrollment or results of our planned and ongoing Clinical Studies, Clinical Trials 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/biotechnology 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.

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.

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 New Loan and Security agreement with SLR Investment Corp., formerly known as Solar Capital Ltd., 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, 2022, our executive officers, directors and their affiliates and 5% stockholders held, in the aggregate, approximately 78% 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 smaller 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 $1.235 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.

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 supply chain, planned and ongoing Clinical Studies and 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 we develop as therapeutics and technologies;
- the timing and outcomes of any Clinical Trials for 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 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, which we refer to as the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, which we refer to as the Federal Forum Provision. We have chosen the United States District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision.

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. Additionally, these forum selection clauses may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

General Risk Factors

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.

We have identified material weaknesses in our internal control over financial reporting. Failure to achieve and maintain effective internal control over financial reporting could harm our business and negatively impact the value of our common stock.

On December 15, 2022, as part of the corporate restructuring, we significantly reduced the size of our finance function, resulting in diminished segregation of duties over financial reporting. Consequently, in connection with the preparation and audit of our financial statements, a material weakness was identified in our internal control over financial reporting as it relates to segregation of duties as of December 31, 2022. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Specifically, we identified the following material weaknesses in our internal control over financial reporting:

- We did not maintain an effective control environment as we did not maintain a sufficient complement of accounting and financial reporting resources commensurate with our financial reporting requirements.
- We did not maintain an effective risk assessment process, whereby our risk assessment was not updated for the changes resulting from the restructuring in December 2022.
- We did not maintain appropriate control activities to support the appropriate segregation of duties over the review of account reconciliations and manual journal entries.
- We did not document, thoroughly communicate and monitor controls processes.

These material weaknesses did not result in any adjustments to our financial statements for the year ended December 31, 2022. However, these material weaknesses could result in a misstatement of our accounts or disclosures that would result in a material misstatement of our annual or interim financial statements that would not be prevented or detected. Refer to Item 9A, Controls and Procedures, for our remediation plan.

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 is required to report upon the effectiveness of our internal control over financial reporting. 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.

In connection with the preparation and audit of our financial statements as of and for the year ended December 31, 2022, material weaknesses were identified in our internal control over financial reporting. We cannot assure you that the material weakness identified will be remediated by us on the timelines currently anticipated, or at all, or that there will not be additional 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.

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

As a public company, we will continue to 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. The rules and regulations applicable to public companies have substantially increased and may further increase our legal and financial compliance costs and to make some activities more time-consuming and costly.

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

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty, our limited personnel after the reorganization in December 2022 may not be sufficient for effective disclosure controls and procedures, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Global economic uncertainty and unfavorable global economic conditions caused by political instability, changes in trade agreements and conflicts, such as the conflict between Russia and Ukraine, could adversely affect our business, financial condition, results of operations or prospects.

Our business, financial condition, results of operations or prospects could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, economic uncertainties in various global markets caused by political instability and conflict, or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our product candidates, if approved, or our inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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 2024, subject to one option to extend the lease for an additional three 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, 2023, there were approximately 28 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.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. The terms of any 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.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is included in Item 12 of this Annual Report, and is incorporated herein by reference.

Unregistered Sales of Equity Securities and Use of Proceeds

Recent Sales of Unregistered Equity Securities

None.

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. [Reserved]

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 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, 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 pioneering a new approach to treat complex diseases using compositions of endogenous metabolic modulators, or EMMs. 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 the treatment of non-alcoholic steatohepatitis, or NASH, and for the treatment of Long COVID (also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19, or "PASC") associated fatigue.

In December 2022, we announced that we discontinued our EMMPACT Phase 2b clinical trial of AXA1125 for the treatment of NASH to focus on AXA1125 for the treatment of Long COVID associated fatigue. We also announced a corporate restructuring and that we have initiated a process to explore a range of strategic alternatives to maximize shareholder value and we have engaged an investment bank to act as a strategic advisor for this process. We expect to devote substantial time and resources to exploring strategic alternatives that our board of directors believes will maximize enterprise value. Despite devoting significant efforts to identify and evaluate potential strategic alternatives, there can be no assurance that this strategic review process will result in us pursuing any transaction or that any transaction, if pursued, will be completed on attractive terms or at all. We have not set a timetable for completion of this strategic review process, and our board of directors has not approved a definitive course of action. Additionally, there can be no assurances that any particular course of action, business arrangement or transaction, or series of transactions, will be pursued, successfully consummated or lead to increased stockholder value or that we will make any additional cash distributions to our stakeholders.

Also, in December 2022, we reduced our workforce by 52 positions, (representing approximately 85% of employees), leaving a core team of individuals to lead the strategic review process.

Funding Overview

Since our inception, we have focused substantially all of our resources on building our proprietary platform, establishing and protecting our intellectual property portfolio, conducting research and development activities, developing our manufacturing process and manufacturing product candidate material, organizing and staffing our company, business planning, raising capital and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations with proceeds from the sale of preferred stock and issuance of debt and with proceeds from our public offerings.

In May 2019, we completed our IPO pursuant to which we issued and sold 3,571,428 shares of common stock. We received proceeds of $64.5 million after deducting underwriting discounts and commissions and other offering expenses.

In May 2020, we completed a follow-on public offering pursuant to which we issued and sold 12,650,000 shares of common stock. We received proceeds of $55.9 million, after deducting underwriting discounts and commissions and other offering costs.

In June 2020, we entered into a sales agreement with SVB Leerink LLC pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $35.0 million from time to time through SVB Leerink. As of December 31, 2022, we sold an aggregate of 3,285,308 shares of common stock under the ATM Offering for net cash proceeds of $14.7 million after deducting commissions and expenses of $0.9 million.

In March 2022, we secured $24.8 million in net proceeds after deducting estimated offering expenses through a registered direct offering with certain institutional purchasers and certain directors and officers of the company named therein. In the registered direct offering, we sold 13,089,002 shares of common stock, at a purchase price of $1.91 per share.

In September 2022, we issued convertible notes in an aggregate principal amount of $6.0 million to existing investor Flagship Pioneering.

In September 2022, we paid SLR approximately $6.4 million, including principal, accrued interest, fees and costs, under the loan and security agreement. In October 2022, the interest only period was extended from January 2023 to July 2023 as we satisfied an equity related condition under the loan and security agreement.

In October 2022, we secured $28.1 million in net proceeds after deducting estimated offering expenses through a registered direct offering of common stock. As part of the registered direct offering, the $6.0 million convertible notes held by funds associated with Flagship Pioneering were automatically converted into our common stock. In total, we sold 20,847,888 shares of common stock at a purchase price of $1.64 per share.

On December 15, 2022, pursuant to a payoff letter, we voluntarily accelerated the debt and paid approximately $21.0 million, in full satisfaction of all obligations, including all outstanding principal, accrued interest, fees, costs, expenses and other amounts chargeable, under the loan and security agreement.

Since our inception, we have incurred significant operating losses. We reported net losses of $81.2 million and $64.6 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $418.4 million. Further, our cash resources have been depleted due to the $27.4 million used to extinguish our long-term debt and satisfy our obligations under the loan and security agreement with SLR. As of December 31, 2022, we had cash and cash equivalents of $17.1 million. Based on our current financial resources and forecasted operating plan, we believe that we will be able to operate into the second quarter of 2023. We expect our corporate restructuring will reduce our operating expenses with the goal of allowing us to pursue any viable strategic alternatives. There is no guarantee that this plan will be successful. We may not be able to successfully pursue any strategic alternatives and, even if certain strategic alternatives may be available, we cannot provide any assurance that the strategic alternatives review process will result in any particular alternative, transaction or value.

As noted elsewhere in this report, there is substantial doubt as to our ability to fund our planned operations for the next twelve months and to continue to operate as a going concern. We have assessed our ability to continue as a going concern, and, based on our need to raise additional capital to finance our future operations, recurring losses from operations incurred since inception, and expectation of continuing operating losses for the foreseeable future, as of March 30, 2023, the issuance date of the consolidated financial statements for the year ended December 31, 2022, we have concluded that there is substantial doubt about our ability to continue as a going concern for a period of one year from the date that these consolidated financial statements are issued.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for any product candidates we may develop. If we obtain regulatory approval for any such product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution.

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

COVID-19 Pandemic

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 pandemic, 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. However, if we or any of the third parties with whom we engage 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 operations and financial condition.

Components of our Consolidated Results of Operations

Revenue

To date, 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 our 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.

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, 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;

- patent-related costs incurred in connection with filing and prosecuting patent applications; 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, Clinical Trials 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.

We anticipate that our future research and development expenses will decrease compared to 2022 levels due to the discontinuation of the NASH clinical trial and reduction in workforce. Many factors can affect the cost and timing of our Clinical Studies and Clinical Trials, including, without limitation, slow patient enrollment and the availability of supplies, including as a result of the COVID-19 pandemic, 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.

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 future general and administrative expenses will decrease from 2022 levels due to our corporate restructuring.

Impairment of Long-Lived Assets

Impairment of long-lived assets consists of:

- Costs attributable to the ceased use of our corporate offices. The impairment was determined by comparing the fair value of the impacted asset group to their carrying value as of the impairment measurement date.

- Costs attributable to the return of leased laboratory equipment to the lessor in January 2023.

Restructuring Charge

In December 2022, we incurred restructuring charges in connection with the reorganization.

Interest Income

Interest income consists of interest earned on our investments in cash equivalents, money market funds, and high-quality fixed income securities.

Interest Expense

Interest expense consists of interest on outstanding borrowings under our loan and security agreement, the amortization expense of the debt discount and debt issuance costs, and interest paid for leased capital equipment.

Loss on Extinguishment of Debt

The loss on extinguishment of debt was related to charges upon the early redemption of debt which consist of: unamortized debt issuance costs and unamortized deferred financing fees; final fees due and payable to the lender; and lender's legal fees. During 2022, we repaid all outstanding principal of $26.0 million on our loan and security agreement. As such, we recognized a $1.5 million loss calculated as the difference between the carrying amount of the debt and the total cash paid upon debt extinguishment.

In addition, we recognized an extinguishment loss of $0.1 million in the year ended December 31, 2022 representing legal fees related to the conversion of notes held by funds associated with Flagship Pioneering into common stock.

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, 2022 and 2021

The following table summarizes our consolidated results of operations for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Operating expenses:			
Research and development	$ 56,984	$ 43,135	$ 13,849
General and administrative	15,815	18,711	(2,896)
Restructuring and impairment charges	4,189	—	4,189
Total operating expenses	76,988	61,846	15,142
Loss from operations	(76,988)	(61,846)	(15,142)
Other income (expense):			
Interest income	504	139	365
Interest expense	(3,021)	(2,917)	(104)
Loss on extinguishment of debt	(1,601)	—	(1,601)
Other income (expense), net	(80)	(4)	(76)
Total other income (expense), net	(4,198)	(2,782)	(1,416)
Net loss	$ (81,186)	$ (64,628)	$ (16,558)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Salary and benefits-related	$ 14,571	$ 13,918	$ 653
Clinical research and outside services	37,666	24,208	13,458
Facility-related and other	4,747	5,009	(262)
Total research and development expenses	$ 56,984	$ 43,135	$ 13,849

Salary and benefits-related costs increased by $0.7 million due to higher headcount and related compensation, offset in part by the reduction in force. Clinical research and outside services costs increased by $13.5 million due to expenses incurred for our Phase 2/2b clinical trials. Facility-related and other costs decreased by $0.3 million due to lower corporate expenses.

General and Administrative Expenses

The following table summarizes our general and administrative expenses incurred during the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Salary and benefits-related	$ 8,821	$ 11,751	$ (2,930)
Other contract services and outside costs	5,923	5,833	90
Facility-related and other	1,071	1,127	(56)
Total general and administrative expenses	$ 15,815	$ 18,711	$ (2,896)

Salary and benefits-related costs decreased by $2.9 million, primarily due to lower stock-based compensation expense from to the forfeiture of stock awards.

Restructuring and Impairment Charges

The following table summarizes our restructuring and impairment charges incurred during the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Employee termination benefits	$ 1,858	$ —	$ 1,858
Impairment of operating lease right-of-use assets	2,116	—	2,116
Impairment of property and equipment	215	—	215
Total restructuring and impairment charges	$ 4,189	$ —	$ 4,189

In December 2022, we recorded charges of $1.9 million, $2.1 million and $0.2 million related to employee termination benefits, impairment of operating lease right-of-use assets, and impairment of property and equipment, respectively, following the reorganization. We paid $0.6 million of employee termination benefits in December 2022 and we paid the remainder in January 2023. In total, we paid approximately $1.9 million in employee severance benefits.

Other Income (Expense), Net

Other income (expense), net was a net expense of $4.2 million for the year ended December 31, 2022, compared to a net expense of $2.8 million for the year ended December 31, 2021. In December 2022, we recognized a $1.5 million loss upon extinguishing our debt with SLR Investment Corp.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have not yet commercialized any product candidates and we do not expect to generate revenue from sales of any product candidates we may develop for several years, if at all. To date, we have funded our operations with proceeds from the sale of preferred and common stock and borrowing of debt.

See “—Funding Overview.”

As of December 31, 2022, we had cash and cash equivalents of $17.1 million. Our cash equivalents as of December 31, 2022 consisted of bank deposits and money market funds, which enables us to achieve our liquidity and capital needs.

Cash Flows

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

	Year Ended December 31,	
	2022	2021
Net cash used in operating activities	$ (69,588)	$ (54,221)
Net cash provided by investing activities	30,923	3,047
Net cash provided by financing activities	32,238	3,158
Net decrease in cash and cash equivalents	$ (6,427)	$ (48,016)

Operating Activities

During the year ended December 31, 2022, operating activities used $69.6 million of cash, primarily resulting from our net loss of $81.2 million, partially offset by non-cash charges for stock-based compensation expense of $3.6 million, impairment of long-lived assets of $2.3 million, and loss on extinguishment of debt of $1.6 million. Additionally, accrued expenses increased to account for NASH clinical trial shut-down costs.

During the year ended December 31, 2021, operating activities used $54.2 million of cash, primarily resulting from our net loss of $64.6 million, partially offset by changes in our operating assets and liabilities of $2.3 million and non-cash charges of $8.1 million, including $6.2 million of stock-based compensation expense.

Investing Activities

During the year ended December 31, 2022, net cash provided by investing activities primarily consisted of $31.3 million in proceeds from sales and maturities of marketable securities.

During the year ended December 31, 2021, net cash provided by investing activities primarily consisted of $26.7 million in proceeds from sales and maturities of marketable securities, partially offset by purchases of marketable securities totaling $23.4 million.

Financing Activities

During the year ended December 31, 2022, net cash provided by financing activities was $32.2 million. We received net proceeds of $59.4 million from the issuance of common stock and short-term convertible notes. These cash inflows were partially offset by repayment of principal, accrued interest, fees and costs of $27.4 million.

During the year ended December 31, 2021, net cash provided by financing activities was $3.2 million, primarily consisting of net proceeds of $4.8 million from the issuance of common stock, partially offset by payments for a terminal fee obligation and debt issuance costs of $1.7 million.

Loan and Security Agreement

On September 2, 2021, we entered into a loan and security agreement with SLR Investment Corp., or SLR, (formerly known as Solar Capital Ltd.), for term loans in an aggregate principal amount of $26.0 million. The loan and security agreement replaced the loan and security agreement between us and SLR, dated as of January 9, 2018 and further amended on October 5, 2018, November 30, 2018 and August 28, 2020 (as amended, the "Prior Loan and Security Agreement").

In September 2022, we paid SLR approximately $6.4 million, including principal, accrued interest, fees and costs. In October 2022, we satisfied an equity related condition under the loan and security agreement that extended the date on which repayment of principal commences from January 2023 to July 2023. On December 15, 2022, we entered into a payoff letter with SLR, under which we voluntarily accelerated the debt and paid SLR approximately $21.0 million, in full satisfaction of all obligations, including all outstanding principal, accrued interest, fees, costs, expenses and other amounts chargeable, under the loan and security agreement. The payoff letter also provided for the termination of all commitments and obligations under the loan and security agreement and release of all liens held by SLR on our assets.

Funding Requirements

As of December 31, 2022, we had cash and cash equivalents of $17.1 million. Based on our current financial resources and forecasted operating plan, we believe that we will be able to operate into the second quarter of 2023. We expect our corporate restructuring will reduce our operating expenses with the goal of allowing us to pursue any viable strategic alternatives. There is no guarantee that this plan will be successful. We may not be able to successfully pursue any strategic alternatives and, even if certain strategic alternatives may be available, we cannot provide any assurance that the strategic alternatives review process will result in any particular alternative, transaction or value. Our cash requirements depend on numerous factors, including, without limitation, expenditures in connection with our research and 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.

Based on our current operating plan, we believe we do not have sufficient cash and cash equivalents to support current operations through a full 12 months from the issuance date of this Annual Report on Form 10-K. 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 re-financings, collaboration agreements, strategic alliances 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 pandemic. 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. The amounts involved in any such transactions, individually or in the aggregate, may be material. These factors individually and collectively raise substantial doubt about our ability to continue as a going concern.

Nasdaq Delisting Notification

On December 30, 2022, we received a deficiency letter from the Listing Qualifications Department, or the Staff, of The Nasdaq Stock Market LLC, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the $1.00 per share minimum bid price requirement for continued inclusion on the Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(a)(1) (which we refer to as the “Minimum Bid Price Requirement”). The Nasdaq deficiency letter has no immediate effect on the listing of our common stock, and our common stock will continue to trade on the Nasdaq Global Market under the symbol “AXLA” at this time.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), or the Compliance Period Rule, we have been provided a period of 180 calendar days, or until June 28, 2023 (the "Compliance Date"), to regain compliance with the Minimum Bid Price Requirement. If, at any time ending June 28, 2023, the bid price for our common stock closes at $1.00 or more for a minimum of ten consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that we have regained compliance with the Minimum Bid Price Requirement and our common stock will continue to be eligible for listing on the Nasdaq Global Market, unless the Staff exercises its discretion to extend this ten-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If we do not regain compliance with the Minimum Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our common stock to The Nasdaq Capital Market, provided that we meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, with the exception of the Minimum Bid Price Requirement, and would need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period. To effect such a transfer, we would also need to pay an application fee to Nasdaq and provide written notice to the Staff of our intention to cure the deficiency during the second compliance period by effecting a reverse stock split if necessary. As part of its review process, the Staff will make a determination of whether it believes we will be able to cure the deficiency. Should the Staff conclude that we will not be able to cure the deficiency, the Staff will provide written notification to us that our common stock will be subject to delisting. At that time, we may appeal the Staff's delisting determination to a Nasdaq Listing and Hearing Review Panel. However, there can be no assurance that, if we receive a delisting notice and appeal the delisting determination by the Staff to the panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Minimum Bid Price Requirement, which could include seeking to affect a reverse stock split. However, there can be no assurance that we will be able to regain, or even pursue, compliance with the Minimum Bid Price Requirement, secure a second period of 180 days to regain compliance, or maintain compliance with any of the other Nasdaq continued listing requirements.

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.

Long-Lived Assets Impairment

Long-lived assets consist of property and equipment and operating lease, right-of-use asset. 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 we consider 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, we compare 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 in loss from operations when estimated undiscounted future cash flows expected to result from the use and eventual disposition 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.

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.

Restructuring

We recognize restructuring charges related to reorganization plans that have been committed to by management when liabilities have been incurred. In connection with these activities, we record restructuring charges at fair value for one-time employee termination benefits when management has committed to a plan of termination, the plan identifies the employees and their expected termination dates, the details of termination benefits are complete, it is unlikely changes to the plan will be made or the plan will be withdrawn and communication to such employees has occurred.

One-time employee termination benefits are recognized in their entirety when communication has occurred and future services are not required. If future services are required, the costs are recorded ratably over the remaining period of service. Contract termination costs to be incurred over the remaining contract term without economic benefit are recorded in their entirety when the contract is canceled.

Stock-Based Compensation

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of company-specific historical and implied volatility data, we base our estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology industries in a similar stage of development as us and that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted. We account for forfeitures as they occur.

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 $1.235 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

Under SEC rules and regulations, as a smaller reporting company, we are not required to provide the information required by this item.

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 stockholders and the Board of Directors 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, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company's recurring losses from operations incurred since inception, the expectation of continuing operating losses for the foreseeable future, and uncertainty around the changes to the business plan, raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, effective January 1, 2022, the Company adopted FASB ASC Topic 842, *Leases*, using the modified retrospective transition approach.

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 30, 2023

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

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

	As of December 31,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 17,147	$ 23,574
Marketable securities	—	31,474
Prepaid expenses and other current assets	876	1,598
Total current assets	18,023	56,646
Property and equipment, net	693	870
Other assets	211	211
Total assets	$ 18,927	$ 57,727
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,707	$ 4,301
Accrued expenses and other current liabilities	7,849	5,849
Current portion of operating lease liability	1,592	—
Total current liabilities	14,148	10,150
Long-term debt, net of discount	—	25,070
Operating lease liability	569	—
Other non-current liabilities	46	499
Total liabilities	14,763	35,719
Commitments and contingencies (Note 11)	—	—
Stockholders' equity:		
Common stock, $0.001 par value; 150,000,000 shares authorized, 74,074,201 and 39,605,701 shares issued and 73,655,220 and 39,186,720 shares outstanding at December 31, 2022 and 2021, respectively	74	40
Additional paid-in capital	422,517	359,261
Treasury stock, 418,981 shares at cost	—	—
Accumulated other comprehensive loss	—	(52)
Accumulated deficit	(418,427)	(337,241)
Total stockholders' equity	4,164	22,008
Total liabilities and stockholders' equity	$ 18,927	$ 57,727

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

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

	Year Ended December 31,	
	2022	2021
Operating expenses:		
Research and development	$ 56,984	$ 43,135
General and administrative	15,815	18,711
Restructuring and impairment charges	4,189	—
Total operating expenses	76,988	61,846
Loss from operations	(76,988)	(61,846)
Other (expense) income:		
Interest income	504	139
Interest expense	(3,021)	(2,917)
Loss on extinguishment of debt	(1,601)	—
Other expense, net	(80)	(4)
Total other (expense) income, net	(4,198)	(2,782)
Net loss	$ (81,186)	$ (64,628)
Net loss per share, basic and diluted	$ (1.49)	$ (1.70)
Weighted average common shares outstanding, basic and diluted	54,355,769	38,110,420
Comprehensive loss:		
Net loss	$ (81,186)	$ (64,628)
Other comprehensive income (loss):		
Unrealized gains (losses) on marketable securities	52	(18)
Comprehensive loss	$ (81,134)	$ (64,646)

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,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (81,186)	$ (64,628)
Adjustment to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	412	288
Share-based compensation expense	3,583	6,243
Non-cash interest expense	513	609
Non-cash lease expense	(183)	—
Long-lived assets impairment	2,331	—
Loss on extinguishment of debt	1,601	—
Other non-cash items	177	925
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	722	94
Accounts payable	382	2,050
Accrued expenses and other current liabilities	2,060	198
Net cash used in operating activities	(69,588)	(54,221)
Cash flows from investing activities:		
Purchases of property and equipment	(426)	(275)
Purchases of marketable securities	—	(23,391)
Proceeds from sales and maturities of marketable securities	31,349	26,713
Net cash provided by investing activities	30,923	3,047
Cash flows from financing activities:		
Proceeds from issuance of common stock, net of issuance costs	53,495	4,779
Proceeds from convertible notes	5,926	—
Proceeds from exercise of common stock options and ESPP	182	236
Principal repayments of debt	(26,000)	—
Payment of terminal fee obligation and debt issuance costs	(1,190)	(1,726)
Repayments of the principal portion of finance lease	(175)	(131)
Net cash provided by financing activities	32,238	3,158
Net decrease in cash and cash equivalents	(6,427)	(48,016)
Cash and cash equivalents, beginning of year	23,574	71,590
Cash and cash equivalents, end of year	$ 17,147	$ 23,574
Supplemental cash flow information:		
Cash paid for interest	$ 2,508	$ 2,309
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of notes into common stock	$ 6,000	$ —
Obtaining a right-of-use asset in exchange for an operating lease liability	$ 3,340	$ —
Purchases of property and equipment included in accounts payable	$ 26	$ 2
Offering costs incurred but unpaid at period end	$ —	$ 20
Property and equipment acquired through capital lease	$ —	$ 534

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

AXCELLA HEALTH INC.
Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share data)

	Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Par Value				
BALANCE - January 1, 2021	38,022,273	$ 38	$ 347,990	$ (34)	$ (272,613)	$ 75,381
Exercise of common stock options	111,833	1	56			57
Issuance of common stock, net of issuance costs of $349	1,331,441	1	4,793			4,794
Issuance of common stock related to ESPP	56,967		179			179
Vesting of restricted stock units	83,187					
Stock-based compensation			6,243			6,243
Unrealized loss on marketable securities				(18)		(18)
Net loss					(64,628)	(64,628)
BALANCE - December 31, 2021	39,605,701	$ 40	$ 359,261	$ (52)	$ (337,241)	$ 22,008
Exercise of common stock options	8,499		6			6
Issuance of common stock, net of issuance costs of $71	34,169,490	34	59,491			59,525
Issuance of common stock related to ESPP	148,416		176			176
Vesting of restricted stock units	142,095					—
Stock-based compensation			3,583			3,583
Unrealized gain on marketable securities				52		52
Net loss					(81,186)	(81,186)
BALANCE - December 31, 2022	74,074,201	$ 74	$ 422,517	$ —	$ (418,427)	$ 4,164

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

1. NATURE OF BUSINESS AND BASIS OF PRESENTATION

Company Overview

Axcella Health Inc., doing business as “Axcella Therapeutics,” and subsidiaries ("Axcella," the "Company," "we" or "us") 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 pioneering a new approach to treat complex diseases using compositions of endogenous metabolic modulators, or EMMs. 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's pipeline includes lead therapeutic candidates for the treatment of Long COVID (also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19, or “PASC”) associated fatigue, and for the treatment of non-alcoholic steatohepatitis, or NASH.

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 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.

To date, the Company has primarily financed its operations with proceeds from the sale of preferred and common stock and borrowing of debt.

In May 2019, the Company completed its initial public offering pursuant to which the Company issued an aggregate of 3,571,428 shares of its common stock for net proceeds of approximately $64.5 million after deducting the underwriting discounts and commissions and other offering expenses.

In May 2020, the Company completed a follow-on public offering pursuant to which the Company issued an aggregate of 12,650,000 shares of its common stock for net proceeds of approximately $55.9 million after deducting the underwriting discounts and commissions and other offering expenses.

In June 2020, the Company entered into a sales agreement with SVB Leerink LLC pursuant to which the Company may offer and sell shares of its common stock having an aggregate offering price of up to $35.0 million from time to time through SVB Leerink, acting as its agent (the “ATM Offering”). As of December 31, 2022, the Company sold an aggregate of 3,285,308 shares of common stock under the ATM Offering for net cash proceeds of $14.7 million after deducting commissions and expenses of $0.9 million. During the year ended December 31, 2022, the Company issued 232,600 shares of common stock in a series of sales under the ATM Offering for an aggregate net proceeds of $0.6 million after deducting nominal commissions and expenses.

In March 2022, the Company secured $24.8 million in net proceeds after deducting estimated offering expenses through a registered direct offering with certain institutional purchasers and certain directors and officers of the company named therein. In the registered direct offering, the Company sold 13,089,002 shares of common stock, at a purchase price of $1.91 per share.

In September 2022, the Company issued convertible notes in an aggregate principal amount of $6.0 million to existing investor Flagship Pioneering.

In October 2022, the Company secured $28.1 million in net proceeds after deducting estimated offering expenses through a registered direct offering of common stock. As part of the registered direct offering, the $6.0 million convertible notes held by funds associated with Flagship Pioneering were automatically converted into the Company's common stock. In total, the Company sold 20,847,888 shares of common stock at a purchase price of $1.64 per share.

In late 2022, the Company used $27.4 million of its cash and cash equivalents to extinguish its long-term debt and satisfy its obligations under the loan and security agreement with SLR Investment Corp.

On December 12, 2022, the Board of Directors approved a reprioritization of the Company's programs and a restructuring of operations to support its streamlined set of priorities. As part of this restructuring, the Board approved a reduction in force of approximately 85% of the Company’s workforce. Since the reorganization, the Company has taken several actions including terminating its EMMPACT Phase 2b clinical trial of AXA1125 for the treatment of NASH to focus on AXA1125 for the treatment of Long COVID associated fatigue, and executing a plan to vacate its facility and to sell its non-leased laboratory equipment.

Under Accounting Standards Update (“ASU”) 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40)* (“ASC 205-40”), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued.

As of December 31, 2022, the Company had an accumulated deficit of $418.4 million, and cash and cash equivalents of $17.1 million. For the year ended December 31, 2022, the Company incurred a loss of $81.2 million and used $69.6 million of cash in operations. The Company expects its reorganization will reduce its operating expenses, however the Company will need to raise additional funding to operate to fund operations. Management has assessed the Company’s ability to continue as a going concern in accordance with the requirements of ASC 205-40 based on the need to raise additional capital to finance its future operations, its recurring losses from operations incurred since inception, and expectation of continuing operating losses for the foreseeable future. As of March 30, 2023, the issuance date of the consolidated financial statements for the year ended December 31, 2022, the Company has concluded that there is substantial doubt about its ability to continue as a going concern for a period of one year from the date that these consolidated financial statements are issued. The accompanying consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

The Company's plans to alleviate its financing requirements include, among other things, pursuing the sale of its common stock, a transaction of the Company or its AXA1125 product candidate for Long COVID, and funding through the establishment of a collaboration(s) with a potential partner(s) to further advance its product pipeline, none of which can be guaranteed or are entirely within the Company's control. As of December 15, 2022, the Company was forced to discontinue some of its operations and develop and implement a plan to further extend payables, reduce overhead and scale back its current operating plan until sufficient additional capital is raised to support further operations. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern, and; therefore, it may be more difficult for the Company to attract investors. Unless the Company is able to raise additional capital to finance its operations, its long-term business plan may not be accomplished, and the Company may be forced to cease, further reduce, or further delay operations. However, the Company does not believe it is probable that those plans can be effectively implemented to mitigate the conditions or events that raise substantial doubt.

The Company's 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").

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany accounts and transactions have been eliminated in consolidation.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

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.

Segment Information

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

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements, the reported amounts of expenses during the reporting period, and disclosure of contingent assets and liabilities. On an on-going basis, the Company evaluates its estimates and assumptions, including those related to recoverability of long-lived assets, useful lives used in depreciation and amortization, income taxes and related valuation allowance, accrued expenses and share-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents include cash held in banks and amounts held in interest-bearing money market accounts. Cash equivalents are carried at cost, which approximates their fair market value. The Company considers all highly liquid investments with a remaining maturity when purchased of three months or less to also be cash equivalents.

Marketable Securities

The Company's marketable securities, which consisted of corporate debt obligations, are classified as available-for-sale and are reported at fair value. Unrealized gains and losses on available-for-sale securities are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity. Realized gains and losses and declines in value determined to be other than temporary are based on the specific identification method and are included as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the consolidated statements of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Concentrations of Credit Risk

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. The Company's cash and cash equivalents consists of bank deposits and money market funds that invest in U.S. treasury securities. Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash equivalents. The Company invests in high-quality financial instruments and its portfolio does not consist of any instrument with a maturity duration in excess of twenty-four months, which we believe limits the Company's credit risk.

In addition, the Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines the allowable investments that the Company believes minimizes the exposure to concentrations of credit risk. The Company has not experienced any credit losses and does not believe that it is subject to significant credit risk.

The Company has a banking relationship with SVB. SVB was closed on March 10, 2023 by the California Department of Financial Protection and Innovation, which appointed the FDIC as receiver. On March 12, 2023, the U.S. Treasury, Federal Reserve, and FDIC announced that SVB depositors will have access to all of their money starting March 13, 2023. While the Company has not experienced any losses in such accounts, the recent failure of SVB potentially exposed the Company to significant credit risk prior to the completion by the FDIC of the resolution of SVB in a manner that fully protected all depositors.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value. 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.

The Company's cash equivalents and marketable securities are carried at fair value, determined according to the fair value hierarchy described above. The carrying values of the Company's accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities. The carrying value of the Company's long-term debt approximates its fair value due to its variable interest rate, which approximates a market interest rate.

Long-Lived Assets - 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
Computer equipment and software	3 years
Office equipment	3 - 5 years
Laboratory equipment	5 years
Furniture and fixtures	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.

Long-Lived Asset - Operating Lease

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, as amended by various subsequently issued ASUs. The standard requires lessees to recognize an operating lease with a term greater than one year on their balance sheets as a right-of-use asset and corresponding lease liability, measured at the present value of the lease payments. Under the standard, disclosures are required to enable financial statement users to assess the amount, timing, and uncertainty of cash flows arising from the leases. Companies are also required to recognize and measure leases existing at, or entered into after, the adoption date using a modified retrospective approach, with certain practical expedients available. Comparative periods prior to adoption have not been retrospectively adjusted.

Effective January 1, 2022, the Company adopted ASU 2016-02, using the required modified retrospective approach and utilizing January 1, 2022 as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, Leases (Topic 840).

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have material financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects an internally developed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

ASC 842 transition practical expedients and application of transition provisions to leases at the transition date

The Company elected the following practical expedients, which must be elected as a package and applied consistently to all of its leases at the transition date (including those for which the entity is a lessee or a lessor): i) the Company did not reassess whether any expired or existing contracts are or contain leases; ii) the Company did not reassess the lease classification for any expired or existing leases (that is, all existing leases that were classified as operating leases in accordance with ASC 840 are classified as operating leases, and all existing leases that were classified as capital leases in accordance with ASC 840 are classified as finance leases); and iii) the Company did not reassess initial direct costs for any existing leases.

For leases that existed prior to the date of initial application of ASC 842 (which were previously classified as operating leases), a lessee may elect to use either the total lease term measured at lease inception under ASC 840 or the remaining lease term as of the date of initial application of ASC 842 in determining the period for which to measure its incremental borrowing rate. In transition to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates.

Application of ASC 842 policy elections to leases post adoption

The Company has made certain policy elections to apply to its leases executed post adoption, or subsequent to January 1, 2022, as further described below.

In accordance with ASC 842, components of a lease should be split into three categories: lease components, non-lease components, and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components.

Entities may elect not to separate lease and non-lease components. Rather, entities would account for each lease component and related non-lease component together as a single lease component. The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

ASC 842 allows for the use of judgment in determining whether the assumed lease term is for a major part of the remaining economic life of the underlying asset and whether the present value of lease payments represents substantially all of the fair value of the underlying asset. The Company applies the bright line thresholds referenced in ASC 842-10-55-2 to assist in evaluating leases for appropriate classification. The aforementioned bright lines are applied consistently to the Company's leases.

Long-Lived Assets Impairment

Long-lived assets consist of property and equipment and operating lease, right-of-use asset. 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 in loss from operations when estimated undiscounted future cash flows expected to result from the use and eventual disposition 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.

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 consumed or the related services are performed.

The Company has entered into various research and development related contracts. The Company records accrued liabilities for research costs incurred but not paid. When measuring 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.

Share-Based Compensation Expense

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 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 the consolidated statements of operations in the same manner in which the award recipient's cash compensation costs are classified.

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, 2022 and 2021, the Company has not identified any uncertain tax positions for which reserves would be required.

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 year ended December 31, 2022, the Company's only element of other comprehensive loss was unrealized gains (losses) on marketable securities.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is calculated by dividing net loss by the weighted average shares outstanding during the period. Diluted net income (loss) per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. All common stock equivalents have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented.

3. MARKETABLE SECURITIES

During the years ended December 31, 2022 and 2021, the Company sold marketable securities worth $15.9 million and $5.9 million, respectively. For the year ended December 31, 2022, the Company recognized realized losses on the sale of those securities of less than $0.1 million, and reclassified amounts out of accumulated other comprehensive loss during the periods. As a result, as of December 31, 2022, the Company did not hold any marketable securities.

As of December 31, 2021, marketable securities by security type consisted of the following (in thousands):

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate obligations	$ 31,526	$ —	$ (52)	$ 31,474

The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2021, the balance in accumulated other comprehensive loss was comprised solely of activity related to marketable securities.

The aggregate fair value of marketable securities by contractual maturity were as follows (in thousands):

Contractual Maturities	December 31, 2021
Mature in one year or less	$ 28,220
Mature in two years or less	3,254
Total	$ 31,474

4. FAIR VALUE MEASUREMENTS

The following tables present the Company's assets that are measured at fair value on a recurring basis and indicate the level within the fair value hierarchy (in thousands):

	Fair value measurements at December 31, 2022 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 14,649	$ —	$ —	$ 14,649
Total	$ 14,649	$ —	$ —	$ 14,649

	Fair value measurements at December 31, 2021 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents				
Money market funds	$ 23,021	$ —	$ —	$ 23,021
Marketable securities:				
Corporate obligations	—	31,474	—	31,474
Total	$ 23,021	$ 31,474	$ —	$ 54,495

As of December 31, 2022 and 2021, the Company's cash equivalents were invested in money market funds and were valued based on Level 1 inputs. The Company's marketable securities consist of corporate obligations which are adjusted to fair value at each balance sheet date, based on quoted prices, which are considered Level 2 inputs. During the years ended December 31, 2022 and 2021, there were no transfers between Level 1, Level 2 and Level 3.

5. PROPERTY AND EQUIPMENT

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

	December 31,	
	2022	2021
Laboratory equipment	$ 3,506	$ 3,426
Leasehold improvements	564	564
Office and computer equipment	303	148
Furniture and fixtures	122	122
Property and equipment, gross	4,495	4,260
Less: accumulated depreciation and amortization	(3,802)	(3,390)
Property and equipment, net	$ 693	$ 870

Depreciation and amortization expense for the years ended December 31, 2022 and 2021 was $0.4 million and $0.3 million, respectively. The Company disposed of lab equipment during the year ended December 31, 2021 totaling $0.3 million.

The Company recognized an impairment charge of $0.2 million during the year ended December 31, 2022 primarily related to the return of leased laboratory equipment to the lessor in January 2023 (Note 14).

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

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

	December 31,	
	2022	2021
Accrued employee compensation and benefits	$ 808	$ 3,005
Accrued external research and development expenses	4,791	2,000
Accrued professional fees	824	601
Accrued employee termination benefits	1,221	—
Other	205	243
Total accrued expenses and other current liabilities	$ 7,849	$ 5,849

7. DEBT

Debt consisted of the following (in thousands):

	December 31,	
	2022	2021
Principal amount of long-term debt	$ —	$ 26,000
Debt discount	$ —	(196)
Deferred financing fees	$ —	(734)
Long-term debt, net of discount	$ —	$ 25,070

In September 2021, the Company entered into a loan and security agreement with SLR Investment Corp., formerly known as Solar Capital Ltd., ("SLR") for term loans in an aggregate principal amount of $26.0 million. The loan and security agreement replaced the prior loan and security agreement between the Company and SLR.

The term loans under the loan and security agreement accrued interest at an annual rate equal to 8.60% plus the greater of (a) the thirty (30) day U.S. Dollar LIBOR rate and (b) 0.10%, payable monthly in arrears. The monthly principal payments of $0.6 million were to be paid over a period of 45 months with a final maturity date of September 1, 2026. The interest only period would be extended provided the Company satisfied certain equity related conditions. The term loans were also subject to a prepayment fee of 3.00% if prepayment occurred within the first year subsequent to September 2, 2021, 2.00% in the second year and 1.00% in the third year through final maturity.

The loan and security agreement also contained certain financial covenants, including an unrestricted minimum cash level until certain clinical trial study data conditions are met. As security for its obligations under the loan and security agreement, the Company granted SLR a first priority perfected security interest in all of the Company’s existing and after-acquired assets, including intellectual property.

In September 2022, the Company paid SLR approximately $6.4 million, including principal, accrued interest, fees and costs. In October 2022, the Company satisfied an equity related condition under the loan and security agreement that extended the date on which repayment of principal commences from January 2023 to July 2023. On December 15, 2022, the Company entered into a payoff letter with SLR, under which the Company voluntarily accelerated the debt and paid SLR approximately $21.0 million, in full satisfaction of all obligations, including all outstanding principal, accrued interest, fees, costs, expenses and other amounts chargeable, under the loan and security agreement. The Company recognized an extinguishment loss of $1.5 million in the year ended December 31, 2022 representing the difference between the reacquisition price and its net carrying amount.

The payoff letter also provided for the termination of all commitments and obligations under the loan and security agreement and release of all liens held by SLR on the Company’s assets.

8. CONVERTIBLE NOTES

On September 20, 2022, the Company received $6.0 million from existing investor Flagship Pioneering through the issuance of convertible notes. The convertible notes mature one year from the date of issuance and bear interest at the rate of 8.00% per annum payable upon the earlier of (i) voluntary conversion of the notes in accordance with the terms therein and (ii) the maturity date. Upon a change of control, the convertible notes and all accrued and unpaid interest shall be due and payable in full. All principal and accrued interest under the convertible notes will automatically convert at the Company's next equity financing at a conversion price equal to the lower of: (a) the closing price of the common stock on the conversion date; or (b) the average closing price of the common stock for the five trading days immediately preceding the conversion date. The convertible notes are subordinate and junior in right of payment to the senior secured debt issued pursuant to the New Loan and Security Agreement with SLR Investment Corp.

The Company determined that the convertible notes contain cash redemption features and share settled put options which do not result in a variable repayment amount, therefore these features do not require bifurcation from the notes. The Company allocated the full proceeds to the convertible notes.

As discussed in Note 1, in October 2022, the Company secured $28.1 million in net proceeds after deducting estimated offering expenses through a registered direct offering of common stock. As part of the registered direct offering, the $6.0 million convertible notes held by funds associated with Flagship Pioneering were automatically converted into the Company's common stock. In total, the Company sold 20,847,888 shares of common stock at a purchase price of 1.64 per share.

The Company recognized an extinguishment loss of $0.1 million in the year ended December 31, 2022 representing legal fees related to the conversion of the notes into common stock.

9. STOCKHOLDERS' EQUITY

2019 Stock Option and Incentive Plan

The 2019 Stock Option and Incentive Plan (the "2019 Plan") was approved by the Company's board of directors on April 29, 2019. 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. Awards under the 2019 plan generally vest ratably over the vesting period (3-4 years) and have a maximum term of 10 years. The number of shares initially reserved for issuance under the 2019 Plan is 905,000, which was increased on January 1, 2020 and will be increased 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 2,317,471 as of December 31, 2022.

2019 Employee Stock Purchase Plan

The 2019 Employee Stock Purchase Plan (the "2019 ESPP") was approved by the Company's board of directors on April 29, 2019. A total of 237,181 shares of common stock were initially reserved for issuance under this plan, which was cumulatively increased on January 1, 2020 and will be increased 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 number of shares available for future grant was 698,005 as of December 31, 2022. The Company recorded $0.1 million of stock-based compensation expense during the years ended December 31, 2022 and 2021.

In connection with all share-based payment awards, total stock-based compensation expense recognized was as follows (in thousands):

	December 31,	
	2022	2021
Research and development	$ 1,484	$ 1,839
General and administrative	2,099	4,404
Total stock-based compensation expense	$ 3,583	$ 6,243

Fair Value of Stock Option Awards

The fair value of stock option awards was estimated using the Black-Scholes option-pricing model. The expected term of these awards was determined using the simplified method, which uses the midpoint between the vesting date and the contractual term. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the stock awards. The expected dividend was zero as the Company had not paid any dividends on its common stock. Finally, as the Company does not have long-term trading history of its common stock, the expected volatility was derived from the average historical stock volatilities of several public companies within the industry that the Company considers to be comparable to the Company's business over a period equivalent to the expected term of the stock-based awards.

The Black-Scholes option pricing model assumptions are included in the table below.

	Year Ending December 31,	
	2022	2021
Risk-free interest rate	2.17 %	0.91 %
Expected option life (in years)	6.06	5.98
Expected dividend yield	— %	— %
Expected volatility	92 %	96 %

The following table summarizes the Company’s stock option activity for the year ended December 31, 2022:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Life (in Years)	Intrinsic Value (in thousands)
Outstanding as of January 1, 2022	6,197,288	$ 5.72		
Granted	2,401,197	1.81		
Exercised	(8,499)	0.72		
Cancelled	(2,053,009)	3.30		
Outstanding as of December 31, 2022	6,536,977	$ 5.05	5.55	$ —
Exercisable as of December 31, 2022	4,496,708	$ 6.00	4.69	$ —
Vested or expected to vest as of December 31, 2022	6,302,190	$ 4.99	5.53	$ —

The intrinsic value of options exercised during the year ended December 31, 2022 was nominal. The intrinsic value of options exercised during the year ended December 31, 2021 was $0.4 million.

The weighted-average grant date fair value of the options granted during the years ended December 31, 2022 and 2021, was $1.09 and $3.87 per share, respectively.

As of December 31, 2022, there was $3.3 million of unrecognized compensation expense related to unvested stock options that is expected to be recognized over a weighted-average period of approximately 2.1 years.

Restricted Stock Units

The fair values of restricted stock units are based on the market value of the Company's common stock on the date of grant. The following table summarizes the Company's restricted stock unit activity for the year ended December 31, 2022:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Outstanding as of January 1, 2022	275,350	$ 4.15
Granted	48,278	1.70
Vested	(142,095)	3.59
Forfeited	(106,300)	3.16
Outstanding as of December 31, 2022	75,233	$ 5.04

As of December 31, 2022, there was $0.2 million of unrecognized compensation expense related to unvested stock options that is expected to be recognized over a weighted-average period of approximately 1.2 years.

10. 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, 2022 and 2021 are as follows:

	December 31,	
	2022	2021
U.S. federal statutory income tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	5.7 %	6.0 %
Permanent differences	(0.1)%	— %
Stock compensation	(0.6)%	(2.2)%
Tax credits	2.9 %	3.1 %
Other	— %	— %
Change in valuation allowance	(28.9)%	(27.9)%
Effective income tax rate	— %	— %

Significant components of the Company's deferred tax asset at December 31, 2022 and 2021 are as follows (in thousands):

	December 31,	
	2022	2021
Net operating loss carryforwards	$ 89,259	$ 82,070
Research and development tax credit carryforwards	13,127	10,892
Start-up costs	14	21
Capitalized research and development costs	13,392	—
Operating lease liabilities	577	—
Depreciation	237	213
Accrued expenses	212	822
Stock-based compensation	3,688	3,316
Other items	1,619	1,366
Total deferred tax assets	122,125	98,700
Valuation allowance	(122,125)	(98,700)
Net deferred tax asset	$ —	$ —

In assessing the realizability of deferred tax assets, the Company considers all relevant positive and negative evidence in determining whether it is more likely than not that some portion or all deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent on several factors, including the generation of sufficient taxable income prior to the expiration of the net operating loss carryforwards. The Company believes it is more likely than not that the results of future operations will not generate sufficient taxable income to realize the full benefits of its deferred tax assets. As such, there is a full valuation allowance against the net deferred tax assets as of December 31, 2022 and 2021. The valuation allowance increased in 2022 by $23.4 million, primarily as a result of net operating losses generated during the period.

As of December 31, 2022, the Company had federal and state net operating loss carryforwards of $329.2 million and $318.3 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, 2019, 2020, 2021 and 2022 can be carried forward indefinitely. As of December 31, 2022, the Company had federal and state research and development tax credit carryforwards of $10.6 million and $3.2 million, respectively. These amounts expire at various dates through 2042. 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. In 2022, the valuation allowance increased by $23.4 million which was primarily driven by the current period net operating loss.

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, 2022, the Company had not yet completed an analysis of whether its net operating loss and research and development credit carryforwards may be limited.

At December 31, 2022 and 2021, the Company had no unrecognized tax benefits. As of December 31, 2022 and 2021, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

For years through December 31, 2022, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company’s research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company’s research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

The Company files income tax returns in the U.S. Federal, California, Massachusetts, New Jersey, New York, and Pennsylvania 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 2019, although carryforward attributes that were generated prior to tax year 2019 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.

11. COMMITMENTS AND CONTINGENCIES

Leases

The Company leases a facility containing 19,200 square feet of laboratory and office space in Cambridge, Massachusetts. The lease expires in April 2024, subject to an option to extend the lease for an additional three years. The lease agreement and most recent amendment contained escalating rent payments.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the year ended December 31, 2022 (in thousands, except weighted average figures):

Operating leases	Year Ended December 31, 2022
Lease cost	
Operating lease cost	$ 1,489
Variable lease cost	711
Total lease cost	$ 2,200
Other information	
Operating cash flows used for operating leases	$ 2,383
Weighted average remaining lease term (years)	1.3
Weighted average discount rate (percentage)	9.0 %

For the year ended December 31, 2022, the Company incurred $2.2 million and in operating lease expense, and made lease payments of $2.4 million, with such amounts reflected in the consolidated statements of cash flows in operating activities.

As the result of adopting ASU 2016-02 using the modified retrospective transition method, the Company did not restate periods prior to the adoption date of January 1, 2022. These periods continue to be presented in accordance with ASC 840. Future minimum lease payments and lease liabilities as of December 31, 2022 were as follows (in thousands):

Maturity of lease liabilities	December 31, 2022
2023	$ 1,722
2024	580
Total future minimum lease payments	$ 2,302
Less: imputed interest	(141)
Total lease liability	$ 2,161
Reported as:	
Operating lease liability	$ 1,592
Operating lease liability, net of current portion	569
Total lease liability	$ 2,161

Other Commitments

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 non-cancelable 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.

12. 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,	
	2022	**2021**
Numerator:		
Net loss	$ (81,186)	$ (64,628)
Denominator:		
Weighted average common shares outstanding, basic and diluted	54,355,769	38,110,420
Net loss per share, basic and diluted	$ (1.49)	$ (1.70)

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

	December 31,	
	2022	**2021**
Options to purchase common stock	6,536,977	6,197,288
Unvested restricted stock units	75,233	275,350
Shares issuable under employee stock purchase plan	—	46,520
	6,612,210	6,519,158

13. 401(k) 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. The Company's matching contributions totaled $0.4 million and $0.3 million for the years ended December 31, 2022 and 2021, respectively.

14. RESTRUCTURING AND IMPAIRMENT CHARGES

The Company incurred approximately $4.2 million in restructuring and impairment charges in its consolidated statement of operations and comprehensive loss related to the corporate restructuring, including the reduction in force, as described in Note 1. The actions associated with the reduction in force were completed in December 2022.

The following table shows the restructuring and impairment charges as of December 31, 2022 (in thousands):

	Year Ended December 31, 2022
Employee termination benefits	$ 1,858
Impairment of operating lease right-of-use assets	2,116
Impairment of property and equipment	215
Total restructuring and impairment charges	$ 4,189

Employee Termination Benefits

Employees affected by the reduction in workforce obtained involuntary termination benefits that are provided pursuant to a one-time benefit arrangement. The affected employees have no requirements to provide future service, therefore the Company recognized the liability for the termination benefits in full at fair value in the current period.

The following table shows the liability related to employee termination benefits as of December 31, 2022 (in thousands):

	Employee Termination Benefits
Accrued employee termination benefits beginning balance	$ —
Employee termination benefits charges incurred during the period	1,858
Amounts paid or otherwise settled during the period	(637)
Accrued employee termination benefits as of December 31, 2022	$ 1,221

Impairment of Operating Lease Right-of-Use Asset

The Company leases laboratory and office space in Cambridge, Massachusetts, under a lease agreement that expires on April 30, 2024.

On January 1, 2022, the Company adopted ASC 842 and recorded a right-of-use asset of $3.3 million and a lease liability of $3.6 million. The standard did not have a material impact on the statement of operations or statement of cash flows. Additionally, there is no tax impact from the adoption as the net increase in deferred tax assets is fully offset with an increase to the valuation allowance.

In December 2022, the Company initiated activities to vacate its corporate offices in Cambridge, Massachusetts, and the activities were completed in January 2023. As a result, the Company performed a recoverability test by comparing the future cash flows attributable to the asset group to the carrying value of the corresponding long-lived, right-of-use asset. Based on this evaluation, the Company determined that the long-lived asset with a carrying value of $2.1 million was no longer recoverable and recorded a right-of-use asset impairment of $2.1 million.

The impairment was determined by comparing the fair value of the impacted asset group to their carrying value as of the impairment measurement date, as required under ASC 360, Property, Plant, and Equipment. The impairment is presented in restructuring and impairment charges on the consolidated statements of operations and comprehensive loss.

The following table shows the asset and liability as of December 31, 2022 (in thousands):

	December 31, 2022
Assets	
Operating lease right-of-use asset	$ —
Liabilities	
Operating lease liabilities (current)	$ 1,592
Operating lease liabilities (noncurrent)	569
Total lease liabilities	$ 2,161

Impairment of Property and Equipment

The Company recognized an impairment charge of $0.2 million during the year ended December 31, 2022 primarily related to the return of leased laboratory equipment to the lessor in January 2023. The Company measured the long-lived asset impairment as the amount by which the carrying value of the asset group exceeds its fair value. The impairment is presented in restructuring and impairment charges on the consolidated statements of operations and comprehensive loss.

15. RELATED-PARTY TRANSACTIONS

In September 2022, the Company issued convertible notes in an aggregate principal amount of $6.0 million to existing investor Flagship Pioneering. Refer to Note 8, Convertible Notes, for further discussion. As discussed in Note 1, in October 2022, the Company sold shares of common stock through a registered direct offering. As part of the registered direct offering, $6.0 million in convertible notes held by funds associated with Flagship Pioneering were converted into common stock.

16. SUBSEQUENT EVENTS

In January 2023, the Company sold its non-leased laboratory equipment for $0.5 million in cash and recorded a gain of $0.1 million representing the difference between the carrying amount and the cash proceeds.

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

None.

Item 9A. Controls and Procedures

Management's Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer ("CEO") and Principal Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of an issuer that are designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

In December 2022, we announced a corporate restructuring whereby we significantly reduced the size of the accounting and financial reporting resources, resulting in diminished segregation of duties. As a result, our management identified material weaknesses in our internal controls over financial reporting as of December 31, 2022. Due to the material weaknesses identified, the CEO and Principal Financial Officer concluded that the disclosure controls were not effective, to provide reasonable assurance that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is accumulated and communicated to management, including the CEO and Principal Financial Officer, as appropriate, to allow timely decisions regarding required disclosure and were not effective to provide reasonable assurance that such information is recorded, processed, summarized and reported within the time periods specified by the SEC's rules and forms.

The material weaknesses we identified were (i) we did not maintain an effective control environment as we did not maintain a sufficient complement of accounting and financial reporting resources commensurate with our financial reporting requirements, (ii) we did not maintain an effective risk assessment process, whereby our risk assessment was not updated for the changes resulting from the restructuring in December 2022, (iii) we did not maintain appropriate control activities to support the appropriate segregation of duties over the review of account reconciliations and manual journal entries, and (iv) we did not document, thoroughly communicate and monitor controls processes. These material weaknesses could result in a misstatement of account balances or disclosures that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected. Had we performed an evaluation of our internal control over financial reporting in accordance with Section 404, additional control deficiencies may have been identified by management, and those control deficiencies could have also represented one or more material weaknesses.

Remediation Plan

Material weaknesses (as defined under the Exchange Act and by the auditing standards of the U.S. Public Company Accounting Oversight Board, or "PCAOB"), were identified in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual financial statements will not be prevented or detected on a timely basis.

We are committed and are taking steps necessary to remediate the control deficiencies that constituted the above material weaknesses by making enhancements to our control environment in 2023, including the following:

- Define user roles within our systems and processes to ensure proper segregation of duties within our financial reporting procedures;

- Engage internal control consultants to assist us in performing a financial reporting risk assessment as well as identifying and designing our system of internal controls necessary to mitigate the risks identified.

Changes in Internal Control over Financial Reporting

As a result of the corporate restructuring, effective December 15, 2022, the size of the accounting and finance function was significantly reduced, not allowing for an appropriate level of segregation of duties over the financial reporting process. Consequently, a change in our internal controls over financial reporting (as defined in Rule 13a-15(f) and 15(d)-15(f) of the Exchange Act) occurred during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

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

Attestation Report of the Registered Public Accounting Firm

This report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting.

Item 9b. Other Information

None.

Item 9c. Disclosures Regarding Foreign Jurisdictions that Prevent Inspections

Not Applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

Executive Officers and Directors

Our executive officers, directors and other key personnel and their respective ages and positions as of March 31, 2023:

Name	Age	Position(s)
Executive Officers		
William R. Hinshaw, Jr.	54	Director, Chief Executive Officer
Paul Fehlner, J.D., Ph.D.	59	Senior Vice President, Chief Legal Officer and Corporate Secretary
Margaret James Koziel, M.D.	63	Senior Vice President and Chief Medical Officer
Non-Employee Directors		
Martin Hendrix, Ph.D.	55	Director
Catherine Angell Sohn, Pharm.D.	70	Director
William D. “Chip” Baird	51	Director
Gary P. Pisano, Ph.D.	61	Director
Cristina M. Rondinone, Ph.D.	62	Director
Paul J. Sekhri	64	Director
Michael Rosenblatt, M.D.	75	Director
Robert Rosiello	65	Director, Chairman
Torben Straight Nissen, Ph.D.	51	Director

The following is a biographical summary of the experience of our executive officers and directors. There are no family relationships among any of our executive officers or directors.

Executive Officers

William R. Hinshaw, Jr. has served as our President and Chief Executive Officer and as a member of our board of directors since June 2018. Prior to joining us, Mr. Hinshaw served in increasing roles of responsibility at Novartis Pharmaceuticals Corporation, a pharmaceutical company, from December 2003 until November 2017, most recently as the Executive Vice President and Head of U.S. Oncology. Mr. Hinshaw holds a B.S. in molecular biology from the University of Wisconsin. We believe that Mr. Hinshaw’s qualifications, attributes and skills, including his experience in operations management and executive leadership, qualify him to serve on our board of directors.

Paul Fehlner, J.D., Ph.D. has served as our Senior Vice President, Chief Legal Officer and Corporate Secretary since September 2020 and previously served as our Senior Vice President and Chief Intellectual Property Officer from April 2018 to September 2020. In addition, Dr. Fehlner has served as a Principal at Life Sciences Innovation LLC, a consulting firm that he founded, since December 2017. From November 2008 through November 2017, Dr. Fehlner served as Global Head of Intellectual Property at Novartis Pharma AG in Basel, Switzerland. Prior to joining Novartis, Dr. Fehlner practiced IP law in leading firms in the U.S. along with working in-house at Rhone-Poulenc Rorer. Dr. Fehlner holds a J.D. from Fordham University School of Law, a Ph.D. in immunology and biochemistry from The Rockefeller University and a B.S. in chemistry from Haverford College.

Margaret James Koziel, M.D. has served as our Senior Vice President and Chief Medical Officer since December 2021 and previously served as our Vice President, Clinical Development from June 2019 to December 2021. Prior to joining Axcella, Dr. Koziel held positions of increasing responsibility at Kaleido Biosciences, Inc., Vertex Pharmaceuticals, Inc., and the Novartis Institute for BioMedical Research (NIBR), working across the full spectrum of clinical development, from target selection through Phase 4 trials. Dr. Koziel also previously served as a Professor and Assistant Vice Provost for Clinical Research at the University of Massachusetts Medical School, staff physician at the Beth Israel Deaconess Medical Center and Associate Professor of Medicine at Harvard Medical School. She obtained her B.A. and M.D. from Dartmouth and her postgraduate medical training at New England Deaconess Hospital and Massachusetts General Hospital, affiliates of Harvard Medical School.

The principal occupation and employment during the past five years of each of our executive officers was carried on, in each case except as specifically identified above, with a corporation or organization that is not a parent, subsidiary or other affiliate of us. There is no arrangement or understanding between any of our executive officers and any other person or persons pursuant to which he or she was or is to be selected as an executive officer.

There are no material legal proceedings to which any of our executive officers is a party adverse to us or our subsidiaries or in which any such person has a material interest adverse to us or our subsidiaries.

Directors

William R. Hinshaw, Jr., biographical information for Mr. Hinshaw, our Chief Executive Officer, is set forth under the heading "Executive Officers" above.

Martin Hendrix, Ph.D., has served as a member of our board of directors since May 2022. Dr. Hendrix joined Nestlé Health Science US in April 2012, and currently serves as its Head of Global Business Development and M&A. In this position, Dr. Hendrix oversees all deal flow of Nestlé Health Science and is also responsible for its venture capital partnerships and direct equity investments. Dr. Hendrix has represented Nestlé on the boards of Enterome, Microbiome Diagnostic Partners, Procise Dx, Bodymed AG, as well as board observer roles for Evelo, Kaleido and Senda. Prior to joining Nestlé, from January 1998 to March 2012, Dr. Hendrix was a research chemist and subsequently a member of the Strategic Planning Group, as well as a Senior Director of Business Strategy at Bayer AG. Dr. Hendrix currently serves on the board of directors of Procise Dx, Bodymed AG, Prometheus Biosciences Inc., and Senda (observer). Dr. Hendrix holds a Ph.D. in Chemistry from The Scripps Research Institute, an M.S. in Chemistry from the Georgia Institute of Technology. We believe that Dr. Hendrix's extensive technical and business experience qualifies him to serve on our board of directors.

Catherine Angell Sohn, Pharm.D., has served as a member of our board of directors since August 2019. Dr. Sohn has over 30 years of biopharmaceutical leadership and operational experience at GlaxoSmithKline and currently serves on the boards of directors of Jazz Pharmaceuticals plc (Nasdaq: JAZZ), Maze Therapeutics (private) and BioEclipse Therapeutics (private). Dr. Sohn is also Adjunct Professor at UCSF, her alma mater. Since January 2011, as President of Sohn Health Strategies, Dr. Sohn has advised CEOs and Boards of life science companies on strategy, strategic product development, partnering/M&A, commercialization of new medicines and vaccines. Dr. Sohn was formerly senior vice president, worldwide business development, and a member of the global executive committee at GlaxoSmithKline's Consumer Healthcare division where she led U.S. and global transactions. Previously she was vice president worldwide strategic product development for the cardiovascular, metabolic and pulmonary therapeutic areas at SmithKline Beecham Pharmaceuticals where along with the senior vice president of R&D, she was responsible for decisions to move assets into phase 1, strategic product development and portfolio prioritization, and where she had global responsibility for commercial strategy and global commercialization, including overseeing the global launch of Coreg for congestive heart failure which became a $1 billion indication. Earlier in her career, as an entrepreneur within a large company, she started the U.S. Vaccine Business, built the team, and led the launch of SB's first vaccine in the U.S. and helped shape the global vaccine portfolio pipeline as a member of the International Vaccine Steering Committee. Subsequently, she led the U.S. commercialization of the company's largest neuroscience product which grew to >$1 billion in sales and as a member of the Global CNS Therapeutic Area Steering Team, led the focus to expand development into anxiety disorders. Dr. Sohn earned a Doctor of Pharmacy degree from the University of California, San Francisco, a Corporate Directors Certificate from Harvard Business School, a Certificate of Professional Development from Wharton, a Certificate from Berkeley Law for ESG: Navigating the Board's Role and is a Certified Licensing Professional Emeritus. We believe that Dr. Sohn's extensive experience with product development, strategic marketing, and business development transactions in the pharmaceutical industry qualifies her to serve on our board of directors.

William D. "Chip" Baird has served as a member of our board of directors since June 2018. Mr. Baird became Chief Financial Officer of 2seventy bio, Inc. when that company spun out of bluebird bio, Inc. He joined bluebird as Chief Financial Officer in February 2019 and previously served as Chief Financial Officer of Amicus Therapeutics, Inc., a pharmaceutical company, from April 2012 to December 2018. Mr. Baird holds an M.B.A. in finance from The Wharton School of the University of Pennsylvania and a B.S.F.S. in international affairs from the Edmund A. Walsh School of Foreign Service of Georgetown University. We believe Mr. Baird's broad experience in pharmaceutical finance and executive management roles qualifies him to serve on our board of directors.

Gary P. Pisano, Ph.D., has served as a member of our board of directors since October 2011. Dr. Pisano is the Harry E. Figgie, Jr. Professor of Business Administration and Senior Associate Dean for Promotions and Tenure at the Harvard Business School. He has served on the Harvard faculty since 1988. Dr. Pisano's research and teaching focus on technology and operations strategy, the management of innovation and intellectual property, and competitive strategy. For more than two decades, he has consulted extensively on these issues with companies in the pharmaceutical, biotechnology, medical device, specialty chemical and healthcare industries. He has previously served as a director of Axovant Sciences Ltd. (Nasdaq: AXON) and Patheon NV (NYSE: PTHN). Dr. Pisano holds a Ph.D. in business administration from the University of California, Berkeley and a B.A. in economics from Yale University. We believe that Dr. Pisano's knowledge of business administration, innovation, and strategy, particularly within the healthcare industry, qualifies him to serve on our board of directors.

Cristina M. Rondinone, Ph.D., has served as a member of our board since June 2018. Since June of 2020, Dr. Rondinone has consulted for pharmaceutical and biotechnology companies at CMR Pharma Consulting and in 2022 became Founder and CEO of a new startup company in stealth mode. Dr. Rondinone served as President of Cellarity Inc. from September 2019 to June 2020. Prior to this position, from March 2011 to September 2019, Dr. Rondinone served in roles of increasing responsibility at MedImmune, LLC, a wholly owned subsidiary of AstraZeneca, most recently as Senior Vice President R&D, Head of Cardiovascular, Renal and Metabolic Diseases Innovative Medicines and Early Development. Dr. Rondinone served in different roles in research and development at Hoffmann-La Roche (2005-2011) and Abbott Laboratories (1998-2005). Dr. Rondinone holds a Docent in molecular medicine from the University of Goteborg, Sweden School of Medicine and a M.Sc. and Ph.D. in biological sciences from the University of Buenos Aires. We believe that Dr. Rondinone's extensive biopharmaceutical research and development experience qualifies her to serve on our board of directors.

Paul J. Sekhri has served as a member of our board of directors since May 2022. Mr. Sekhri is a Director of Longboard Pharmaceuticals, Inc., Ipsen S.A., Compugen Ltd., Pharming N.V., where he is Chairman, Oryn Therapeutics, and Veeva Systems. He most recently served as the chief executive officer of eGenesis where he is now a member of the Board and a Senior Advisor to the Chairman. Before eGenesis, Mr. Sekhri served as president and chief executive officer of Lycera Corp. Prior to Lycera, Mr. Sekhri served as Senior Vice President, Integrated Care at Sanofi. Prior to Sanofi, he served as group executive vice president, global business development, and chief strategy officer for Teva Pharmaceuticals Industries, Ltd., and earlier, operating partner and head of the Biotechnology Operating Group at TPG Biotech. Previously, Mr. Sekhri founded Cerimon Pharmaceuticals where he served as president and chief executive officer. Prior to founding Cerimon, he was president and chief business officer of ARIAD Pharmaceuticals. Earlier in his career, Mr. Sekhri held various senior positions at Novartis AG, including senior vice president, head of global search and evaluation, business development and licensing, and global head, early commercial development. Mr. Sekhri completed graduate work in neuroscience at the University of Maryland School of Medicine in Baltimore and received his B.S. in zoology from the University of Maryland, College Park. We believe that Mr. Sekhri's extensive business and financial experience qualifies him to serve on our board of directors.

Michael Rosenblatt, M.D. has served as a member of our board of directors since May 2022. Dr. Rosenblatt has held major leadership roles in academia and the biopharmaceutical industry. He is a Senior Partner and former Chief Medical Officer at Flagship Pioneering. He is the former Chief Medical Officer of Merck. Prior to that he was Dean of Tufts University School of Medicine. Before that, he held the Robert Ebert Professorship in Molecular Medicine and then the George R. Minot Professorship of Medicine at Harvard Medical School (HMS). He served as the President of Beth Israel Deaconess Medical Center (BIDMC). Previously, he was the Harvard Faculty Dean and Senior Vice President for Academic Programs at BIDMC. Dr. Rosenblatt has also served as Director of the Harvard-MIT Division of Health Sciences and Technology. From 1981 to 1984, he served as Chief of the Endocrine Unit, Massachusetts General Hospital. He is a founder of ProScript and Radius Pharmaceuticals. He was a member of the Board of Scientific Counselors of the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH. He has been elected to the presidency of the American Society of Bone and Mineral Research, to the American Society of Clinical Investigation, the Association of American Physicians, and to Fellowship in the American Association for the Advancement of Science and the American College of Physicians. He received his undergraduate degree summa cum laude from Columbia and his M.D. magna cum laude from Harvard. His internship, residency, and endocrinology training were all at the Massachusetts General Hospital. We believe that Dr. Rosenblatts's extensive drug development and medical experience qualifies him to serve on our board of directors.

Robert Rosiello has served as a member of our board of directors since October 2022. Mr. Rosiello is an Executive Partner at Flagship Pioneering, which he joined in 2018 and where he focuses on building capability to help originate, manage, and grow new Flagship companies. He also works with senior leadership to drive Flagship's strategy, institution building, and growth initiatives. From September 1984 to June 2015, Mr. Rosiello worked at McKinsey & Company advising CEOs and boards of leading health care, technology, and consumer companies. He served as a senior partner for 18 years and was a member of McKinsey's Senior Partner Review and Compensation Committees. Mr. Rosiello led the work that shifted McKinsey's recruiting toward non-MBAs and developed innovative leadership training for McKinsey's senior partners. He also led significant pro bono work for Save the Children, Americares, Carnegie Corporation, and Fairfield University. From July 2015 to August 2016, Mr. Rosiello was both Executive Vice President and Chief Financial Officer at Valeant Pharmaceuticals, where he led the finance, human resources, and IT functions. He led Valeant's financial restatement and regained timely reporting status with the SEC. He currently serves on the Board and Executive Committee of Catholic Charities of New York and the Central Selection Committee of the Morehead-Cain Foundation. He previously served on the Boards of the Pew Research Center and Inari Agriculture. Mr. Rosiello received his B.A. in economics from the University of North Carolina, where he was a Morehead Scholar and graduated Phi Beta Kappa, an M.Sc. in economics from the London School of Economics, and an M.B.A. from Harvard Business School. We believe that Mr. Rosiello's extensive business and financial experience qualifies him to serve on our board of directors.

Torben Straight Nissen, Ph.D., has served as a member of our board of directors since November 2022. Dr. Straight Nissen is an executive partner at Flagship Pioneering, which he joined in November 2016. Dr. Straight Nissen also serves as the interim CEO of Repertoire Immune Medicines. Dr. Straight Nissen served on the board of directors of Ring Therapeutics, Inc. from August 2018 to December 2021 and since March 2021 has served as founding chief executive officer of FL84 Inc. From November 2016 to July 2019, he served as president of Rubius Therapeutics (NASDAQ: RUBY); he also served on the board of directors of Rubius from November 2016 to August 2018. From July 2011 to November 2016 Dr. Straight Nissen held positions of increasing responsibility at Pfizer, with his last position as Vice President, heading up Pfizer's Worldwide R&D Strategic Portfolio Management. In this role, he oversaw Pfizer's portfolio spanning from discovery up to Phase 3 trials across multiple therapeutic areas, including oncology, inflammation and immunology, rare diseases, cardiovascular and metabolic disease, neuroscience, and vaccines. Previously, he was responsible for the portfolio, strategy and operations functions within Pfizer's BioTherapeutics Division and ensured efficient advancement of protein therapeutics, cell therapies, gene therapies and vaccines from discovery through development. He also served as chief operating officer for the Centers for Therapeutic Innovation, a pioneering R&D unit within Pfizer that drives product development partnerships with world-leading academic medical centers. As COO, Dr. Straight Nissen headed up that organization's portfolio management, business development, finance, and operations functions, and he was one of the key drivers behind establishing the unit. Prior to joining Pfizer, Dr. Straight Nissen served as chief operating officer at Ascendis Pharma (NASDAQ: ASND) from April 2008 to June 2011, advancing the company's portfolio of new, innovative prodrugs from discovery to clinical proof-of-concept. Earlier, Dr. Straight Nissen served in various leadership positions at Maxygen, a molecular evolution and advanced protein engineering company, including the role of managing director of R&D and senior vice president of global project management. He began his career at Novo Nordisk with a focus on protein engineering. Dr. Straight Nissen holds a Ph.D. in molecular biology and biochemical engineering from the Technical University of Denmark and Carlsberg Laboratories and a Master of Science degree in chemical engineering from the Technical University of Denmark. We believe that Dr. Straight Nissen's extensive business, financial, and scientific experience qualifies him to serve on our board of directors.

There are no family relationships between or among any of our directors or executive officers. The principal occupation and employment during the past five years of each of our directors was carried on, in each case except as specifically identified above, with a corporation or organization that is not a parent, subsidiary or other affiliate of us. There is no arrangement or understanding between any of our directors and any other person or persons pursuant to which he or she is to be selected as a director.

There are no material legal proceedings to which any of our directors is a party adverse to us or our subsidiaries or in which any such person has a material interest adverse to us or our subsidiaries.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers, and persons holding more than 10% of our common stock to report their initial ownership of the common stock and other equity securities and any changes in that ownership in reports that must be filed with the SEC. The SEC has designated specific deadlines for these reports, and we must identify in this Annual Report on Form 10-K those persons who did not file these reports when due.

Based solely on a review of reports furnished to us, or written representations from reporting persons, we believe all directors, executive officers, and 10% owners timely filed all reports regarding transactions in our securities required to be filed for 2022 by Section 16(a) under the Exchange Act, except that Mr. Epstein filed two late Forms 4 for the transactions that occurred on February 18, 2022 that was filed on February 23, 2022 and on May 19, 2022 that was filed on June 3, 2022, each due to an administrative error, and Mr. Sekhri filed one late Form 4 for the transaction that occurred on May 19, 2022 that was filed on May 25, 2022 due to an administrative error.

No Change in Nominating Procedure

There were no changes made during 2022 to the procedure by which our shareholders may recommend nominees to our board.

Audit Committee

William D. "Chip" Baird, Martin Hendrix, Ph.D., and Gary P. Pisano, Ph.D., serve on the audit committee, which is chaired by Mr. Baird. Our board of directors has determined that each member of the audit committee is "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable Nasdaq rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated Mr. Baird as an "audit committee financial expert," as defined under the applicable rules of the SEC. During the fiscal year ended December 31, 2022, the audit committee met four times. The report of the audit committee is included under "Report of the Audit Committee." The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions;

- reviewing quarterly earnings releases;
- reviewing and overseeing our ESG commitments with respect to risk assessment and management policies and activities, including financial controls, whistleblower policies, and compliance; and
- reviewing and overseeing our information security and technology risks, including cybersecurity and data protection programs and policies to manage those risks.

All audit and non-audit services, other than de minimis non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Oversight of Cybersecurity Matters. Our audit committee is responsible for the general oversight of our information security and technology risks, including our cybersecurity and data protection policies and programs. As part of our cybersecurity risk mitigation, we provide employees with annual cybersecurity training and we engage third parties to review our security controls and enhance our information and security team, including providing ongoing response and monitoring. We also have entered into a cybersecurity insurance policy. We have not experienced any material information security breaches within the last three years.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the corporate governance section of our website, which is located at https://ir.axcellatx.com/corporate-governance/documents-and-charters. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation

Our named executive officers, or NEOs, for the year ended December 31, 2022 who appear in the Summary Compensation table are:

- William R. Hinshaw, Jr., our chief executive officer;
- Paul Fehlner, J.D., Ph.D, our chief legal officer;
- Margaret James Koziel, M.D., our chief medical officer; and
- Robert Crane, our former chief financial officer.

2022 Summary Compensation Table

The following table presents the compensation awarded to, earned by or paid to each of our named executive officers for the years indicated.

Name and Principal Position	Year	Salary ($)	Stock Awards ($)	Option Awards ($)[1]	Non-Equity Incentive Plan Compensation ($)[2]	All Other Compensation ($)	Total ($)
William R. Hinshaw, Jr.	2022	571,875		435,679	291,741	8,061[4]	1,307,356
President and CEO	2021	546,250		1,913,241[3]	275,275	8,700[4]	2,743,466
Paul Fehlner, J.D., Ph.D	2022	398,491		86,215	150,769	8,700[4]	644,175
Chief Legal Officer							
Margaret James Koziel, M.D.	2022	415,000		41,133	157,389	7,380[4]	620,902
Senior Vice President and Chief Medical Officer							
Robert Crane[5]	2022	214,103		401,801	121,812	8,202[4]	745,918
Former Senior Vice President and Chief Financial Officer							

(1) The amounts reported represent the aggregate grant date fair value of stock options awarded to the named executive officers in 2022 and 2021, as applicable, calculated in accordance with FASB ASC Topic 718. Such grant date fair value does not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value are set forth in Note 9 to our audited consolidated financial statements in this Annual Report. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting or exercise of the applicable awards. The amount reported for Mr. Crane includes the grant date fair value of a performance-based option award assuming probable achievement. Assuming maximum achievement, the grant date fair value is $801,551.

(2) The amounts reported represent cash incentive compensation based on the board of directors' assessment of the achievement of company and individual performance objectives for the years ended December 31, 2022, and December 31, 2021, respectively. The cash incentive compensation for 2022 performance was paid in two installments, with the first installment paid in August 2022 and based on achievement of objectives for the first half of 2022, and the second installment paid in February 2023 and based on achievement of objectives for the second half of 2022. The cash incentive compensation for 2021 performance was paid in February 2022. The amount reported for Mr. Crane includes a one-time cash bonus of $75,000 paid in February 2022 and $46,812 cash incentive compensation paid in August 2022.

(3) In 2021, Mr. Hinshaw was granted a total of 375,000 time-based option awards.

(4) The amounts reported represent matching contributions under the Company's 401(k) plan.

(5) Robert Crane's employment terminated effective December 15, 2022. In connection with his termination, Mr. Crane forfeited 325,000 of performance-based option awards granted to him in 2022. On December 16, 2022, Mr. Crane entered into a consulting agreement, and, in addition to receiving cash compensation consideration in January 2023 under the arrangement, the vesting period for his service-based option awards was extended to February 24, 2023. Mr. Crane will forfeit an aggregate 568,750 option awards.

Narrative to Summary Compensation Table

Our board of directors and compensation committee review compensation annually for all employees, including our executives. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. We target a general competitive position, based on independent third-party benchmark analytics to inform the mix of compensation of base salary, bonus or long-term incentives.

Our compensation committee discharges our board of directors' responsibilities relating to compensation of our directors and executives, oversees our company's overall compensation structure, policies and programs, and reviews our processes and procedures for the consideration and determination of director and executive compensation. Our compensation committee typically reviews and approves grants and awards under equity-based plans for all service providers, including our executive officers. In addition, our compensation committee reviews and recommends to the board of directors for determination the corporate goals and objectives that may be relevant to the compensation of our chief executive officer, and evaluates our chief executive officer's performance, and recommends to the board of directors for determination our chief executive officer's equity and non-equity compensation. Our board of directors discusses the compensation committee's recommendations and ultimately approves the compensation of our executive officers without members of management present.

Annual base salary

Each named executive officer's base salary is a fixed component of annual compensation for performing specific duties and functions and has been established by our board of directors taking into account each individual's role, responsibilities, skills, and experience. Base salaries for our named executive officers are reviewed annually by our compensation committee, typically in connection with our annual performance review process, and adjusted from time to time, based on the recommendation of the compensation committee, to realign salaries with market levels after considering individual responsibilities, performance, and experience.

Cash bonus

Our annual bonus program is intended to reward our named executive officers for meeting objective or subjective performance goals for a fiscal year. From time to time, our board of directors or compensation committee may approve annual bonuses for our named executive officers based on individual performance, company performance, or as otherwise determined appropriate.

Name	Target Bonus (% of base salary)
William R. Hinshaw, Jr.	55
Paul Fehlner, J.D., Ph.D	40
Margaret James Koziel, M.D.	40
Robert Crane	40

Long-term equity incentives

Our equity grant program is intended to align the interests of our named executive officers with those of our stockholders and to motivate them to make important contributions to our performance. We granted awards to our named executive officers in 2022, as described in the "Outstanding Equity Awards at 2022 Fiscal Year End Table."

Outstanding Equity Awards at 2022 Fiscal Year End Table

The following table presents information regarding all outstanding equity awards held by each of our named executive officers on December 31, 2022.

	Option Awards					Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock that have not Vested (#)	Market Value of Shares or Units of Stock that have not Vested ($) [1]
William R. Hinshaw	939,028[2]	0[2]		6.21	6/21/2028		
President and CEO	57,000[3]	3,800[3]		13.83	3/22/2029		
	117,525[4]	39,175[4]		4.12	1/2/2030		
	164,063[5]	210,937[5]		6.59	2/8/2031		
	0[6]	275,000[6]		1.63	2/7/2032		
	0[6]	100,000[6]		5.00	2/7/2032		
Paul Fehlner, J.D., Ph.D	97,828[7]	0[7]		6.21	4/24/2028	42,500[10]	13,919[10]
Chief Legal Officer	13,500[8]	4,500[8]		3.40	12/18/2029		
	16,875[9]	13,125[9]		4.73	9/15/2030		
	37,188[5]	47,812[5]		6.59	2/8/2031		
	0[6]	70,000[6]		1.63	2/7/2032		
Margaret James Koziel, M.D.	18,200[11]	2,600[11]		9.31	6/27/2029	13,125[16]	4,298[16]
Senior Vice President and Chief Medical Officer	7,688[12]	2,562[12]		4.12	1/2/2030		
	5,500[13]	5,500[13]		5.04	11/10/2030		
	13,584[5]	17,466[5]		6.59	2/08/2031		
	3,750[14]	6,250[14]		4.11	6/25/2031		
	18,750[15]	56,250[15]		2.60	12/10/2031		
	0[6]	33,397[6]		1.63	2/7/2032		
Robert Crane	0[17]	200,000[17]		1.63	5/25/2023		
Former Senior Vice President and Chief Financial Officer	0[17]	125,000[17]		1.63	5/25/2023		

(1) Based on $0.33 per share, the last sale price of Axcella common stock on December 30, 2022.

(2) 25% of this option vested and became exercisable on May 31, 2019, and the remainder vested in 12 equal quarterly installments thereafter.

(3) This option was granted on March 22, 2019. Following the closing of our initial public offering on May 13, 2019, the vesting period for the stock option commenced subject to approval of performance criteria by the Board of Directors, which occurred on May 22, 2019. 25% of this option vested and became exercisable on March 1, 2020, and the remainder shall vest in 12 equal quarterly installments thereafter.

(4) 25% of this option vested and became exercisable on January 2, 2021, with the remainder to vest in 12 equal quarterly installments thereafter.

(5) 25% of this option vested and became exercisable on February 9, 2022, with the remainder vesting in 12 equal quarterly installments thereafter.

(6) 25% of this option shall vest and become exercisable on February 8, 2023, with the remainder vesting in 12 equal quarterly installments thereafter.

(7) 25% of this option vested and became exercisable on April 2, 2019, and the remainder vested in 12 equal quarterly installments thereafter.

(8) 25% of this option vested and became exercisable on December 18, 2020, and the remainder shall vest in 12 equal quarterly installments thereafter.

(9) 25% of this option vested and became exercisable on September 16, 2021, and the remainder shall vest in 12 equal quarterly installments thereafter.

(10) 1/3 of the restricted stock units vested on February 9, 2023 and the remaining 2/3 of the grant shall vest on February 9, 2024.

(11) 25% of the shares underlying this option vested and became exercisable on June 27, 2020, with the remainder vesting in 12 equal quarterly installments thereafter.

(12) 25% of the shares underlying this option vested and became exercisable on January 2, 2021, with the remainder vesting in 12 equal quarterly installments thereafter.

(13) 25% of the shares underlying this option vested and became exercisable on November 10, 2021, with the remainder vesting in 12 equal quarterly installments thereafter.

(14) 25% of the shares underlying this option vested and became exercisable on June 25, 2022, with the remainder vesting in 12 equal quarterly installments thereafter.

(15) 25% of this option vested and became exercisable on December 10, 2022, with the remainder vesting in 12 equal quarterly installments thereafter.

(16) 25% of the restricted stock units vested on August 31, 2021, with the remainder vesting in 12 equal quarterly installments thereafter.

(17) 25% of each option was scheduled to vest on February 8, 2023, with the remainder vesting in 12 equal quarterly installments thereafter. Mr. Crane was terminated effective December 15, 2022. His separation agreement provided for continued vesting during a consulting period, which ended on February 24, 2023. A total of 81,250 shares vested and became exercisable on February 8, 2023.

Employment arrangements with our named executive officers

William R. Hinshaw, Jr.

Under our Amended and Restated Employment Agreement with Mr. Hinshaw, dated December 20, 2018, or the Hinshaw Employment Agreement, he will continue to serve as our President and Chief Executive Officer on an at will basis. Mr. Hinshaw initially received a base salary of $500,000 per year, which is subject to periodic review and adjustment. Mr. Hinshaw is also eligible for an annual performance bonus targeted at 55% of his base salary and is eligible to participate in the employee benefit plans generally available to our employees, subject to the terms of those plans.

The Hinshaw Employment Agreement further provides that if Mr. Hinshaw's employment is terminated by us without Cause (as defined in the Hinshaw Employment Agreement) or Mr. Hinshaw resigns for Good Reason (as defined in the Hinshaw Employment Agreement), he will be entitled to receive: (i) base salary continuation for 12 months following termination, or the Hinshaw Severance Amount, and, (ii) if Mr. Hinshaw is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, 12 months of COBRA premiums for himself and his eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law). Payment of the Hinshaw Severance Amount shall immediately cease if Mr. Hinshaw breaches the terms of the Restrictive Covenants Agreement between him and us. In lieu of the severance payments and benefits set forth above, in the event Mr. Hinshaw's employment is terminated by us without Cause or he resigns for Good Reason, in either case within 12 months following a Change in Control (as defined in the Hinshaw Employment Agreement), he will be entitled to receive: (i) a lump sum cash amount equal to 1.5 times the sum of (A) his current base salary (or his base salary in effect prior to the Change in Control, if higher) plus (B) his target annual cash incentive compensation for the year of termination, (ii) if Mr. Hinshaw is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, 18 months of COBRA premiums for himself and his eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law), and (iii) notwithstanding anything to the contrary provided in the applicable award agreement, accelerated vesting of 100% of all time-based stock options and other stock-based awards subject to time-based vesting, or "Time-Based Equity Awards", held by Mr. Hinshaw.

On February 14, 2023, the severance provisions of the Hinshaw Employment Agreement were amended as described below under the heading "—Retention Agreements."

Margaret Koziel

Under our Employment Agreement with Dr. Koziel, dated December 1, 2021, or the Koziel Employment Agreement, Dr. Koziel was engaged to serve as our Senior Vice President and Chief Medical Officer an at will basis. Dr. Koziel initially received a base salary of $415,000 per year, which is subject to periodic review and adjustment. Dr. Koziel is also eligible for an annual performance bonus targeted at 40% of her base salary and is eligible to participate in the employee benefit plans generally available to our employees, subject to the terms of those plans.

The Koziel Employment Agreement further provides that if Dr. Koziel's employment is terminated by us without Cause (as defined in the Koziel Employment Agreement) or Dr. Koziel resigns for Good Reason (as defined in the Koziel Employment Agreement), she will be entitled to receive: (i) base salary continuation for nine months following termination, or the Koziel Severance Amount, and, (ii) if Dr. Koziel is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, nine months of COBRA premiums for herself and her eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law). Payment of the Koziel Severance Amount shall immediately cease if Dr. Koziel breaches the terms of the Restrictive Covenants Agreement between her and us. In lieu of the severance payments and benefits set forth above, in the event Dr. Koziel's employment is terminated by us without Cause or she resigns for Good Reason, in either case within 12 months following a Change in Control (as defined in the Koziel Employment Agreement), she will be entitled to receive: (i) a lump sum cash amount equal to one times the sum of (A) her current base salary (or her base salary in effect prior to the Change in Control, if higher) plus (B) her target annual cash incentive compensation for the year of termination, (ii) if Dr. Koziel is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, 12 months of COBRA premiums for herself and her eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law), and (iii) notwithstanding anything to the contrary provided in the applicable award agreement, accelerated vesting of 100% of all Time-Based Equity Awards held by Dr. Koziel.

On February 14, 2023, the severance provisions of the Koziel Employment Agreement were amended as described below under the heading "—Retention Agreements."

Paul Fehlner

Under our Amended and Restated Employment Agreement with Dr. Fehlner, dated December 20, 2018 and amended September 16, 2020, or the Fehlner Employment Agreement, Dr. Fehlner serves as our Chief Legal Officer and Corporate Secretary on an at will basis. Dr. Fehlner initially received a base salary of $370,000 per year, which is subject to periodic review and adjustment. Dr. Fehlner is also eligible for an annual performance bonus targeted at 40% of his base salary and is eligible to participate in the employee benefit plans generally available to our employees, subject to the terms of those plans.

The Fehlner Employment Agreement further provides that if Dr. Fehlner's employment is terminated by us without Cause (as defined in the Fehlner Employment Agreement) or Dr. Fehlner resigns for Good Reason (as defined in the Fehlner Employment Agreement), he will be entitled to receive: (i) base salary continuation for nine months following termination, or the Fehlner Severance Amount, and, (ii) if Dr. Fehlner is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, nine months of COBRA premiums for himself and his eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law). Payment of the Fehlner Severance Amount shall immediately cease if Mr. Fehlner breaches the terms of the Restrictive Covenants Agreement between him and us. In lieu of the severance payments and benefits set forth above, in the event Dr. Fehlner's employment is terminated by us without Cause or he resigns for Good Reason, in either case within 12 months following a Change in Control (as defined in the Fehlner Employment Agreement), he will be entitled to receive: (i) a lump sum cash amount equal to one times the sum of (A) his current base salary (or his base salary in effect prior to the Change in Control, if higher) plus (B) his target annual cash incentive compensation for the year of termination, (ii) if Dr. Fehlner is enrolled in our health care program immediately prior to the date of termination and properly elects to receive COBRA benefits, 12 months of COBRA premiums for himself and his eligible dependents at our normal rate of contribution for employees for coverage at the level in effect immediately prior to the date of termination (or a monthly cash payment in lieu thereof if we determine we cannot pay such amounts without potentially violating applicable law), and (iii) notwithstanding anything to the contrary provided in the applicable award agreement, accelerated vesting of 100% of all time-based stock options and other stock-based awards subject to Time-Based Equity Awards held by Dr. Fehlner.

On February 14, 2023, the severance provisions of the Fehlner Employment Agreement were amended as described below under the heading "—Retention Agreements."

Robert Crane

Under our Employment Agreement with Mr. Crane, dated January 24, 2022, or the Crane Employment Agreement, he was engaged to serve as our Chief Financial Officer on an at will basis. Mr. Crane initially received a base salary of $250,000 per year, which was subject to periodic review and adjustment. Mr. Crane was also eligible for an annual performance bonus targeted at 40% of his base salary and is eligible to participate in the employee benefit plans generally available to our employees, subject to the terms of those plans.

Retention Agreements

On February 14, 2023, we entered into retention agreements, or the Retention Agreements, with each of (i) Mr. Hinshaw, (ii) Dr. Koziel, and (iii) Dr. Fehlner to provide an incentive for their continued service with us subsequent to the restructuring event on December 14, 2022.

The Retention Agreements provide for retention bonuses of cash and equity in the event of certain actions by us as further described below. In connection with the retention bonuses provided under the Retention Agreements, each of Mr. Hinshaw, Dr. Koziel and Dr. Fehlner agreed to waive their rights to severance payments provided under their respective employment agreements in the event of a Terminations Without Cause or for Good Reason (as such terms are currently defined in their respective employment agreements).

The Company will pay $517,500 to Mr. Hinshaw in the event of (i) an affirmative decision by the board of directors that the Company will cease to do business, (ii) Mr. Hinshaw's Termination Without Cause or resignation for Good Reason (as such terms are currently defined in the Hinshaw Employment Agreement) or (iii) the board of directors approving a sale of the Company or a corporate transaction that allows the Company to continue its operations, with fifty percent of the total retention payment payable on June 30, 2023 and the remainder payable on September 30, 2023.

The Company will pay $280,125 to Dr. Koziel in the event of (i) an affirmative decision by the board of directors that the Company will cease to do business, (ii) Dr. Koziel's Termination Without Cause or resignation for Good Reason (as such terms are currently defined in the Koziel Employment Agreement) and (iii) the board of directors approving a sale of the Company or a corporate transaction that allows the Company to continue its operations, with fifty percent of the total retention payment payable on June 30, 2023 and the remainder payable on September 30, 2023.

The Company will pay $270,123 to Dr. Fehlner in the event of (i) an affirmative decision by the board of directors that the Company will cease to do business, (ii) Dr. Fehlner's Termination Without Cause or resignation for Good Reason (as such terms are currently defined in the Fehlner Employment Agreement) and (iii) the board of directors approving a sale of the Company or a corporate transaction that allows the Company to continue its operations, with fifty percent of the total retention payment payable on June 30, 2023 and the remainder payable on September 30, 2023.

In addition, the Company may, subject to review by the board of directors, offer a further equity incentive grant to each of Mr. Hinshaw, Dr. Koziel and Dr. Fehlner equal to 50% of such individual's 2023 target annual bonus to continue employment with the Company in the event of a transaction referenced in (iii) above of an appropriate scale and that allows the Company to continue its operations indefinitely. Such equity incentive would vest fifty percent (50%) on the date six (6) months after grant, with the remaining fifty percent (50%) vesting on the date twelve (12) months after grant, provided that such individual remains employed by the Company on each vesting day.

Other agreements

We have also entered into employee confidentiality, inventions, non-solicitation and non-competition agreements with each of our named executive officers. Under such agreements, each named executive officer has agreed (1) not to compete with us during his or her employment and for a period of one year after the termination of such employment, (2) not to solicit our employees during his or her employment and for a period of one year after the termination of such employment, (3) to protect our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his or her employment.

Additional Narrative Disclosure

401(k) Savings Plan. We maintain a 401(k)-retirement savings plan for the benefit of our employees, including our named executive officers, who satisfy certain eligibility requirements. Under the 401(k) plan, eligible employees may elect to defer a portion of their compensation, within the limits prescribed by Internal Revenue Code of 1986, as amended, (the "Code") on a pre-tax or after tax (Roth) basis through contributions to the 401(k) plan. We are permitted to make discretionary profit-sharing contributions to the 401(k) plan. In 2020 the Company began matching 50% of every employee's first 6% of contributions and the contributions will be 100% vested after 1 year of employment. The 401(k) plan is intended to qualify under Section 401(a) of the Code. As a tax qualified retirement plan, pre-tax contributions to the 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until distributed from the 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the 401(k) plan.

Health and Welfare Benefits. All of our full-time employees, including our named executive officers, are eligible to participate in our health and welfare plans, including medical and dental benefits, short-term and long-term disability insurance, and life insurance. We believe these perquisites are necessary and appropriate to provide a competitive compensation package to our named executive officers.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. Our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. In line with this philosophy, we do not provide guaranteed bonuses to the above NEOs, and the bonuses to the above NEOs are only awarded upon approval of the compensation committee (or in the case of our CEO, the board) based upon satisfactorily meeting goals set by the board of directors. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Rule 10b5-1 Sales Plans

Our policy governing transactions in our securities by directors, officers, and employees permits our officers, directors, and certain other persons to enter into trading plans complying with Rule 10b5-1 under the Exchange Act. Generally, under these trading plans, the individual relinquishes control over the transactions once the trading plan is put into place. Accordingly, sales under these plans may occur at any time, including possibly before, simultaneously with, or immediately after significant events involving our company.

2022 Director Compensation Table

The table below shows all compensation earned by each individual who served as non-employee member of our board of directors during 2022 for their services as directors in 2022, other than Mr. Hinshaw. Amounts paid to Mr. Hinshaw are presented below in the Summary Compensation Table.

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)[1]	Option Awards ($)[1][3]	Non-Equity Incentive Plan Compensation ($)	Nonqualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
Martin Hendrix, Ph.D	41,236		52,628				93,864
Catherine Angell Sohn, Pharm.D.	57,165		25,952				83,117
William D. “Chip” Baird	67,500		25,952				93,452
Gary P. Pisano, Ph.D.	47,500		25,952				73,452
Cristina M. Rondinone, Ph.D.	44,000		25,952				69,952
Paul Sekhri	33,832		52,628				86,460
Michael Rosenblatt	34,725		52,628			10,000[2]	97,353
Robert Rosiello	15,750[4]		29,680				45,430
Torben Straight Nissen	9,000[4]		29,680				38,680

(1) The amounts reported represent the aggregate grant date fair value of the stock options awarded to the non-employee directors in the fiscal year ended December 31, 2022, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in Note 9 to our audited Consolidated Financial Statements included in this Annual Report. The amounts reported in this column reflect the accounting cost for these stock options and stock awarded and do not correspond to the actual economic value actually received by the non-employee directors or that may be received by the non-employee directors upon the exercise of the stock options or any sale of the underlying shares of common stock.

(2) The amount reported represents $10,000 in cash payments made to Mr. Rosenblatt in consideration for services on the Scientific Advisory Board.

(3) As of December 31, 2022, each non-employee director held unexercised options to purchase the number of shares of the Company's common stock as set forth below:

	Option Awards[1]	
Name	**Exercisable (#)**	**Unexercisable (#)**
Martin Hendrix, Ph.D	6,667	33,333
Catherine Angell Sohn, Pharm.D.	53,000	20,000
William D. "Chip" Baird	93,031	20,000
Gary P. Pisano, Ph.D.	42,000	20,000
Cristina M. Rondinone, Ph.D.	88,144	20,000
Paul Sekhri	6,667	33,333
Michael Rosenblatt	19,898	33,333
Robert Rosiello	—	40,000
Torben Straight Nissen	—	40,000

(1) The amounts reported represent the aggregate number of unexercised options to purchase shares of the Company's common stock held by each non-employee director, including awards granted prior to the completion of the Company's IPO in May of 2019.

(4) The annual retainers earned by Mr. Rosiello and Dr. Straight Nissen were prorated based on the date they joined the board of directors.

Non-Employee Director Compensation

Under our director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of each committee receives a higher retainer for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment is prorated for any portion of such quarter that the director is not serving on our board of directors. The annual retainer paid to the chairman of the board is $70,000. The fees paid to non-employee directors, other than our chairman, for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Annual Retainer
Board of Directors:	
All non-employee members, except chairman	$ 40,000
Audit Committee:	
Members	$ 7,500
Chairman	$ 15,000
Compensation Committee:	
Members	$ 5,000
Chairman	$ 10,000
Nominating and Corporate Governance Committee:	
Members	$ 4,000
Chairman	$ 8,000

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of directors and committee meetings.

In addition, each new non-employee director elected to our board of directors will be granted an initial, one-time equity award of an option to purchase 40,000 shares of our common stock, which shall vest in equal quarterly installments during the 12 quarters following the grant date, subject to continued service as a director through such vesting date. On the date of each annual meeting of stockholders of Axcella, each non-employee director will receive an annual equity award of an option to purchase 20,000 shares of common stock, which shall vest on the earlier of the one-year anniversary of the grant date and Axcella's next annual meeting of stockholders, subject to continued service as a director through such vesting date.

This program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

The Directors have agreed to suspend their cash remuneration for service on the board until the Company has clarity on its financial condition.

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

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our common stock as of March 15, 2023, by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own 5% or more of our common stock.

The column entitled "Shares Beneficially Owned" is based on a total of 73,679,105 shares of our common stock outstanding as of March 15, 2023.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of March 15, 2023, are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Axcella Therapeutics, P.O. Box 1270, Littleton, Massachusetts 04160.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% or Greater Stockholders:		
Flagship Pioneering[(1)]	29,251,545	39.7%
FMR LLC[(2)]	11,033,193	15.0%
Nestlé S.A.[(3)]	11,105,438	15.1%
HarbourVest Partners, LLC[(4)]	6,207,929	8.4%
Directors, Named Executive Officers and Other Executive Officers		
William R. Hinshaw, Jr.[(5)]	1,539,201	2.1%
Paul Fehlner, J.D., Ph.D.[(6)]	258,972	*
Margaret James Koziel, M.D.[(7)]	115,302	*
Robert Crane[(8)]	126,614	*
Martin Hendrix, Ph.D.[(9)]	10,000	*
Catherine Angell Sohn, Pharm.D.[(10)]	60,097	*
William D. “Chip” Baird[(11)]	93,031	*
Gary P. Pisano, Ph.D.[(12)]	133,798	*
Cristina M. Rondinone, Ph.D.[(13)]	88,144	*
Paul Sekhri[(14)]	10,000	*
Michael Rosenblatt[(15)]	23,231	*
Robert Rosiello[(16)]	3,333	*
Torben Straight Nissen[(17)]	3,333	*
All executive officers and directors as a group (13 persons)	2,465,056	3.3%

*Represents beneficial ownership of less than one percent.

(1) Based solely on a Schedule 13D/A filed with the SEC on October 17, 2022, consists of (i) 2,035,830 shares of common stock held by Flagship VentureLabs IV, LLC (“VentureLabs IV”) (ii) 14,101,638 shares of common stock held by Flagship Ventures Fund IV, L.P. (Flagship Ventures Fund IV General Partner LLC) (iii) 2,004,657 share of common stock held by Flagship Ventures Fund IV-Rx, L.P (Flagship Ventures Fund IV General Partner LLC) (iv) 1,761,029 shares of common stock held by Flagship Ventures Fund 2007, L.P. (Flagship Ventures 2007 General Partner LLC) (v) 6,299,611 shares of common stock held by Flagship Ventures Opportunities Fund I, L.P. (Flagship Ventures Opportunities Fund I General Partner LLC) (vi) 3,048,780 shares of common stock held by FPA, L.P. Noubar B. Afeyan, Ph.D. is the sole manager of Flagship Fund IV GP, Flagship Fund 2007 GP and Flagship Opportunities GP, and he may be deemed to beneficially own the shares directly held by the Flagship Fund IV Funds, Flagship Fund 2007, and Flagship Opportunities. Effective May 11, 2020, Mr. Kania retired from Flagship Pioneering, Inc. and as manager of Flagship Fund IV GP and Flagship Fund 2007 GP. The address of each of the entities and individuals listed above is 55 Cambridge Parkway, Suite 800E, Cambridge, MA 02142.

(2) Based solely on a Schedule 13G/A filed with the SEC on February 9, 2023, FMR LLC has sole voting power with respect to 11,033,193 shares and sole dispositive power over 11,033,193 shares and Abigail P. Johnson has sole dispositive power over 11,033,193 shares. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company ("FMR Co. LLC"), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

(3) Based solely on a Schedule 13G/A filed with the SEC on February 2, 2023, (i) Société des Produits Nestlé S.A. ("SPN") and (ii) Nestlé S.A. ("Nestlé"), the ultimate parent of SPN, each has shared voting power and shared dispositive power with respect to 11,105,438 shares. Nestlé disclaims beneficial ownership of such shares of Common Stock except to the extent of its pecuniary interest therein. The principal executive office of SPN and Nestlé is Avenue Nestlé 55, CH-1800, Vevey Switzerland.

(4) Based solely on a Schedule 13G/A filed with the SEC on February 14, 2023, consists of 6,207,929 shares common stock owned directly by SMRS-TOPE LLC. HarbourVest Partners, LLC ("HarbourVest") is the General Partner of HarbourVest Partners L.P., which is the Manager of HVST-TOPE LLC, which is the Managing Member of SMRS-TOPE LLC. Each of HarbourVest, HarbourVest Partners L.P. and HVST-TOPE LLC may be deemed to have a beneficial interest in the shares held by SMRS-TOPE LLC. SMRS-TOPE LLC has the sole power to vote or to direct the vote of; and, to dispose or to direct the disposition of 6,207,929 shares of common stock. HarbourVest, HarbourVest Partners L.P. and HVST-TOPE LLC may be deemed to have shared power to vote or to direct the vote of; and, to dispose or to direct the disposition of 6,207,929 shares of common stock. Voting and investment power over the securities owned directly by SMRS-TOPE LLC is exercised by the Investment Committee of HarbourVest. Each of HarbourVest, HarbourVest Partners L.P. and HVST-TOPE LLC and the members of the HarbourVest Investment Committee disclaim beneficial ownership of the shares held directly by SMRS-TOPE LLC. The principal business office of each HarbourVest Partners, LLC, HarbourVest Partners L.P., HVST-TOPE LLC and SMRS-TOPE LLC is One Financial Center, Boston, MA 02111.

(5) Consists of 83,928 shares of common stock and 1,455,273 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(6) Consists of 58,081 shares of common stock and 200,891 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(7) Consists of 24,883 shares of common stock and 90,419 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(8) Consists of 45,364 shares of common stock and 81,250 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(9) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(10) Consists of 7,097 shares of common stock and 53,000 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(11) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(12) Consists of 91,798 shares of common stock and 42,000 shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(13) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(14) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(15) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(16) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

(17) Consists entirely of shares of common stock underlying options exercisable within 60 days of March 15, 2023.

Securities Authorized for Issuance under Equity Compensation Plans

The following table sets forth information as of December 31, 2022, regarding shares of common stock that may be issued under our equity compensation plans.

	Equity Compensation Plan Information		
Plan Category	**Number of securities to be issued upon exercise of outstanding options, warrants and rights**	**Weighted average exercise price of outstanding options, warrants and rights**	**Number of securities remaining available for future issuance under equity compensation plan (excluding securities in first column)**
Equity compensation plans approved by security holders[1]	6,612,210[2]	$5.05	3,015,476[3][4]
Equity compensation plans not approved by security holders	—	—	—
Total	6,612,210	$5.05	3,015,476

(1) Includes the Axcella Health Inc. Amended and Restated 2010 Stock Incentive Plan (the "2010 Plan"), the 2019 Plan and the Axcella Health Inc. 2019 Employee Stock Purchase Plan (the "2019 Employee Stock Purchase Plan").

(2) Includes 6,536,977 of common stock issuable upon the exercise of outstanding stock options and 75,233 shares of common stock issuable upon settlement of restricted stock units.

(3) As of December 31, 2022, there were 2,317,471 shares available for grant under the 2019 Plan and 698,005 shares available for grant under the 2019 Employee Stock Purchase Plan. As of the closing of our initial public offering, no additional equity awards may be granted under the 2010 Plan. The shares of common stock underlying any awards granted under the 2010 Plan or 2019 Plan that are forfeited, canceled, reacquired by us prior to vesting, satisfied without the issuance of stock, or otherwise terminated (other than by exercise) and the shares of common stock that are withheld upon exercise of a stock option or settlement of such award to cover the exercise price or tax withholding will be added to the shares of common stock available for issuance under the 2019 Plan.

(4) The 2019 Plan provides that an additional number of shares will automatically be added to the shares authorized for issuance under the 2019 Plan on January 1 of each year. The number of shares added each year will be equal to the lesser of: (i) 4% of the outstanding shares on the immediately preceding December 31 or (ii) such amount as determined by the compensation committee of our board of directors. The 2019 Employee Stock Purchase Plan provides that an additional number of shares will automatically be added to the shares authorized for issuance under the 2019 Employee Stock Purchase Plan on January 1 of each year through January 1, 2029. The number of shares added each year will be equal to the least of: (i) 1% of the outstanding shares on the immediately preceding December 31, (ii) 237,181 shares or (iii) such amount as determined by the compensation committee of our board of directors.

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

Other than the compensation agreements and other arrangements described under "2022 Summary Compensation Table" and "2022 Director Compensation Table " in this Annual Report on Form 10-K and the transactions described below, since January 1, 2022, there has not been and there is not currently proposed, any transaction or series of similar transactions to which we were, or will be, a party in which the amount involved exceeded, or will exceed, $120,000 and in which any director, executive officer, holder of five percent or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

Agreements with our stockholders

Investors' Rights Agreement

In connection with the initial closing of our Series E Preferred Stock financing on November 30, 2018, we entered into a fifth amended and restated investors' rights agreement, or investors' rights agreement, with certain of our stockholders, including affiliates of Flagship Pioneering Funds, or Flagship. The investors' rights agreement, among other things, granted investors party thereto certain registration rights (the "Registration Rights"), including demand registration rights, short-form registration rights, and piggyback registration rights, with respect to shares of our common stock, including shares of common stock issued or issuable upon conversion of our convertible preferred stock.

The Registration Rights will terminate on the earlier to occur of May 13, 2024, or, as to each holder, such earlier time at which such holder (i) can sell all shares held by it in compliance with SEC Rule 144(b) (1)(i) or (ii) holds 1% or less of our common stock and all registrable securities held by such holder can be sold in any three-month period without registration in compliance with SEC Rule 144.

Agreement with Flagship Pioneering

In December 2008, we entered into a services agreement with Flagship Ventures Management, Inc., now known as Flagship Pioneering, Inc., an affiliate of the Flagship Pioneering Funds, under which Flagship Pioneering, Inc. provides us with advisory and administrative services on an as-needed basis. The agreement, which is invoiced monthly, may be terminated by either party upon 30 days' prior written notice. Our transactions with Flagship Pioneering, Inc. were immaterial for the year ended December 31, 2022, for services provided under the services agreement.

Limitation of Liability and Indemnification of Officers and Directors

Our restated certificate of incorporation contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by the Delaware General Corporation Law, or DGCL. Consequently, our directors are not personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases, or redemptions as provided in Section 174 of the DGCL; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated bylaws require us to indemnify our directors and officers to the maximum extent not prohibited by the DGCL and allow us to indemnify other employees and agents as set forth in the DGCL. Subject to certain limitations, our amended and restated bylaws also require us to advance expenses incurred by our directors and officers for the defense of any action for which indemnification is required or permitted.

We have entered, and intend to continue to enter, into separate indemnification agreements with our directors, officers and certain of our key employees, in addition to the indemnification provided for in our restated certificate of incorporation and amended and restated bylaws. These agreements, among other things, require us to indemnify our directors, officers and key employees for certain expenses, including attorneys' fees, judgments, penalties, fines and settlement amounts actually incurred by these individuals in any action or proceeding arising out of their service to us or our subsidiaries or any other company or enterprise to which these individuals provide services at our request. Subject to certain limitations, our indemnification agreements also require us to advance expenses incurred by our directors, officers and key employees for the defense of any action for which indemnification is required or permitted.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, upon consideration of a potential related party transaction, the material facts as to the related party's relationship or interest in the transaction are disclosed to our board of directors prior to their consideration of such transaction, and the transaction is not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approve the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

In connection with our initial public offering, we adopted a written related party transactions policy that provides that such transactions must be approved by our audit committee. This policy became effective on May 9, 2019. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members.

Director Independence

Applicable Nasdaq Stock Market LLC, or Nasdaq, rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act and that compensation committee members satisfy independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In addition, in affirmatively determining the independence of any director who will serve on a company's compensation committee, Rule 10C-1 under the Exchange Act requires that a company's board of directors must consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including: the source of compensation to the director, including any consulting, advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors has determined that all members of the board of directors, except Mr. Hinshaw, are independent directors, including for purposes of the rules of Nasdaq and the SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. There are no family relationships among any of our directors or executive officers. Mr. Hinshaw is not an independent director under these rules because he is an executive officer of Axcella.

Item 14. Principal Accounting Fees and Services

Our independent public accounting firm is Deloitte & Touche, LLP, Boston, Massachusetts, PCAOB Auditor ID 34.

Axcella incurred the following fees from Deloitte & Touche LLP for the audit of the consolidated financial statements and for other services provided during the years ended December 31, 2022, and 2021.

Fee Category	Fiscal Year 2022 ($)	Fiscal Year 2021 ($)
Audit and audit-related fees[(1)]	$628,893	$588,307
Tax fees	—	—
All other fees	—	—
Total Fees	$628,893	$588,307

(1) Consists of fees for the audit of our annual financial statements, reviews of quarterly financial statements included in Quarterly Reports on Form 10-Q, services provided in connection with SEC filings, including consents and comfort letters, and a subscription to the Deloitte Accounting Research Tool.

Audit Committee Pre-approval Policy and Procedures

Our audit committee has adopted policies and procedures relating to the approval of all audit and non-audit services that are to be performed by our independent registered public accounting firm. This policy provides that we will not engage our independent registered public accounting firm to render audit or non-audit services unless the service is specifically approved in advance by our audit committee, or the engagement is entered into pursuant to the pre-approval procedure described below.

From time to time, our audit committee may pre-approve specified types of services that are expected to be provided to us by our independent registered public accounting firm during the next 12 months. Any such pre-approval details the particular service or type of services to be provided and is also generally subject to a maximum dollar amount.

During our 2022 and 2021 fiscal years, no services were provided to us by Deloitte & Touche LLP other than in accordance with the pre-approval policies and procedures described above.

Part IV

Item 15. Exhibits and Financial Statement Schedules

(a) Documents Filed as Part of this Annual Report

1. *Financial Statements*

The financial statements of Axcella Health Inc. are included in Item 8 of this Annual Report on Form 10-K.

2. *Financial Statement Schedules*

All financial statements schedules are omitted as they are either not required or the information is otherwise included in the consolidated financial statements and related notes.

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 17, 2019).
3.3	Amendment to the Amended and Restated Bylaws of Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on May 8, 2020).
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 (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 23, 2020).
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# First Amendment to Amended and Restated Employment Agreement between the Registrant and Paul Fehlner, dated September 16, 2020 (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, 2020).

10.7# Employment Agreement, by and between the Company and Margaret Koziel, dated as of December 1, 2021 (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 December 7, 2021).

10.8# Employment Agreement, by and between the Company and Robert Crane, dated as of January 24, 2022 (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 February 7, 2022).

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 Sixth Lease Extension and Modification Agreement to the Lease Agreement between Rivertech Associates II, LLC and the Registrant, dated as of October 1, 2020 (incorporated by reference to Exhibit 10.18 to the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 17, 2021).

10.15 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).

10.16 Second Amendment to Loan and Security Agreement, dated November 30, 2018 (incorporated by reference to Exhibit 10.14 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).

10.17 Third Amendment to Loan and Security Agreement, dated August 28, 2020, between the Registrant and Solar Capital Ltd. (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 August 31, 2020).

10.18^ Loan and Security Agreement, dated September 2, 2021, by and between the Registrant and SLR Investment Corp.. (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 September 7, 2021).

10.19 Securities Purchase Agreement, dated as of September 20, 2022, by and among Axcella Health Inc. and certain funds affiliated with Flagship Pioneering, as purchasers (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 September 23, 2022).

10.20 First Amendment to Securities Purchase Agreement, dated as of September 30, 2022, by and among Axcella Health Inc. and the purchasers party thereto (Incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38901) filed with the Securities and Exchange Commission on November 1, 2022).

10.21 Form of Convertible Promissory Note (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on September 23, 2022).

10.22	Form of Securities Purchase Agreement dated as of October 13, 2022 by and among Axcella Health, Inc. and the purchasers thereto (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 October 13, 2022).
10.23#	Retention Agreement, dated February 14, 2023, by and between Axcella Health Inc. and William Hinshaw (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 February 17, 2023).
10.24#	Retention Agreement, dated February 14, 2023, by and between Axcella Health Inc. and Margaret Koziel (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on February 17, 2023).
10.25#	Retention Agreement, dated February 14, 2023, by and between Axcella Health Inc. and Paul Fehlner (Incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-38901) filed with the Securities and Exchange Commission on February 17, 2023).
10.26#	Employment Agreement, by and between the Company and Daniel Kirby, dated as of May 26, 2022 (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38901) filed with the Securities and Exchange Commission on August 12, 2022).
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Deloitte & 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.
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.)

---

* 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.

^ Certain exhibits and schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Company hereby undertakes to furnish supplementally a copy of any omitted exhibit or schedule upon request by the SEC.

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 30, 2023 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 Marie Washburn, 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 30, 2023
/s/ Robert Rosiello Robert Rosiello	Chairman, Director	March 30, 2023
/s/ Marie Washburn Marie Washburn	Vice President, Finance and Corporate Controller (Principal Financial Officer and Principal Accounting Officer)	March 30, 2023
/s/ William D. "Chip" Baird William D. "Chip" Baird	Director	March 30, 2023
/s/ Martin Hendrix Martin Hendrix	Director	March 30, 2023
/s/ Torben Straight Nissen Torben Straight Nissen	Director	March 30, 2023
/s/ Gary P. Pisano Gary P. Pisano	Director	March 30, 2023
/s/ Cristina M. Rondinone Cristina M. Rondinone	Director	March 30, 2023
/s/ Michael Rosenblatt Michael Rosenblatt	Director	March 30, 2023
/s/ Paul J. Sekhri Paul J. Sekhri	Director	March 30, 2023
/s/ Catherine Angell Sohn Catherine Angell Sohn	Director	March 30, 2023

[THIS PAGE INTENTIONALLY LEFT BLANK]

BOARD OF DIRECTORS

Robert Rosiello
Board Chairman
Executive Partner, Flagship Pioneering

William D. Baird
Chief Financial Officer, 2seventy bio

Martin Hendrix, Ph.D.
Head of Global Business Development and M&A at Nestlé Health Science

William Hinshaw, Jr.
President & Chief Executive Officer

Gary Pisano, Ph.D.
Harry E. Figgie Professor of Business Administration, Harvard Business School

Cristina M. Rondinone, Ph.D.
Founder, CMR Pharma Consulting

Michael Rosenblatt, M.D.
Senior Partner, Flagship Pioneering

Paul Sekhri
Board Member and Advisor to the Life Science Industry

Catherine Angell Sohn, PharmD.
Adjunct Professor, University of California San Francisco

Torben Straight Nissen, Ph.D.
Senior Partner, Flagship Pioneering, CEO of Repertoire and Founding CEO of FL84

EXECUTIVE OFFICERS

William Hinshaw, Jr.
President & Chief Executive Officer

Paul Fehlner, J.D., Ph.D.
Senior Vice President, Chief Legal Officer and Corporate Secretary

PRINCIPAL EXECUTIVE OFFICES

P.O. Box 1270
Littleton, Massachusetts, 01460

PUBLIC ACCOUNTING FIRM

Deloitte & Touche LLP
200 Berkeley St 10th floor
Boston, MA 02116

CORPORATE INFORMATION

https://axcellatx.com/
Trading Symbol: AXLA (NASDAQ)

INVESTOR RELATIONS

ir@axcellatx.com
(857) 320-2200

TRANSFER AGENT

Computershare
6200 S. Quebec St.
Greenwood Village CO 80111
(800) 736-3001

SEC Form 10-K

A copy of our Form 10-K filed with the Securities and Exchange Commission (SEC) is available free of charge on the SEC's website at www.sec.gov or from the company's investor relations department by emailing ir@axcellatx.com or sending a written request to Axcella's investor relations department at:

Investor Relations

Axcella Health Inc.
P.O. Box 1270
Littleton, Massachusetts, 01460

P.O. Box 1270
Littleton, Massachusetts, 01460
(857) 320-2200
https://axcellatx.com/