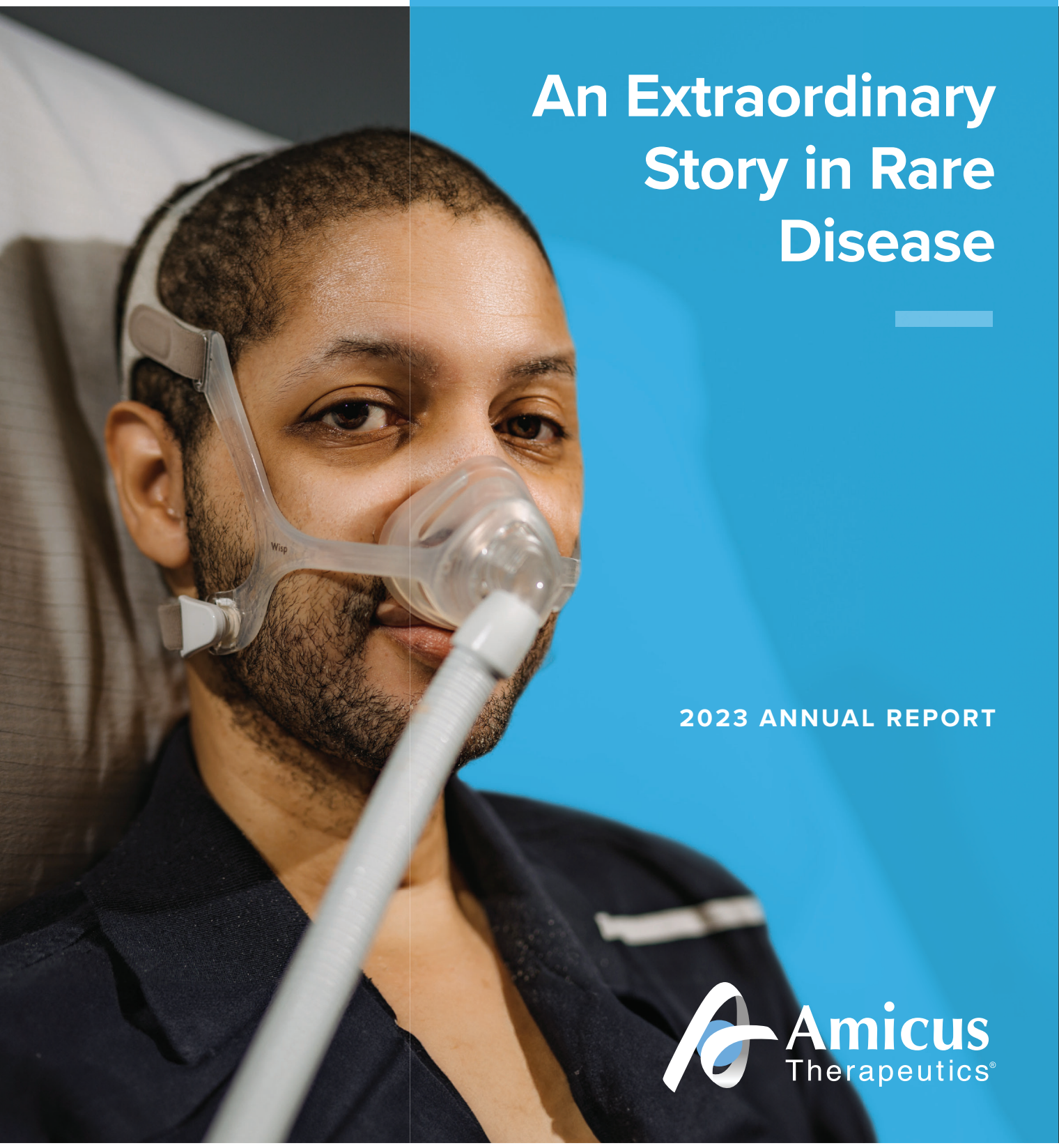


An Extraordinary Story in Rare Disease

2023 ANNUAL REPORT

Amicus Therapeutics®

To Our Shareholders

Everyday Amicus is driven by a shared sense of purpose and commitment to people around the world living with a rare disease. Our work is founded in the belief that every person living with a rare disease deserves access to effective treatments and that together we can be the difference.

Our accomplishments in 2023 represent the dedication Amicus brings to the rare disease community as we continued our mission of transforming the lives of people living with rare diseases. The accomplishments were transformational and pillared around our three value drivers:

- Receiving regulatory approvals of our second commercial therapy, Pombiliti™ + Opfolda™, in the United States, European Union, and the United Kingdom
- Increasing access to Galafold with over 2,400 people living with Fabry disease around the world
- Delivering on our commitment of non-GAAP profitability in the fourth quarter of the year

Following the approval of our second commercial therapy, we are committed more than ever to increasing our leadership in rare diseases and achieving our next level of growth. A growth defined by delivering our therapies to those in need, advancing our ongoing studies to enhance our medical and scientific leadership in Fabry and Pompe disease, and leveraging our strong infrastructure to create long-term value. I am confident our pursuit of excellence and innovation on behalf of people living with rare diseases will position us for success and create value for all our stakeholders.

As we reflect on the past year and set our sights on the year ahead, I would like to recognize the many people who have made Amicus an extraordinary story in rare disease. Thank you to the patients and their families who inspire us, to our employees for their passion and drive, and to you, our shareholders, for supporting our mission.

Sincerely,

Bradley Campbell
President and Chief Executive Officer

Bradley L. Campbell
President and Chief Executive Officer

A Rare Company.

Amicus Therapeutics is a global, patient-dedicated biotechnology company focused on developing and delivering high-quality medicines for people living with rare diseases.

as of December 31, 2023

$399M
Net Product Sales

500+
Dedicated Employees Globally

Focused Rare Disease
Pipeline
in Fabry Disease and Pompe Disease

2 Approved Therapies
Galafold® and Pombiliti™ + Opfolda™

Global Footprint in
20+ Countries

Non-GAAP
Profitability
Achieved in Q4 2023[1]

1. Amicus defines non-GAAP Net (Loss) Income as GAAP Net (Loss) Income excluding the impact of share-based compensation expense, changes in fair value of contingent consideration, loss on impairment of assets, depreciation and amortization, acquisition related income (expense), loss on extinguishment of debt, restructuring charges and income taxes.

An Extraordinary Story in Rare Disease

Amicus, the Latin word for friend, signifies our collaborative approach to developing medicines by incorporating the patient perspective every step of the way. Our company was founded by an entrepreneur who embarked on a life-long journey to transform the lives of those living with devastating conditions when two of his children were diagnosed with a rare disease. That spirit of empathy, compassion, and tenacity permeates our culture and influences all aspects of our approach to advancing cutting-edge technologies.

2023 Pombiliti™ + Opfolda™ approved – first and only two-component therapy for Late-Onset Pompe disease

2022 More than 2,000 patients on Galafold®

2016 Galafold® approved – first and only approved oral treatment option for Fabry disease

2013 Entry into biologics through acquisition of Callidus and Pompe enzyme replacement therapy

2007 Amicus initial public offering (NASDAQ: FOLD)

2006 First Fabry patient treated in an Amicus clinical trial

2002 Amicus is founded on the pharmacological chaperone technology from Mt. Sinai School of Medicine

Reaching Patients Across the Globe

Amicus is a global organization, united by a passion for making a difference.

Our global footprint spans over 20 countries, including our global headquarters in Princeton, NJ and international headquarters in Marlow, U.K. Additional international office locations include Australia, Canada, France, Japan, Germany, Italy, the Netherlands, and Spain.

Core Value Drivers

Galafold: Building a Leadership Position in the Treatment of Fabry Disease

2,400+ patients and $388M global sales in FY23

Projecting Galafold revenue growth of 11-16% at CER[1] in 2024

Fastest growing treatment for Fabry disease globally

Pombiliti + Opfolda: Resetting Treatment Expectations for People Living with Late-onset Pompe Disease

Approved and launched in the U.S., EU, and the U.K., the three largest Pompe markets

Growing patient and physician demand across all three markets

Focus on securing broad patient access and initiating multiple successful launches throughout 2024

Non-GAAP Profitability achieved in 4Q 2023: On-track to achieve first full year of non-GAAP profitability in 2024

Continue to drive double-digit revenue growth for Galafold

Advance the ongoing commercial launch of Pombiliti + Opfolda

Targeted investment in next-generation therapies for Fabry disease and Pompe disease

Leverage global commercial infrastructure to become a leader in rare diseases

1. Constant Exchange Rates; 2024 Galafold revenue guidance utilizes actual exchange rate as of December 31, 2023.

Fabry Disease

Fabry disease is a rare, progressive genetic disorder characterized by a defective gene (GLA) that causes an enzyme deficiency. This enzyme is responsible for breaking down disease substrate that, when deficient in patients with Fabry disease, builds up in the kidneys, one of the organ systems impacted by Fabry disease.

Galafold® (migalastat) is an oral pharmacological chaperone of alpha-Galactosidase A (alpha-Gal A) for the treatment of Fabry disease in adults who have amenable galactosidase alpha gene (GLA) variants.

40+
countries with regulatory approval

60-65%
market share of treated amenable patients

90%+
compliance and adherence rates

Galafold®
(migalastat)

Natalie
Living with Fabry Disease

Jeff
Living with Late-Onset Pompe Disease

Pompe Disease

Pompe disease is a progressive, debilitating, and life-threatening rare Lysosomal Disorder that results from a deficiency in an enzyme GAA. Signs and symptoms of Pompe disease can be severe and debilitating and include progressive muscle weakness throughout the body, particularly the heart and skeletal muscles. This leads to accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease.

Pombiliti™ (cipaglucosidase alfa-atga) + Opfolda™ (miglustat) is a two-component therapy that consists of cipaglucosidase alfa-atga, a bis-M6P-enriched rhGAA that facilitates high-affinity uptake through the M6P receptor while retaining its capacity for processing into the most active form of the enzyme, and the oral enzyme stabilizer, miglustat, that's designed to reduce loss of enzyme activity in the blood.

Approved and launched in the three largest Pompe markets: U.S., EU, and U.K.

First and only two-component therapy for the treatment of late-onset Pompe disease.

Resetting therapeutic expectations for Pompe with Pombiliti + Opfolda: **Improvement is Possible**

Pombiliti™ + Opfolda™
(cipaglucosidase alfa-atga) (miglustat) 65 mg capsules

Corporate Responsibility

Strengthening our corporate culture as we grow to positively impact as many people living with rare diseases as possible

Corporate Responsibility

At Amicus, we have a shared purpose of improving public health, patient experiences, and outcomes with a focus on educational, advocacy, and access initiatives related to the disease areas in which we focus our development and therapeutic programs.

Healing Beyond Disease

The rare disease community always has a voice within Amicus. This is shown through our corporate social responsibility initiative Healing Beyond Disease – our unique promise to further serve the needs of the rare disease community in extraordinary ways.

Healing Beyond Disease is inspired by and adaptive to rare disease communities and reflects the existing generosity of our corporate culture.

Time

Evolve volunteerism company-wide to further our commitment to the rare disease patient community with information and incentives for employees

Talent

Leverage the expertise within Amicus to empower organizations and individuals impacted by rare diseases to accomplish their mission

Treasure

Advance philanthropy for rare diseases by providing a broader opportunity for financial support and contributions

Pledge

Designate a portion of sales from any Amicus marketed drug and reinvest back into that specific disease until there is a cure

Bridges

Build rare bridges across the globe to provide access to our medicines in the near and in the long-term in the developed and developing world

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2023

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 001-33497

Amicus Therapeutics, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**71-0869350**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)
47 Hulfish Street, Princeton, NJ	**08542**
(Address of Principal Executive Offices)	(Zip Code)

(609) 662-2000
(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	FOLD	NASDAQ Global Market

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "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 283,196,538 shares of voting common equity held by non-affiliates of the registrant, computed by reference to the closing price as reported on The NASDAQ Global Market, as of the last business day of the registrant's most recently completed second fiscal quarter (June 30, 2023) was $3,556,948,517. Shares of voting and non-voting stock held by executive officers, directors, and holders of more than 10% of the outstanding stock have been excluded from this calculation because such persons or institutions may be deemed affiliates. This determination of affiliate status is not a conclusive determination for other purposes.

The number of shares outstanding of the registrant's common stock, $0.01 par value per share, as of February 13, 2024 was 295,382,614 shares.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2024 Annual Meeting of Stockholders which is to be filed subsequent to the date hereof are incorporated by reference into Part III of this Annual Report on Form 10-K.

PART I

We have filed applications to register certain trademarks in the United States and abroad, including AMICUS THERAPEUTICS and design, AMICUS ASSIST and design, CHART and design, AT THE FOREFRONT OF THERAPIES FOR RARE AND ORPHAN DISEASES, HEALING BEYOND DISEASE, OUR GOOD STUFF, Galafold® and design, Pombiliti™ and design, Opfolda™ and design.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks, uncertainties, and assumptions. Forward-looking statements are all statements, other than statements of historical facts, that discuss our current expectation and projections relating to our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, and objectives of management. These statements may be preceded by, followed by or include the words "aim," "anticipate," "believe," "can," "could," "estimate," "expect," "forecast," "intend," "likely," "may," "might," "outlook," "plan," "potential," "predict," "project," "seek," "should," "will," "would," the negatives or plurals thereof, and other words and terms of similar meaning, although not all forward-looking statements contain these identifying words.

We have based these forward-looking statements on our current expectations and projections about future events. Although we believe that our assumptions made in connection with the forward-looking statements are reasonable, we cannot assure you that the assumptions and expectations will prove to be correct. You should understand that the following important factors could affect our future results and could cause those results or other outcomes to differ materially from those expressed or implied in our forward-looking statements:

- the scope, progress, results and costs of clinical trials for our drug candidates;
- the cost of manufacturing drug supply for our commercial, clinical and preclinical studies, including the cost of manufacturing Pombiliti™ (also referred to as "ATB200" or "cipaglucosidase alfa");
- the future results of preclinical research and subsequent clinical trials for pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates;
- any changes in regulatory standards relating to the review of our product candidates;
- any changes in laws, rules or regulations affecting our ability to manufacture, transport, test, develop, or commercialize our products, including Galafold®, Pombiliti™ + Opfolda™, or our product candidates;
- the costs of commercialization activities, including product marketing, sales, and distribution;
- the emergence of competing technologies and other adverse market developments;
- the estimates regarding the potential market opportunity for our products and product candidates;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl");
- our ability to successfully commercialize Pombiliti™ + Opfolda™ (together, also referred to as "AT-GAA") in the E.U., U.K., and U.S., and elsewhere, if regulatory applications are approved;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and Pombiliti™ + Opfolda™;
- our ability to obtain reimbursement for Galafold® and Pombiliti™ + Opfolda™;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold® and Pombiliti™ + Opfolda™;
- our ability to obtain market acceptance of Galafold® and Pombiliti™ + Opfolda™, or any other product developed or acquired that has received regulatory approval;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims, including Hatch-Waxman litigation;
- the impact of litigation that has been or may be brought against us or of litigation that we are pursuing or may pursue against others, including Hatch-Waxman litigation;
- the extent to which we acquire or invest in businesses, products, and technologies;
- our ability to successfully integrate acquired products and technologies into our business, or successfully divest or license existing products and technologies from our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;

- our ability to establish licensing agreements, collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other economic benefits from any such collaborators;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards, including climate reporting requirements at the local, state and national levels;
- our ability to successfully protect our information technology systems and maintain our global operations and supply chain without interruption;
- our ability to accurately forecast revenue, operating expenditures, or other metrics impacting profitability;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

In light of these risks and uncertainties, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A "— Risk Factors", a summary of which may be found below, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Those factors and the other risk factors described herein are not necessarily all of the important factors that could cause actual results or developments to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors also could harm our results. Our forward-looking statements do not reflect the potential impact of any future collaborations, alliances, business combinations, partnerships, strategic out-licensing of certain assets, the acquisition of preclinical-stage, clinical-stage, marketed products or platform technologies or other investments we may make. Consequently, there can be no assurance that actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, us. Given these uncertainties, investors are cautioned not to place undue reliance on such forward-looking statements.

You should read this Annual Report on Form 10-K and the documents that we incorporate by reference in this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. These forward-looking statements speak only as of the date of this report. We undertake no obligation, and specifically decline any obligation, to publicly update or revise any forward-looking statements, even if experience or future developments make it clear that projected results expressed or implied in such statements will not be realized, except as may be required by law.

Summary Risk Factors

The following is a summary of the principal risks that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face and is qualified in its entirety by reference to the more detailed descriptions included in Part I, Item 1A "— Risk Factors". This summary should be read together with those more detailed descriptions, along with our other SEC filings before making an investment decision.

- We depend heavily on sales of Galafold® in Europe, the U.S. and Japan. If we are delayed or unable to commercialize Galafold® successfully, our business could be materially harmed.
- If we are not able to obtain, or delayed in obtaining, required regulatory approvals, we will not be able to commercialize our products or product candidates, materially impairing our ability to generate revenue.
- If we are unable to establish and maintain sales and marketing capabilities, or relationships, to market and sell our products or, if approved, product candidates, their commercialization may suffer.
- If the market opportunities for our products or product candidates are smaller than we believe they are, then our revenues may be adversely affected, and our business may suffer.
- Galafold®, Pombiliti™ + Opfolda™, or any of our product candidates that receive regulatory approval may fail to achieve the degree of market acceptance necessary for commercial success.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- A variety of risks associated with international operations, including the U.S. and China relations, could adversely affect our business, particularly as it relates to products or product candidates for which we have a sole supplier.
- Our products or any product candidates receiving approval may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives.
- If we are found to have promoted off-label uses by regulatory authorities, we may become subject to significant liability.
- Product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.
- If applicable regulatory authorities approve generic or biosimilar products with claims that compete with our products or any of our product candidates, it could reduce our sales.
- We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on an alternative for which there is a greater likelihood of success.
- Our products or product candidates may have side effects that could impact their regulatory approval or commercialization.
- Any product or product candidate we obtain marketing approval for could be subject to restrictions or withdrawal from the market and we may be subject to penalties or enforcement actions if we fail to comply with regulatory requirements.
- Certain relationships will be subject to anti-kickback, fraud and abuse, anti-bribery and corruption and other laws and regulations, which could expose us to criminal, civil, or contractual penalties, reputational harm and diminished earnings.
- If clinical trials of our product candidates do not produce results satisfactory to regulatory authorities, the development and commercialization of our product candidates may not be completed.
- If we experience unforeseen events in connection with our clinical trials, potential regulatory approval or commercialization of our product candidates could be delayed or prevented.
- If we experience delays or difficulties in the enrollment of our clinical trials, regulatory approvals could be delayed or prevented.
- Initial clinical trial results do not ensure that the trial will be successful and success in preclinical or early stage clinical trials does not ensure success in later-stage clinical trials.
- If our competitors obtain orphan drug exclusivity for their products and we do not, we may be unable to have competing products approved in the applicable jurisdiction for a significant period of time.
- Failure to obtain or maintain regulatory approval outside the U.S. would prevent us from marketing our products abroad.
- Our gene therapy product candidates are based on novel technologies, which makes it difficult to predict the time and cost of their development and subsequently obtaining regulatory approval.

- Our use of third parties to manufacture our products or product candidates may increase the risk that we will not have sufficient quantities of our products or product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We may be unable to enter into agreements with third-party manufacturers, or unable to do so on acceptable terms.
- We rely on third parties to distribute our products who may not perform satisfactorily.
- We rely on third parties to conduct certain preclinical activities and our clinical trials, who may not perform satisfactorily.
- We may not be successful in maintaining or establishing collaborations, which could adversely affect our ability to develop and, particularly in international markets, commercialize products.
- Materials necessary to manufacture our products or product candidates may not be available on commercially reasonable terms, which may delay their development and commercialization.
- Manufacturing issues may arise that could increase costs or delay commercialization.
- We have incurred significant losses and anticipate that we will continue to incur losses in the future.
- We may never become profitable even though we currently generate revenue from the sale of products.
- If we require, and fail to obtain, additional necessary financing, we may be unable to complete the development and commercialization of our products and product candidates.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies, Galafold®, Pombiliti™ + Opfolda™, or product candidates.
- We may not have sufficient cash flow from our business to pay our substantial debt.
- Foreign currency exchange rate fluctuations could harm our financial results.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- Our executive officers, directors and principal stockholders maintain the ability to exert significant influence and control over matters submitted to our stockholders for approval.
- We do not anticipate paying cash dividends so capital appreciation, if any, will be our stockholders sole source of gain.
- Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.
- If we are unable to obtain and maintain sufficiently broad patent protection, our ability to successfully commercialize our technology and products may be adversely affected.
- We currently are and may become involved in lawsuits to protect or enforce our patents or other intellectual property.
- Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights which could have a material adverse effect on the success of our business.
- We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.
- If we fail to comply with our obligations in our intellectual property licenses, we could lose material license rights.
- Failure to secure trademark registrations could adversely affect our business.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- Our employees, independent contractors, principal investigators, consultants and vendors may engage in misconduct or improper activities which could lead to significant liability and harm our reputation.
- If our enterprise risk program, global risk committee and other compliance methods are not effective, our business, financial condition and operating results may be adversely affected.
- The increased focus on environmental, social and governance ("ESG") matters and emission reporting by investors, governmental bodies and other stakeholders, as well as existing and proposed laws related to these topics, may adversely affect our business and reputation.
- Our business activities involve the use of hazardous materials which could subject us to significant adverse consequences if we fail to comply with the applicable laws regulating their use.
- Unfavorable global economic conditions such as global crises, health epidemics, military conflicts, geopolitical and trade disputes, including between the U.S. and China, or other factors, may adversely affect our business and financial results.

PART I

Item 1. BUSINESS

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We seek to deliver the highest quality therapies that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. Our two marketed therapies are Galafold®, the first oral monotherapy for people living with Fabry disease who have amenable genetic variants, and Pombiliti™ + Opfolda™, a novel treatment designed to improve uptake of active enzyme into key disease relevant tissues for adults living with late-onset Pompe disease.

Galafold® (also referred to as "migalastat") is approved in over 40 countries around the world, including the United States ("U.S."), European Union ("E.U."), United Kingdom ("U.K."), and Japan. Additionally, Galafold® has been granted orphan drug designation in the U.S., E.U., U.K., Japan, and several other countries.

Pombiliti™ + Opfolda™ (also referred to as "cipaglucosidase alfa-atga/miglustat") was approved in 2023 in the three largest Pompe markets: the U.S., the E.U., and the U.K. Multiple regulatory submissions and reimbursement processes with global health authorities are currently underway. Additionally, Pombiliti™ + Opfolda™ has been granted orphan drug designation in the U.S., E.U., U.K., Japan and several other countries.

Our Strategy

Our strategy is to create, manufacture, test, and deliver the highest quality medicines for people living with rare diseases through internally developed, jointly developed, acquired, or in-licensed products and product candidates. We are leveraging our global capabilities to develop and broaden our franchises in Fabry and Pompe disease, with focused discovery work on next-generation therapies and novel technologies.

Highlights of our progress include:

- *Commercial and regulatory success in Fabry disease*. For the year ended December 31, 2023, Galafold® revenue was $387.8 million of consolidated revenue, which represented an increase of $58.7 million compared to the prior year. We continue to see strong commercial momentum and expansion into additional geographies.
- *Pompe disease program milestones*. For the year ended December 31, 2023 Pombiliti™ + Opfolda™ revenue was $11.6 million of consolidated revenue. Pombiliti™ + Opfolda™ were approved by the European Commission ("EC") in June 2023, the Medicines and Healthcare products Regulatory Agency ("MHRA)" of the United Kingdom in August 2023, and the U.S. Food and Drug Administration ("FDA") in September 2023.
- *Pipeline advancement and growth.* We are leveraging our global capabilities to develop and broaden our franchises in Fabry and Pompe disease, with focused discovery work on next-generation therapies and novel technologies.
- *Financial strength.* Total cash, cash equivalents, and marketable securities as of December 31, 2023 was $286.2 million.

Our Commercial Products and Product Candidates

Galafold® (migalastat HCl) for Fabry Disease

Our oral precision medicine Galafold® was granted accelerated approval by the FDA in August 2018 for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene ("GLA") variant based on in vitro assay data. Galafold® was approved in the E.U. and U.K. in May 2016 as a first-line therapy for long-term treatment of adults and adolescents, aged 16 years and older, with a confirmed diagnosis of Fabry disease and who have an amenable mutation (variant). Marketing authorization approvals as well as approvals for adolescents aged 12 years and older weighing 45 kg or more have been granted in over 40 countries around the world. We plan to continue to launch Galafold® in additional countries, including for adolescents aged 12 years and older.

As an orally administered monotherapy, Galafold® is designed to bind to and stabilize an endogenous alpha-galactosidase A ("alpha-Gal A") enzyme in those patients with genetic variants identified as amenable in a Good Laboratory Practice ("GLP") cell-based amenability assay.

Next-Generation for Fabry Disease

We are committed to continued innovation for all people living with Fabry disease. As part of our long-term commitment, we are also continuing discovery for next-generation genetic medicines and have an academic research collaboration agreement to explore next-generation pharmacological chaperones for Fabry disease.

Fabry Disease Background

Patients with Fabry disease have an inherited deficiency of the alpha-Gal A enzyme that would normally degrade the lipid substrate globotriaosylceramide in the lysosome. Genetic variants that cause changes in the amino acid sequence of alpha-Gal A result in an unstable enzyme that does not efficiently fold into its correct three-dimensional shape and cannot be trafficked properly in the cell, even if it has the potential for biological activity. Galafold® is an oral small molecule pharmacological chaperone that is designed to bind to and stabilize a patient's own endogenous target protein. This is considered a precision medicine because Galafold® targets only patients with GLA variants amenable to Galafold®.

Fabry disease is an X-linked disease caused by mutations in the GLA gene, which encodes the alpha-Gal A enzyme. These mutations can cause alpha-Gal A to be either absent or deficient. When alpha-Gal A is absent or deficient in the substrates, GL-3 and lyso-Gb3 accumulate, leading to damage of cells within affected parts of the individual's body and causing the various pathologies seen in Fabry disease. Fabry disease leads to progressive, irreversible organ damage, typically involving the nervous, cardiac, and renal systems, as well as multiple other tissues. The symptoms can be severe, differ from patient to patient, and begin at an early age, resulting in significant clinical, humanistic, and healthcare costs. Fabry disease requires lifelong medical intervention to manage the complications of this devastating disease across multiple organ systems.

Fabry disease is a relatively rare disorder. The annual incidence of Fabry disease in newborn males has been historically estimated to be 1:40,000-1:60,000 (Journal of the American Medical Association January 1999 and The Metabolic and Molecular Bases of Inherited Disease 8th edition 2001). However, more recent newborn screening studies in Italy, Taiwan, Austria, Spain and the U.S., which collectively screened more than 500,000 male and female newborns, found the incidence of GLA mutations to be between 1:2,445 to 1:8,454, more than ten times higher than previous estimates for classic patients (American Journal of Human Genetics 2006, Human Mutation 2009, the Lancet 2011, Journal of Pediatrics 2017, and Journal of the American Medical Association Pediatrics 2018). When looking at only male newborns within these studies, the incidence of Fabry disease mutations is as high as 1:1,316 – 1:7,575 (Circulation in Cardiovascular Genetics 2009, American Journal of Human Genetics 2006, European Journal of Pediatrics 2017).

We believe that approximately 35-50% of the Fabry disease patient population may benefit from treatment with Galafold® as a monotherapy. Additionally, we expect that as awareness of late-onset symptoms of Fabry disease grows, the number of patients diagnosed with the disease will increase. Increased awareness of Fabry disease, particularly for specialists not accustomed to treating Fabry disease patients, may lead to increased testing and diagnosis of patients with the disease.

Currently, three other products, all ERTs, are approved for the treatment of Fabry disease: agalsidase beta by Sanofi Aventis, pegunigalsidase alfa-iwxj by Chiesi Farmaceutici and agalsidase alfa by Takeda, the last of which is not approved in the U.S.

Pombiliti™ (cipaglucosidase alfa-atga) + Opfolda™ (miglustat) for Pompe Disease

We have leveraged our biologics capabilities to develop Pombiliti™ + Opfolda™, a novel treatment paradigm for late-onset Pompe disease. Pombiliti™ + Opfolda™ were approved by the EC in June 2023, the MHRA in August 2023, and the FDA in September 2023. Additional regulatory submissions and reimbursement processes with global health authorities are currently underway.

Pombiliti™ + Opfolda™ consists of a uniquely engineered rhGAA enzyme, cipaglucosidase alfa-atga, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with miglustat that functions as an enzyme stabilizer. Miglustat binds to and stabilizes cipaglucosidase alfa-atga reducing inactivation of rhGAA in circulation to improve the uptake of active enzyme into key disease relevant tissues. Miglustat is not an active ingredient that contributes directly to glycogen reduction.

In addition, clinical studies are ongoing in pediatric patients for both the late-onset Pompe disease ("LOPD") and infantile-onset Pompe disease ("IOPD") populations.

Next-Generation for Pompe Disease

We are committed to continued innovation for all people living with Pompe disease. As part of our long-term commitment, we are also continuing discovery for next-generation genetic medicines for Pompe disease.

Pompe Disease Background

Pompe disease is a lysosomal storage disorder that results from a deficiency in an enzyme, GAA. Signs and symptoms of Pompe disease can be severe and debilitating and include progressive muscle weakness throughout the body, particularly the heart and skeletal muscles. GAA deficiency causes accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease. Pompe disease ranges from a rapidly fatal infantile form with severe cardiac involvement to a more slowly progressive, late-onset form primarily affecting skeletal muscle. All forms are characterized by severe muscle weakness that worsens over time. In the early-onset form, patients are usually diagnosed shortly after birth and often experience enlargement of the heart and severe muscle weakness. In late-onset Pompe disease, symptoms may not appear until late childhood or adulthood and patients often experience progressive muscle weakness.

According to reported estimates of the Acid Maltase Deficiency Association, the United Pompe Foundation, and the Lysosomal Disease Program at Massachusetts General Hospital, there are 5,000-10,000 patients with Pompe disease worldwide. Pompe disease is a rare genetic disease with a traditionally used incidence rate of 1:40,000 (European Journal of Human Genetics 1999). However, it's increasingly recognized that the incidence rate varies among different ethnic groups, forms of the disease (infantile onset vs late onset Pompe Disease) and countries (Molecular Genetics and Metabolism Reports 2021). With the advent of new-born screening and adoption by several states in the U.S. and elsewhere, more definitive incidence rate data is beginning to be gathered with rates as low as 1:10,152 (Current Treatment Options Neurology 2022). Based on a recent study of population genetic prevalence, the revised estimated incidence rate is now believed to be 1:23,232 (Molecular Genetics and Metabolism Reports 2021). As additional newborn screening data is gathered worldwide, a clearer picture of the disease epidemiology will emerge.

Currently, two products, both ERTs, are approved for the treatment of Pompe disease: alglucosidase alfa and avalglucosidase alfa-ngpt by Sanofi Aventis.

Strategic Alliances and Arrangements

We will continue to evaluate business development opportunities as appropriate to build stockholder value and provide us with access to the financial, technical, clinical, and commercial resources and intellectual property necessary to develop and market technologies or products with a focus on rare and orphan diseases. We are exploring potential collaborations, alliances, and various other business development opportunities on a regular basis. These opportunities may include business combinations, partnerships, the strategic out-licensing of certain assets, or the acquisition of preclinical-stage, clinical-stage, or marketed products or platform technologies consistent with our strategic plan to develop and provide therapies to patients living with rare and orphan diseases.

Intellectual Property

Patents and Trade Secrets

Our success depends in part on our ability to maintain proprietary protection surrounding our product candidates, technology, and know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by filing U.S. and foreign patent applications related to our proprietary technology, including both new inventions and improvements of existing technology, that are important to the development of our business, unless this proprietary position would be better protected using trade secrets. Our patent strategy includes obtaining patent protection, where possible, on compositions of matter, methods of manufacture, methods of use, combination therapies, dosing and administration regimens, formulations, therapeutic monitoring, screening methods, and assays. We also rely on trade secrets, know-how, continuing technological innovation, in-licensing, and partnership opportunities to develop and maintain our proprietary position. Lastly, we monitor third parties for activities that may infringe our proprietary rights, as well as the progression of third-party patent applications that may have the potential to create blocks to our products or otherwise interfere with the development of our business. We are aware, for example, of U.S. patents, and corresponding international counterparts, owned by third parties that contain claims related to ERTs, and small molecules for stabilizing enzymes. If any of these patents were to be asserted against us, there is no assurance that a court would find in our favor or that, if we choose or are required to seek a license, a license to any of these patents would be available to us on acceptable terms or at all.

We own or hold license rights to several issued patents and numerous pending and issued applications, filed in the U.S., Europe, Japan, and other jurisdictions that are related to Galafold® and our ongoing clinical programs:

- We own issued U.S. patents that cover the use of migalastat, the active pharmaceutical ingredient in Galafold®, in the treatment of Fabry disease, which expire between 2027 and 2042 and are listed in the FDA Orange Book. Foreign counterparts of the U.S. patents are pending or issued in Europe, Japan, and certain other jurisdictions. Further, we have pending U.S. patent applications, as well as their foreign counterparts covering various aspects of Galafold®, including composition-of-matter methods of treating a patient diagnosed with Fabry disease, and methods of manufacturing. Any patents issuing from these applications will expire between 2036 and 2043. We anticipate listing these patents in the FDA Orange Book if issued.
- We own several issued U.S. patents that cover various aspects of Opfolda™ and Pombiliti™, a pharmacological chaperon/ERT combination in the treatment of Pompe disease, which expire between 2033 and 2037. Several of the issued U.S. patents are listed in the FDA Orange Book for Opfolda™. Foreign counterparts to the issued patents are pending or issued in Europe, Japan, and certain other jurisdictions. We also have pending U.S. patent applications, as well as foreign counterpart applications, covering various aspects of compositions, methods of treatment, methods of manufacture, and formulations. Any patents issuing from these pending applications will expire between 2033 and 2043. We also filed Patent Term Extension application at the U.S. Patent and Trademark Office ("USPTO"), requesting that the term of certain issued U.S. patent covering cipaglucosidase alfa, the active pharmaceutical ingredient in Pombiliti™, be extended pursuant to 35 U.S.C. § 156.
- From our agreement with the University of Pennsylvania ("Penn"), we have a license to Penn’s patent portfolio pertaining to vector and other platform technologies for treating Pompe disease and Fabry disease.

Patent term extensions and adjustments, supplementary protection certificates, and pediatric exclusivity periods are not reflected in the expiration dates listed above and may extend protection.

In addition to our clinical programs, we actively monitor and file patent applications in the U.S. and in foreign countries on relevant technologies and pre-clinical programs. For example, we own or hold license rights to U.S. and foreign patents or patent applications covering the following:

- Next-generation Fabry chaperones;
- Gene therapy protein engineering technology;
- Gene therapy (e.g., Pompe, Fabry) and ERT (e.g., CDKL5) programs and their use to treat specified diseases. We cannot be certain, however, that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents.

- Individual patents extend for varying periods depending on the effective date of filing of the patent application or the date of patent issuance, and the legal term of the patents in the countries in which they are obtained. Generally, patents issued in the U.S. are effective for 20 years from the earliest nonprovisional filing date. This period may be shortened by terminal disclaimer or further extended by patent term adjustment or extension. The term of foreign patents varies in accordance with provisions of applicable local law, but typically is 20 years from the earliest nonprovisional filing date.

The U.S. Drug Price Competition and Patent Term Restoration Act of 1984, and amendments thereto, more commonly known as the Hatch-Waxman Act, provides for an extension of one patent, known as a Hatch-Waxman statutory extension, for each New Chemical Entity ("NCE") to compensate for a portion of the time spent in clinical development and regulatory review. However, the maximum extension is five years and the extension cannot extend the patent beyond 14 years from the New Drug Application ("NDA") approval. Similar extensions are available in European countries, known as Supplemental Protection Certificate ("SPC") extensions, Japan, and other countries. However, in the U.S. we will not know what, if any, extensions are available until a drug is approved. In addition, in the U.S., under provisions of the Best Pharmaceuticals for Children Act, we may be entitled to an additional six-month period of patent protection or market exclusivity for completing pediatric clinical studies in response to an FDA issued Pediatric Written Request before said exclusivities expire.

In the fourth quarter of 2022, we received Paragraph IV Certification Notice Letters from Teva Pharmaceuticals USA, Inc. ("Teva"), Aurobindo Pharma Limited ("Aurobindo"), and Lupin Limited ("Lupin") in connection with Abbreviated New Drug Applications (“ANDA”) filed with the FDA requesting approval to market generic Galafold®. In November 2022, we filed four lawsuits against Teva, Lupin, and Aurobindo in the U.S. District Court for the District of Delaware for infringement of our Orange Book-listed patents and will vigorously enforce our Galafold® intellectual property rights. Lupin, Aurobindo and Teva supplemented their Paragraph IV Certifications in 2023. In the fourth quarter of 2023, a stipulation order to stay litigation with respect to Lupin was ordered. Additionally, in the first quarter of 2024, a stipulation was filed with the court and approved by the presiding judge, whereby the parties agreed to accept our definition of the terms that were in dispute. As such, the scheduled Markman hearing was deemed unneeded and cancelled.

The patent positions of companies like ours are generally uncertain and involve complex legal, technical, scientific, and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in promptly filing patent applications on new discoveries, and in obtaining effective claims and enforcing those claims once granted. We focus special attention on filing patent applications for formulations and delivery regimens for our products in development to further enhance our patent exclusivity for those products. We seek to protect our proprietary technology and processes, in part, by contracting with our employees, collaborators, scientific advisors, and our commercial consultants to ensure that any inventions resulting from the relationship are disclosed promptly, maintained in confidence until a patent application is filed, and preferably until publication of the patent application, and assigned to us or subject to a right to obtain a license. We do not know whether any of our owned patent applications or those patent applications that are licensed to us will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, invalidated, circumvented, or be found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products and reduce the term of patent protection that we may have for our products. Neither we nor our licensors can be certain that we were the first to invent the inventions claimed in our owned or licensed patents or patent applications. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us and the rights granted under any issued patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing, and regulatory review of a potential product, it is possible that any related patent may expire prior to or shortly after commencing commercialization, thereby reducing the advantage of the patent to our business and products.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our trade secret technology and processes, in part, by entering into confidentiality agreements with commercial partners, collaborators, employees, consultants, scientific advisors, and other contractors, and by contracting with our employees and some of our commercial consultants to ensure that any trade secrets resulting from such employment or consulting are owned by us. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be discovered independently by others. To the extent that our consultants, contractors, or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Collaboration and License Agreements

We have acquired rights to develop and commercialize our product candidates through licenses granted by various parties. We have certain obligations under these acquisitions or licensing agreements, including diligence obligations and payments, which are contingent upon achieving various development, regulatory and commercial milestones. Also, pursuant to the terms of some of these license agreements, when and if commercial sales of a product commence, we may be obligated to pay royalties to such third parties on net sales of the respective products.

The following summarizes our material rights and obligations under those licenses:

University of Pennsylvania

In December 2022, we entered into a license agreement with Penn pursuant to which we obtained a license with respect to the pre-clinical research and development of next-generation parvovirus gene therapy products for the treatment of Pompe disease and Fabry disease. Under the agreement, we will be responsible for clinical development and commercialization of the licensed products for the indications and Penn is eligible to receive certain milestone and royalty payments with respect to licensed products for each indication, up to an aggregate of $86.5 million per indication. Royalty payments are based on net sales of licensed products on a licensed product-by-licensed product and country-by-country basis.

GlaxoSmithKline

In July 2012, as amended in November 2013, we entered into an agreement with GlaxoSmithKline ("GSK"), pursuant to which Amicus obtained global rights to develop and commercialize Galafold® as a monotherapy and in combination with ERT for Fabry disease (“Collaboration Agreement”). Under the terms of the Collaboration Agreement, GSK is eligible to receive post-approval and sales-based milestones up to $40 million, as well as tiered royalties in the mid-teens in eight major markets outside the U.S.

Manufacturing

We continue to rely on contract manufacturers to supply the active biopharmaceutical ingredients and finished goods for our products and product candidates. The active biopharmaceutical ingredients and final formulations for these products are manufactured under current Good Manufacturing Practice ("cGMP"). The components in the final formulation for each product are commonly used in other biopharmaceutical products and are well characterized ingredients. Although we rely on contract manufacturers, we have personnel with extensive manufacturing and quality experience to oversee our contract manufacturers. We have implemented appropriate controls for assuring the quality of both active biopharmaceutical ingredients and final drug products. Product specifications will be established in concurrence with regulatory bodies at the time of product registration. Our current arrangement with third-party manufacturers provide sufficient quantities of our program materials to meet anticipated clinical and commercial demands.

Competition

Overview

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. In addition, several large pharmaceutical companies are increasingly focused on developing therapies for the treatment of rare diseases through organic growth, acquisitions, and partnerships. While we believe that our technologies, knowledge, experience, and scientific resources, provide us with competitive advantages, we face potential competition from many different sources, including commercial enterprises, academic institutions, government agencies, and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with both existing and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise associated with research and development, regulatory approvals, and marketing approved products. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient, and/or are less expensive than products that we may develop. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive to buyers.

Major Competitors

Our major competitors include pharmaceutical and biotechnology companies in the U.S. and abroad that have approved therapies or therapies in development for lysosomal storage disorders. Other competitors are pharmaceutical and biotechnology companies that have approved therapies or therapies in development for rare diseases for which pharmacological chaperone technology, or next-generation ERT may be applicable. Additionally, we are aware of several early-stage, niche pharmaceutical, and biotechnology companies whose core business revolves around protein misfolding; however, we are not aware that any of these companies are currently working to develop products that would directly compete with ours. We are also aware of several pharmaceutical and biotechnology companies who are developing various treatments for novel ERTs and gene therapy. The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, convenience, and price.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. The following table lists our principal competitors and publicly available information on the status of their clinical-stage product offerings:

Competitor [1]	Indication	Product	Class of Product	Status	2023 Sales
					(in millions)
	Fabry Disease	Fabrazyme®	ERT	Marketed	€991
	Pompe Disease	Myozyme®/ Lumizyme®	ERT	Marketed	€783
Sanofi	Pompe Disease	Nexviazyme®/ Nexviadyme®	ERT	Marketed	€425
	Fabry Disease	Venglustat	Oral glucosylceramide synthase ("GCS") Inhibitor	Phase 3	N/A
Takeda [2]	Fabry Disease	Replagal®	ERT	Marketed	¥71,300
Chiesi [3]	Fabry Disease	ELFABRIO®	ERT	Marketed	$14.7
Idorsia	Fabry Disease	Lucerastat	Oral GCS Inhibitor	Phase 3	N/A
AceLink	Fabry Disease	AL1211	Oral GCS Inhibitor	Phase 1/2	N/A
Sangamo	Fabry Disease	Isaralgagene civaparvovec	Gene Therapy	Phase 1/2	N/A
4DMT	Fabry Disease	4D-310	Gene Therapy	Phase 1/2	N/A
Bayer	Pompe Disease	ACTUS-101	Gene Therapy	Phase 1/2	N/A
Astellas	Pompe Disease	AT845	Gene Therapy	Phase 1/2	N/A
Roche	Pompe Disease	SPK-3006	Gene Therapy	Phase 1/2	N/A
Maze	Pompe Disease	MZE001	Oral glycogen synthase ("GYS1") Inhibitor	Phase 1/2	N/A

[1] Reflects commercial products and product candidates for which IND has been filed or are in clinical development.
[2] Reflects running 12 month revenue as of December 31, 2023, as Takeda's fiscal year ends on March 31, 2024.
[3] Reflects sales through September 30, 2023.

Government Regulation

FDA Approval Process

In the U.S., biopharmaceutical products, including gene therapies, are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, Public Health Services Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of biopharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to file a marketing application, to issue complete response letters or to not approve pending NDAs or BLAs, or to issue warning letters, untitled letters, Form 483s, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, litigation, government investigation, and criminal prosecution.

Biopharmaceutical product development in the U.S. typically involves nonclinical laboratory and animal tests, the submission to the FDA of an Investigational New Drug application ("IND"), which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required varies substantially based upon the type, complexity, and novelty of the product or disease. Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal studies to assess the characteristics, potential safety, and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The results of preclinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls, and at least one proposed clinical trial protocol. Long-term preclinical safety evaluations, such as animal tests of reproductive toxicity and carcinogenicity, continue during the IND phase of development. Reproductive toxicity studies are required to allow inclusion of women of childbearing potential in clinical trials, whereas carcinogenicity studies are required for registration. The results of these long-term studies would eventually be described in product labeling.

A 30-day review period after the submission and receipt of an IND is required prior to the commencement of clinical testing in humans. The IND becomes effective 30 days after its receipt by the FDA, and trials may begin at that point unless the FDA notifies the sponsor that the investigations are subject to a clinical hold.

Clinical trials usually involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with applicable government regulations, Good Clinical Practice ("GCP"), as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an Institutional Review Board ("IRB"), for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support an NDA or BLA for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on pharmacodynamics effects and effectiveness.

Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication or indications, dosage tolerance, and optimum dosage, and identify common adverse effects and safety risks. If a compound demonstrates evidence of efficacy and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients over longer treatment periods, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

The FDA has established the Office of Tissue and Advanced Therapies within the Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review.

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving gene therapies. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire. NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

After completion of the required clinical testing, an NDA or BLA is prepared and submitted to the FDA for the determination of efficacy and safety. FDA approval of the NDA or BLA is required before marketing of the product may begin in the U.S. The NDA or BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA or BLA is substantial. Under federal law, the submission of most NDAs and BLAs is additionally subject to a substantial application user fee; although for orphan drugs these fees are waived, and the holder of an approved NDA or BLA may also be subject to annual product and establishment user fees. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs and BLAs. Marketing applications are assigned review status during the filing period. Review status could be either standard or priority. Most such applications for standard review are reviewed within 12 months under PDUFA V (two months for filing plus ten months for review). The FDA attempts to review a drug candidate that is eligible for priority review within six months, as discussed below. The review process may be extended by the FDA for three additional months to evaluate major amendments submitted during the pre-specified PDUFA V review clock. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for public review, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA may also undertake an audit of nonclinical and clinical trial sites. The FDA will not approve the product candidate unless compliance with cGMP is satisfactory and the NDA or BLA contains data that provide substantial evidence that the drug is safe and effective in the indication studied and to be marketed. During the product approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product candidate. A REMS could include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the NDA or BLA without a REMS, if required.

After the FDA evaluates the NDA or BLA and the manufacturing facilities, it issues an approval letter or a complete response letter. Complete response letters outline the deficiencies in the submission that prevent approval and may require substantial additional testing or information for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in an amendment submitted to the NDA or BLA, the FDA will then issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type and extent of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA or BLA approval, the FDA may require substantial post-approval commitments or requirements to conduct additional testing and/or surveillance to monitor the drug's safety or efficacy and may impose other conditions, including distribution and labeling restrictions which can materially affect the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained, problems are identified following initial marketing, or post-marketing commitments are not met.

The Hatch-Waxman Act

In seeking approval for a drug through an NDA, applicants are required to list with the FDA certain patent(s) with claims that cover the applicant's product or approved method of use. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug product that has the same route of administration, active ingredients strength, and dosage form as the listed drug and has been shown through bioequivalence testing to be, in most cases, therapeutically equivalent to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed "innovator" drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid is called a Paragraph 4 certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant submits a Paragraph 4 certification to the FDA, the applicant must also send notice of the Paragraph 4 certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph 4 certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph 4 certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

Patent term and data exclusivity run in parallel. An ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired ("New Chemical Entity Market Exclusivity"). Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph 4 certification that challenges a listed patent, in which case the submission may be made four years following the original product approval.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which the FDA cannot grant effective approval of an ANDA based on that listed drug for the same new dosage form, route of administration or combination, or new use.

Other Regulatory Requirements

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, communications regarding unindicated uses, industry-sponsored scientific and educational activities, and promotional activities involving the internet. Products approved under Subpart H or Subpart E carry additional post-marketing considerations and requirements.

Drugs may be promoted only for approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, new safety information, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA, NDA supplement, BLA, or BLA supplement before the change can be implemented. New efficacy claims require submission and approval of an NDA supplement and BLA supplement for each new indication.

The efficacy claims typically require new clinical data similar to those included in the original application. The FDA uses the same procedures and actions in reviewing NDA and BLA supplements as it does in reviewing NDAs and BLAs. Additional exclusivity may be granted for new efficacy claims. Generic ANDAs cannot be labeled for these types of claims until the new exclusivity period expires.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA or BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk evaluation and mitigation strategies, and surveillance to monitor the effects of an approved product, or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to cGMP, after approval. Drug manufacturers and certain subcontractors are required to register their establishments with FDA and certain state agencies and are subject to routine inspections by the FDA during which the agency inspects manufacturing facilities to access compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first NDA or BLA applicant with FDA orphan drug designation for a particular active ingredient to receive FDA approval of the designated drug for the disease indication for which it has such designation, is entitled to a seven-year exclusive marketing period ("Orphan Drug Exclusivity") in the U.S. for that product, for that indication. During the seven-year period, the FDA may not finally approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the license holder cannot supply sufficient quantities of the product. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition, provided that the sponsor has conducted appropriate clinical trials required for approval. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee for the orphan indication.

Pediatric Information

Under the Pediatric Research Equity Act of 2007 ("PREA"), NDAs or supplements to NDAs and BLAs or supplements to BLAs must contain data 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 drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Fast Track Designation

Under the Fast Track program, the sponsor of an IND may request the FDA to designate the drug candidate as a Fast Track drug if it is intended to treat a serious condition and fulfill an unmet medical need. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Once the FDA designates a drug as a Fast Track candidate, it is required to facilitate the development and expedite the review of that drug by providing more frequent communication with and guidance to the sponsor.

In addition to other benefits such as greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA or BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's review period as specified under PDUFA V for filing and reviewing an application does not begin until the last section of the NDA or BLA has been submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

Breakthrough Therapy designation is intended to expedite the development and review of a candidate that is planned for use to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A Breakthrough Therapy designation conveys all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program. The FDA also has an organizational commitment to involve senior management in such guidance.

Priority Review

Under FDA policies, a drug candidate is eligible for priority review, or review within six months from filing for a new molecular entity ("NME") or six months from submission for a non-NME if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis, or prevention of a disease, rather than the standard review of ten months under current PDUFA guidelines. A Fast Track designated drug candidate would ordinarily meet the FDA's criteria for priority review. The FDA makes its determination of priority or standard review during the 60-day filing period after an initial NDA or BLA submission.

Accelerated Approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. This approval mechanism is provided for under 21CRF314 Subpart H and Subpart E. In this case, clinical trials are conducted in which a surrogate endpoint is used as the primary outcome for approval. A surrogate endpoint is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, that 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. This surrogate endpoint substitutes for a direct measurement of how a patient feels, functions, or survives and is considered reasonably likely to predict clinical benefit. Such surrogate endpoints may be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to 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. When the Phase 4 commitment is successfully completed, the biomarker is deemed to be a surrogate endpoint. Failure to conduct required post-approval studies or confirm a clinical benefit during post-marketing studies, could lead the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA, an ANDA, or a BLA. A fourth alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the safety and efficacy data of an existing product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the submission of an NDA for which at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon certain preclinical or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already-approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent as an ANDA applicant. Thus approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph 4 certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Biologics Price Competition and Innovation Act

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which was enacted as part of the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 ("PPACA") created an abbreviated approval pathway for biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-licensed reference biological product via an approved BLA. Biosimilarity to an approved reference product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity is demonstrated in steps beginning with rigorous analytical studies or "fingerprinting", in vitro studies, in vivo animal studies, and generally at least one clinical study, absent a waiver from the Secretary of Health and Human Services. The biosimilarity exercise tests the hypothesis that the investigational product and the reference product are the same. If at any point in the stepwise biosimilarity process a significant difference is observed, then the products are not biosimilar, and the development of a stand-alone NDA or BLA is necessary. In order to meet the higher hurdle of interchangeability, a sponsor must demonstrate that the biosimilar product can be expected to produce the same clinical result as the reference product, and for a product that is administered more than once, that the risk of switching between the reference product and biosimilar product is not greater than the risk of maintaining the patient on the reference product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being evaluated by the FDA. Under the BPCIA, a reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product.

Anti-Kickback, False Claims Laws, the Prescription Drug Marketing Act and Other Regulations

Our activities are subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil False Claims Act, and laws and regulations pertaining to limitations on and reporting of healthcare provider payments (physician sunshine laws). These laws and regulations are interpreted and enforced by various federal, state and local authorities including CMS, the Office of Inspector General for the U.S. Department of Health and Human Services, the U.S. Department of Justice, individual U.S. Attorney offices within the Department of Justice, and state and local governments. These laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order, or arranging for or recommending the purchase, lease or order of, any good or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. civil False Claims Act (which can be enforced through “qui tam,” or whistleblower actions, by private citizens on behalf of the federal government), prohibits any person from, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment of government funds or knowingly making, using or causing to be made or used, a false record or statement material to an obligation to pay money to the government or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the U.S. federal government;
- U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal liability and amends provisions on the reporting, investigation, enforcement, and penalizing of civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of or payment for healthcare benefits, items or services by a healthcare benefit program, which includes both government and privately funded benefits programs; similar to the U.S. 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;

- state laws and regulations, including state anti-kickback and false claims laws, that may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payer, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and
- the Physician Payments Sunshine Act, implemented as the Open Payments program, and its implementing regulations, requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to certain payments made in the preceding calendar year and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; beginning in 2022, applicable manufacturers are required to report such information regarding payments and transfers of value provided, as well as ownership and investment interests held, during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.

Violations of any of these laws or any other governmental regulations that may apply to us, may subject us to significant civil, criminal and administrative sanctions including penalties, damages, fines, imprisonment, and exclusion from government funded healthcare programs, such as Medicare and Medicaid, and/or adverse publicity. Moreover, government entities and private litigants have asserted claims under state consumer protection statutes against pharmaceutical and medical device companies for alleged false or misleading statements in connection with the marketing, promotion and/or sale of pharmaceuticals.

Physician Drug Samples

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act (the "PDMA") imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling, and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

Regulation Outside the U.S.

In addition to regulations in the U.S., we are subject to a variety of regulations in other jurisdictions governing clinical studies, commercial sales, and distribution of our products. Most countries outside the U.S. require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the U.S. before we can commence clinical studies or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval.

To obtain regulatory approval of an orphan drug under the E.U. regulatory system, we are mandated to submit a marketing authorization application ("MAA") to be assessed in the centralized procedure. The centralized procedure, which came into operation in 1995, allows applicants to obtain a marketing authorization that is valid throughout the E.U. It is compulsory for medicinal products manufactured using biotechnological processes, for orphan medicinal products and for human products containing a new active substance which was not authorized in the community before 20 May 2004 (date of entry into force of Regulation (EC) No 726/2004) and which are intended for the treatment of AIDS, cancer, neurodegenerative disorder, or diabetes. The centralized procedure is optional for any other products containing new active substances not authorized in the community before 20 May 2004 or for products which constitute a significant therapeutic, scientific, or technical innovation or for which a community authorization is in the interests of patients at community level. When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the European Medicines Agency ("EMA"), to be assessed by the Committee for Medicinal Products for Human Use ("CHMP"). The procedure results in a commission decision, which is valid in all E.U. member states. Centrally-authorized products may be marketed in all member states. Under the centralized procedure, full copies of the MAA are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's scientific assessment of the medicinal product and prepare draft reports. Once the draft reports are prepared (other experts might be called upon for this purpose), they are sent to the CHMP, whose comments or objections are communicated to the applicant. The rapporteur is therefore the privileged interlocutor of the applicant and continues to play this role, even after the MAA has been granted approval.

The rapporteur and co-rapporteur then assess the applicant's replies, submit them for discussion to the CHMP and, taking into account the conclusions of this debate, prepare a final assessment report. Once the evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the authorization. When the opinion is favorable, it shall include the draft summary of the product's characteristics, the package leaflet and the texts proposed for the various packaging materials. The time limit for the evaluation procedure is 210 days. The EMA then has fifteen days to forward its opinion to the commission. This is the start of the second phase of the procedure: the decision-making process. The Agency sends to the commission its opinion and assessment report, together with annexes containing: the SmPC ("Annex 1"); the particulars of the Marketing Authorization Holder ("MAH") responsible for batch release, the particulars of the manufacturer of the active substance and the conditions of the marketing authorization ("Annex 2"); and the labelling and the package leaflet ("Annex 3"). The annexes are translated into the 22 other official languages of the E.U. During the decision-making process, the commission services verify that the marketing authorization complies with Union law. The commission has fifteen days to prepare a draft decision. The medicinal product is assigned a community registration number, which will be placed on its packaging if the marketing authorization is granted. During this period, various commission directorates-general are consulted on the draft marketing authorization decision.

The draft decision is then sent to the Standing Committee on Medicinal Products for Human Use, (member states have one representative each in both of these committees) for their opinions. The centralized procedure provides for the grant of a single marketing authorization that is valid for all E.U. member states. The "decentralized procedure" provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, 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 cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

We have obtained an orphan medicinal product designation in the E.U. from the EMA for Galafold® for the treatment of Fabry disease and the combination product, ATB200/AT2221, for the treatment of Pompe disease. Applications from persons or companies seeking "orphan medicinal product designation" for products they intend to develop for the diagnosis, prevention, or treatment of life-threatening or very serious conditions that affect not more than 5 in 10,000 persons in the E.U. are reviewed by the Committee for Orphan Medicinal Products ("COMP"). In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating, or serious and chronic condition in the E.U. and that without incentives it is unlikely that sales of the drug in the E.U. would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the E.U. of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation provides opportunities for fee reductions, protocol assistance and access to the centralized procedure before and during the first year after marketing approval. Fee reductions are not limited to the first year after marketing approval for small and medium enterprises. In addition, if a product which has an orphan drug designation subsequently receives EMA marketing approval for the indication for which it has such designation, the product is entitled to orphan market exclusivity, which means the EMA may not approve any other application to market a similar drug for the same indication for a period of 10 years. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Competitors may receive marketing approval of different drugs or biologics for the indications for which the orphan product has exclusivity. In order to do so, however, they must demonstrate that the new drugs or biologics are clinically superior over the existing orphan product. This demonstration of clinical superiority may be done at the time of initial approval or in post-approval studies, depending on the type of marketing authorization granted.

In March 2016, the EMA launched an initiative, the Priority Medicines ("PRIME") scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

We have obtained a positive opinion for our pediatric investigation plan ("PIP") in the E.U. for Galafold® for the treatment of Fabry disease as well. A PIP is a development plan aimed at ensuring that the necessary data are obtained to support the authorization of a medicine for children, through studies in children. All applications for marketing authorization for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. This requirement also applies when a marketing-authorization holder wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized and covered by intellectual property rights. Several rewards and incentives for the development of pediatric medicines for children are available in the E.U. Medicines authorized across the E.U. with the results of studies from a PIP included in the product information are eligible for an extension of their supplementary protection certificate by six months. This is the case even when the studies' results are negative. For orphan medicines, the incentive is an additional two years of market exclusivity. Scientific advice and protocol assistance at the agency are free of charge for questions relating to the development of pediatric medicines. Medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate are eligible for a pediatric-use marketing authorization ("PUMA"). If a PUMA is granted, the product will benefit from 10 years of market protection as an incentive.

Effective January 1, 2021, following the U.K. exit of the E.U., the MHRA is the U.K.'s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules apply in Northern Ireland than in England, Wales and Scotland (together Great Britain, "GB"); broadly, Northern Ireland continues to follow the E.U. regulatory regime, but its national competent authority remains the MHRA. The MHRA has published a draft guidance outlining the various aspects of the U.K. regulatory regime for medicines in GB and in Northern Ireland. The guidance includes clinical trials, marketing authorizations, importing, exporting and pharmacovigilance and is relevant to any business involved in the research, development or commercialization of medicines in the U.K. The new guidance has been given effect via the Human Medicines Regulations ("Amendment etc.") ("E.U. Exit") Regulations 2019 (the "Exit Regulations"). The U.K. regulatory regime largely mirrors that of the E.U.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing E.U. marketing authorizations ("MAs") for centrally authorized products were automatically converted ("grandfathered") into U.K. MAs free-of-charge on January 1, 2021. Amicus has completed the necessary baseline submission for conversion and was granted Marketing Authorization on August 4, 2021 for Galafold® with an effective date of January 1, 2021.

There is no pre-marketing authorization orphan designation. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the GB market, e.g. the prevalence of the condition in GB (rather than the E.U.) must not be more than 5 in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB or E.U./European Economic Area, wherever is earliest. Galafold® and Pombiliti™ + Opfolda™ have been granted orphan designation by the MHRA.

The PIP application process for applicants is simplified by offering an expedited assessment where possible, and by mirroring the submission format, content and terminology of the E.U.-PIP system. The MHRA is taking decisions on PIP and waiver opinions, modifications and compliance statements to support pediatric market authorization decisions, while acknowledging that Northern Ireland continues to be part of the E.U.'s system for pediatric medicines development including agreement of E.U. PIPs or waivers.

The MHRA has maintained the early access to medicine scheme ("EAMS"). EAMS is designed to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization when there is a clear unmet medical need. Medicines with a positive EAMS opinion could be made available to patients 12-18 months ahead of formal marketing authorization. As the initial step in this process, the applicant must apply for and be granted a Promising Innovative Medicine ("PIM") designation. The designation is issued after an MHRA scientific designation meeting on the basis of non-clinical and clinical data available on the product, in a defined disease area. Following designation, the applicant is expected to complete a clinical development program within a reasonable time period, in order to continue with an application under the EAMS. In January 2020, the MHRA issued a PIM designation for AT-GAA for the treatment of late-onset Pompe disease and subsequently granted a positive opinion under EAMS in June 2021.

We have obtained orphan drug designation in Japan for migalastat for the treatment of Fabry Disease. We also have other Orphan Drug applications approved in other world markets including Switzerland, Australia, South Korea and Taiwan. The Ministry of Health, Labor, and Welfare, based on the opinion of the Pharmaceutical Affairs and Food Sanitation Council, grants orphan status to drugs intended to address serious illnesses with high unmet medical need that affect fewer than 50,000 patients in Japan. In 2020, orphan drug designation was granted in Japan for AT-GAA for the treatment of Pompe disease. Orphan designation provides certain benefits and incentives, including priority review for marketing authorization and a period of 10 years of market exclusivity if the drug candidate is approved for the designated indication.

U.S. Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or the FCPA, generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our industry is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently, the Securities and Exchange Commission ("SEC") and Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. Violations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Enforcement actions may be brought by the Department of Justice or the SEC, and recent enacted legislation has expanded the SEC's power to seek disgorgement in all FCPA cases filed in federal court and extended the statute of limitations in SEC enforcement actions in intent-based claims such as those under the FCPA from five years to ten years.

United States Healthcare Reform

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system, including implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the Affordable Care Act that have been implemented since enactment and are of importance to the commercialization of our products and product candidates, if approved, are the following:

- an annual, nondeductible fee on any entity that manufactures, or imports specified branded prescription drugs or biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the U.S. civil False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- 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;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements to report certain financial arrangements with physicians and teaching hospitals;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been significant ongoing judicial, administrative, executive and legislative efforts to modify or eliminate the Affordable Care Act. For example, the Tax Act enacted on December 22, 2017, repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code, commonly referred to as the individual mandate. Other legislative changes have been proposed and adopted since passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than $1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or the CARES Act, which was designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 to March 31, 2022 and adjusted the sequester to 1% for the period between April 1, 2022 and June 30, 2022. As of July 2, 2022, the 2% sequester reduction resumed. The sequester will remain in place through 2030. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The Affordable Care Act has also been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court. On June 17, 2021, the Supreme Court ruled that the plaintiffs lacked standing to challenge the law as they had not alleged personal injury traceable to the allegedly unlawful conduct. As a result, the Supreme Court did not rule on the constitutionality of the ACA or any of its provisions.

Further changes to and under the Affordable Care Act remain possible but it is unknown what form any such changes or any law proposed to replace or revise the Affordable Care Act would take, and how or whether it may affect our business in the future. We expect that changes to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry. We also expect that the Affordable Care Act, as well as other healthcare reform measures that have 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 our products and product candidates, if approved. Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers.

The Inflation Reduction Act of 2022 (the "IRA") contains substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D to penalize price increases that outpace inflation, and requires manufacturers to provide discounts on Part D drugs. Substantial penalties can be assessed for noncompliance with the drug pricing provisions in the IRA. Orphan drugs that treat only one rare disease are exempt from the IRA's drug negotiation program. The IRA could have the effect of reducing the prices we can charge and reimbursement we receive for our products, if approved, thereby reducing our profitability, and could have a material adverse effect on our financial condition, results of operations, and growth prospects. The effects of the IRA on our business and the pharmaceutical industry in general is not yet known.

Human Capital

At Amicus, one of our founding principles is that we believe in each other to foster teamwork and respect for each individuals' contribution. Our passion for making a difference unites us. Supporting our global employees and valuing their differences is an essential part of the core values and culture at Amicus. Tied to these values and culture, we believe our success and our ability to help patients depends on our capability to attract, develop and retain key personnel.

We are committed to fostering an inclusive workplace where every voice is heard and valued, resulting in a dimensional way of thinking that is used when meeting Company goals. This ensures that every employee feels they are treated fairly which is evidenced through our most recent engagement survey where we came within 2% of the global benchmark for Justice/ Fairness.

As of December 31, 2023, we had 517 full-time employees. As of December 31, 2023, 58% of our global workforce, 31% of our executive management team and 30% of our Board of Directors were women. We are committed to ensuring a diverse, equitable, and inclusive culture where all employees are provided equal opportunities.

Our Mission to 'Always Put Patients First' helps keep our employees engaged with this sense of purpose. We support engagement through communicating frequently and transparently with our employees through a variety of communication methods, including video and written communications, town hall meetings, round tables, employee pulse surveys, and Company intranet, and we acknowledge individual contributions through a number of reward and recognition programs. We believe these engagement efforts keep employees informed about our strategy, culture and purpose and motivated to do their best work.

We believe in a strong compliance culture and provide robust trainings to employees on our code of conduct and the various policies contained therein. As part of our commitment to our employees, these trainings cover our zero-tolerance policy

towards the use of child labor, forced labor, or other forms of modern slavery, educating our workforce on discrimination and harassment, and periodically refreshing the organization's understanding of our global anti-bribery and corruption policy.

We support and develop our employees through global development programs that build and strengthen employees' leadership skills through global leadership development programs, targeted development for high-potential talent, development plans and career paths, tuition reimbursement, and the ability to attend industry conferences and trainings, and patient-mission focused Lunch and Learns. Additionally, we strive to attract and retain the most talented employees in the industry and across the globe by offering competitive compensation and benefits that support their health, financial and emotional well-being. Our compensation philosophy is based on rewarding each employee's individual contributions and striving to achieve equal pay for equal work regardless of gender, race or ethnicity.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. The address of our global headquarters is 47 Hulfish Street, Princeton, NJ 08542 and our telephone number is 609-662-2000. Our website address is *www.amicusrx.com*. We make available free of charge on our website our annual, quarterly, and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the U.S. Securities and Exchange Commission.

Information relating to our corporate governance, including our Code of Business Conduct for Employees, Executive Officers and Directors (the "Code of Conduct"), Corporate Governance Guidelines, and information concerning our senior management team, Board of Directors, including Board Committees and Committee charters, and transactions in our securities by directors and executive officers, is available free of charge on our website at *www.amicusrx.com* under the "Investors — Corporate Governance" caption and in print to any stockholder upon written request to our Chief Legal Officer at the address set forth on the cover of this Annual Report. Any waivers or material amendments to the Code will be posted promptly on our website.

ITEM 1A. RISK FACTORS

You should carefully consider these risk factors, together with all of the other information included in this Annual Report on Form 10-K, including our Consolidated Financial Statements and the related notes thereto, before you decide whether to make an investment in our securities. The risks set forth below are not the only risks we face. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially and adversely affect our business, prospects, financial condition, cash flows, liquidity, funds from operations, results of operations, stock price and ability to service our indebtedness. In such case, the value of our common stock and the trading price of our securities could decline, and you may lose all or a significant part of your investment. Some statements in the following risk factors constitute forward looking statements. Please refer to the explanation of the qualifications and limitations on forward-looking statements under "Forward-Looking Statements" of this Form 10-K.

Risks Related to our Ability to Generate and Sustain Revenue

We depend heavily on sales of our first product, Galafold®, in Europe, the U.S., Japan, and other geographies. Moreover, if we are unable to commercialize Galafold® successfully, or experience significant delays in doing so, our business could be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of Galafold® for the treatment of Fabry disease and rely upon sales of Galafold® primarily in Europe and growing sales in the U.S., Japan, and other geographies. Our ability to generate material product revenues will depend heavily on the successful development, regulatory approval, and commercialization of Galafold®. We will continue to study Galafold® in Phase 4 studies. If the results of the Phase 4 studies negatively change the benefit/risk profile of Galafold®, the commercial success of Galafold® may be substantially diminished. Any adverse market event with respect to Galafold®, including failure to obtain and maintain sufficient market acceptance, could have a material adverse effect on our business, financial condition and results of operations. If our sales of Galafold® were to decrease, or such sales were substantially or completely displaced in the market, or if we are unable to achieve and maintain sufficient market acceptance of Galafold® by physicians, patients, third-party payors and others in the medical community, or if we fail to receive commercial approval in any additional jurisdictions, it could have a material adverse effect on our business, financial condition and results of operations. In addition, if Galafold® or similar products from our competitors were to become the subject of litigation and/or an adverse governmental action requiring us or such competitors, as applicable, to cease sales of Galafold®, such an event could have a material adverse effect on our business, financial condition and results of operations. In addition, the entry into the market of competitors with new or generic treatments, including oral, ERT and gene therapies, may erode the market for Galafold® and have a material impact on our business.

Any delay or impediment in our ability to obtain regulatory approval in any region to commercialize, or, when approved, obtain coverage and adequate reimbursement from third parties, including government payors, for Galafold® may cause us to be unable to meet our revenue guidance or to generate the revenues necessary to continue our research and development pipeline activities, thereby adversely affecting our business and our prospects for future growth.

Further, the success of Galafold® will depend on a number of factors, including the following:

- obtaining a sufficiently broad label in each territory that would not unduly restrict patient access;
- obtaining additional foreign approvals for Galafold®;
- continuing to build and maintain an infrastructure capable of supporting product sales, marketing, and distribution of Galafold® in the U.S., Europe, Japan and other territories where we pursue commercialization directly;
- maintaining commercial manufacturing arrangements with third-party manufacturers;
- maintaining commercial distribution agreements with third-party distributors;
- launching commercial sales of Galafold®, where approved, whether alone or in collaboration with others;
- acceptance of Galafold®, where approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including potential generics and gene therapies;

- successfully identifying new patients who could benefit from Galafold®;
- a continued acceptable safety profile of Galafold®;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting and enforcing our rights in our intellectual property portfolio; and
- obtaining and maintaining a commercially viable price.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize Galafold®, which would materially harm our business and ability to meet our financial goals and debt covenants.

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

Our products, Galafold® and Pombiliti™ + Opfolda™, and product candidates and the activities associated with their development and commercialization, including their testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, commercialization and reimbursement are subject to comprehensive regulation by the European Medicines Agency ("EMA"), the Pharmaceutical and Medical Devices Agency ("PMDA"), the Food and Drug Administration ("FDA"), and other regulatory agencies in the U.S. and by comparable authorities in other countries. Failure to obtain regulatory approval for our products and product candidates will prevent us from commercializing our products in jurisdictions beyond those in which we have obtained regulatory approval for our product or in any jurisdictions for our product candidates.

Securing marketing approval for all our product candidates, requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. We will continue to rely on third parties to assist us with filing and supporting the applications necessary to obtain marketing approvals for product candidates in this process. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that any of our products or product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.

Obtaining approval for all of our product candidates, whether those currently in our pipeline or those we acquire or in-license in the future, is highly uncertain and we may fail to obtain regulatory approval in any or all jurisdictions. The review processes and the processes of regulatory authorities, including the FDA, EMA and PMDA, are extensive, lengthy, expensive, and uncertain, and such regulatory authorities may delay, limit, or deny the approval of any of our product candidates for many reasons, including, but not limited to:

- our failure to demonstrate to the satisfaction of the applicable regulatory authorities that any of our product candidates, are safe and effective for a particular indication;
- the results of clinical trials may not meet the level of statistical significance or other efficacy or safety parameters required by the applicable regulatory authorities for approval;
- the applicable regulatory authority may disagree with the number, design, size, conduct, or implementation of our clinical trials or conclude that the data fail to meet statistical or clinical significance;
- the applicable regulatory authority may not find the data from preclinical studies and clinical trials sufficient to demonstrate that the product candidate's clinical and other benefits outweigh its safety risks;
- the applicable regulatory authority may disagree with our interpretation of data from preclinical studies or clinical trials, and may reject conclusions from preclinical studies or clinical trials, or determine that primary or secondary endpoints from clinical trials were not met, or reject safety conclusions from such studies or trials;
- the applicable regulatory authority may not accept data generated at one or more of our clinical trial sites;
- the applicable regulatory authority may determine that we did not properly oversee our clinical trials or follow the regulatory authority's advice or recommendations in designing and conducting our clinical trials;

- an advisory committee, if convened by the applicable regulatory authority, may recommend against approval of our application or may recommend that the applicable regulatory authority require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, or even if an advisory committee, if convened, makes a favorable recommendation, the respective regulatory authority may still not approve the product candidate;
- the applicable regulatory authority may only approve a limited label for less than the full indicated population, as a second line or rescue therapy, or impose other label restrictions; and
- the applicable regulatory authority may identify deficiencies in the chemistry, manufacturing, and control sections of our application, our manufacturing processes, facilities, or analytical methods or those of our third-party contract manufacturers or be unable to complete any necessary manufacturing inspections of our third-party manufacturers which may lead to significant delays in the approval of our product candidates or to the rejection of our applications altogether.

The process of obtaining marketing approvals is expensive, may take many years, 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 product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process 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. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we are unable to establish and maintain sales and marketing capabilities or enter into agreements with third parties to market and sell our products or product candidates, if approved, we may not be successful in commercializing Galafold®, Pombiliti™ + Opfolda™, or any product candidate if and when they are approved.

To achieve commercial success for any approved product, we must continue to develop and maintain a sales and marketing organization or outsource commercialization to third parties. We have established our own sales and marketing capabilities to promote Galafold® in Europe, Japan, the U.S. and other foreign jurisdictions with a targeted sales force and have leveraged these resources to support the launch of Pombiliti™ + Opfolda™ in those same jurisdictions. We anticipate using these capabilities to support other product candidates if approved. We have also entered into distribution agreements with third parties to market our products in jurisdictions in which we do not have our own sales and marketing capabilities. There are risks involved with establishing and maintaining our own sales and marketing capabilities and entering into arrangements with third parties to perform these services for our products or any of our product candidates, if approved. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate, if approved, for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Similarly, if we enter into agreements with third parties, including the out licensing of our products or product candidates, we may choose to reduce or eliminate our sales and marketing operations and thereby lose our commercialization investment.

Factors that may inhibit our efforts to successfully commercialize Galafold®, Pombiliti™ + Opfolda™, or our product candidates if and when they are approved by regulatory authorities, on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization;
- misconduct by independent sales and marketing organizations that expose us to fines, penalties and other restrictions on our ability to effectively market and sell our products; and

- efforts by our competitors to commercialize products at or about the time when our product candidates would be coming to market.

We may also co-promote or out license our products or product candidates, if approved, in various markets with pharmaceutical and biotechnology companies in instances where we believe that a larger sales and marketing presence will expand the market or accelerate penetration. If we do enter into co-promote or out licensing arrangements with third parties, our product revenues will be lower than if we directly sold and marketed our products and any revenues received under such arrangements will depend on the skills and efforts of others.

We may not be successful in entering into distribution arrangements and marketing alliances with third parties. Our failure to enter into these arrangements on favorable terms could delay or impair our ability to commercialize our products and product candidates, if approved, and could increase our costs of commercialization. Dependence on distribution arrangements and marketing alliances to commercialize our products and product candidates will subject us to a number of risks, including:

- we may not be able to control the amount and timing of resources that our distributors may devote to the commercialization of our products or product candidates, if approved;
- our distributors may experience financial difficulties;
- our distributors may experience compliance related issues and associated government investigations;
- our distributors may require transfer of the marketing authorization for our products and product candidates, if approved, and may refuse to relinquish them at the end of the distribution relationship;
- our distributors may be out of compliance with applicable anti-bribery and corruption laws with an adverse effect on operations and expose us to liability;
- business combinations or significant changes in a distributor's business strategy may also adversely affect a distributor's willingness or ability to complete its obligations under any arrangement; and
- these arrangements are often terminated or allowed to expire, which could interrupt the marketing and sales of a product and decrease our revenue.

If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue at our current guidance, meet our debt obligations, and may not ever become profitable.

If the market opportunities for our products or product candidates are smaller than we believe they are, then our revenues may be adversely affected, and our business may suffer.

Each of the diseases that our products and product candidates are being developed to address is rare and by definition has small patient populations. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products and product candidates are based on estimates.

Currently, most reported estimates of the prevalence of these diseases are based on studies of small subsets of the population of specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the broader world population. In addition, as new studies are performed the estimated prevalence of these diseases may change. There can be no assurance that the prevalence of Fabry disease, Pompe disease, or other rare diseases in the study populations, particularly in these newer studies, accurately reflects the prevalence of these diseases in the broader world population. If our estimates of the prevalence of Fabry disease, Pompe disease, or other rare diseases or of the number of patients who may benefit from treatment with our products or product candidates prove to be incorrect, the market opportunities for our products and product candidates, if approved, may be smaller than we believe they are, our prospects for generating revenue at our guidance levels may be adversely affected and our business may suffer.

Galafold® and Pombiliti™ + Opfolda™, or any of our product candidates that receive regulatory approval, may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Galafold® and Pombiliti™ + Opfolda™, as well as any of our product candidates that receive regulatory approval may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to competitive or alternative treatments, including generics and gene therapies;
- the prevalence and severity of any side effects;
- the ability to offer our products and product candidates, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- competition from other products for the same or similar indications; and
- sufficient third-party coverage or reimbursement.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the U.S., E.U., U.K. and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of Galafold®, Pombiliti™ + Opfolda™ and any of our product candidates that receive marketing approval, and we may fail to meet our revenue targets as a result.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current products, Galafold®, Pombiliti™ + Opfolda™ and product candidates, as well as any products we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology and gene therapy companies worldwide. For example, several large pharmaceutical and biotechnology companies currently market and sell products for the treatment of lysosomal storage disorders, including Fabry disease and Pompe disease. These Fabry products include Sanofi Aventis' Fabrazyme®, Takeda's Replagal®, and Chiesi's Elfabrio, as well as other Fabry treatment products in development. As of 2022, Galafold® also faces potential generic competition, with Hatch-Waxman litigation currently on-going. In addition, Sanofi markets and sells Myozyme®, Lumizyme®, Nexviazyme®, and Nexviadyme® for the treatment of Pompe disease. We are also aware of other enzyme replacement and substrate reduction therapies in development by third parties for Fabry and Pompe, as well as potential gene therapies for both Fabry and Pompe and our other product candidates.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or noncompetitive. Our competitors may also obtain FDA, EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours, could achieve regulatory exclusivity and block us from approval and marketing our products for a significant period of time. We may also face competition from off-label use of other approved therapies. There can be no assurance that developments by others will not render our product candidates or any acquired products obsolete or noncompetitive either during the research phase or once the products reach commercialization.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, prosecuting intellectual property rights and marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs or advantageous to our business. In addition, if we obtain regulatory approvals for our product candidates, manufacturing efficiency and marketing capabilities are likely to be significant competitive factors. We currently rely on third-party manufacturers for our products and all of our product candidates. Further, many of our competitors have substantial resources and expertise in conducting collaborative arrangements, sourcing in-licensing arrangements, manufacturing and acquiring new business lines or businesses that are greater than our own.

A variety of risks associated with international operations could materially adversely affect our business.

Galafold®, Pombiliti™ + Opfolda™, and any of our product candidates that may be approved in the future for commercialization in the E.U., U.K. or in other foreign countries are or will be subject to additional risks related to international operations or entering into international business relationships, including:

- different regulatory requirements for maintaining approval of drugs in foreign countries;
- reduced protection for contractual and intellectual property rights in some countries;
- unexpected changes in taxes, tariffs, trade barriers and regulatory requirements;
- economic weakness, including rising interest rates, inflation and political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- our ability, and our commercialization partners ability, to comply with local laws, rules and regulations, including those relating to modern slavery;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anti-corruption laws in other jurisdictions;
- tighter restrictions on privacy and the collection and use of patient data; and
- business interruptions resulting from geopolitical actions (including war and terrorism), pandemic diseases, or natural disasters (including earthquakes, typhoons, floods and fires).

Moreover, there are complex regulatory, tax, labor and other legal requirements imposed by the E.U., U.K., and many of the individual countries in Europe, Asia and Latin America with which we will need to comply. Many U.S.-based biopharmaceutical companies have found the process of marketing their own products in Europe and other international geographies to be very challenging.

In addition, Pombiliti™ is currently manufactured in the People's Republic of China ("PRC") by WuXi Biologics Co., Ltd. ("WuXi"). The PRC, and WuXi specifically, has faced increased scrutiny by the U.S. government, which could impact our ability to supply Pombiliti™ to meet our forecasted future demand, as WuXi is our sole supplier. This risk is discussed in greater detail below under the heading "Risks Related to the Manufacture of our Products and Product Candidates and our Dependence on Third Parties".

Following the receipt of marketing approval of our products or any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations and practices that govern marketing approvals, pricing, commercialization, coverage and reimbursement for new drug products vary widely from country to country and product to product. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries, including almost all of the member states of the European Economic Area, require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, including the European market, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted and approved products are subject to re-reviews, class reviews and other governmental controls which can negatively impact pricing originally approved. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact any revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. This is particularly true in the case of gene therapies for which payors and manufacturers must develop different pricing models for this growing area. Current pricing for gene therapies may not be sustainable in the future which would have a negative impact on our revenues and business.

Our ability to successfully commercialize Galafold®, Pombiliti™ + Opfolda™, or any product candidate if approved, will also depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the European and U.S. healthcare industries and elsewhere is cost containment. It is currently unknown what impact, if any proposed changes by the federal and state governments in the U.S. and similar changes in foreign countries may have on pricing and reimbursement, particularly with respect to government programs such as Medicare and Medicaid and Pharmacy Benefit Managers for commercial plans, and including reimportation, reference pricing and limitations on manufacturer price increases.

Prices at which we or our customers seek reimbursement for our products can be subject to challenge, reduction or denial by the government and other payers. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for pharmaceutical products. We cannot be sure that coverage and reimbursement will continue to be available for Galafold®, Pombiliti™ + Opfolda™, or any product candidate that we commercialize or may commercialize, and if coverage and reimbursement are available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, Galafold®, Pombiliti™ + Opfolda™, or any product candidate for which we obtain marketing approval. Obtaining reimbursement for our product candidates when approved may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients and the pricing and reimbursement of competitive products. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product for which we obtain marketing approval.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system, including implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. In the United States, the Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

There have been significant ongoing judicial, administrative, executive and legislative efforts to modify or eliminate the Affordable Care Act.

Changes to and under the Affordable Care Act remain possible but it is unknown what form any such changes or any law proposed to replace or revise the Affordable Care Act would take, and how or whether it may affect our business in the future. We expect that changes to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry. We also expect that the Affordable Care Act, as well as other healthcare reform measures that have 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 our products and product candidates, if approved. Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers.

Recently, the Inflation Reduction Act of 2022 (the "IRA") contains substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D to penalize price increases that outpace inflation, and requires manufacturers to provide discounts on Part D drugs. Substantial penalties can be assessed for noncompliance with the drug pricing provisions in the IRA. Although the IRA exempts orphan drugs that treat only one rare disease from the drug pricing negotiation provisions, we do not know if additional drug pricing reforms could eliminate this exemption and therefore affect the prices we can charge and reimbursement we receive for our products and product candidates, if approved, thereby reducing our profitability. Any change to the exemption could have a material adverse effect on our financial condition, results of operations, and growth prospects. The effects of the IRA on the pharmaceutical industry in general are not yet known.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted in the U.S. for uses that are not approved by the FDA as reflected in the product's approved labeling or prior to regulatory approval. Further, any labeling approved by the FDA for Galafold®, Pombiliti™ + Opfolda™,or any of our product candidates may include restrictions on use, limit use to specific populations or include various other limitations. The FDA may impose further requirements or restrictions on the distribution or use of any of our other product candidates as part of a Risk Evaluation and Mitigation Strategies ("REMS") plan. Physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label provided the company did not promote such use. If we are found to have promoted such off-label uses, we may become subject to significant liability. Similarly, the FDA strictly regulates the promotion of investigational products prior to approval, known as pre-approval promotion. The federal government has levied large civil and criminal fines and / or other penalties against companies for alleged improper promotion and has investigated and / or prosecuted several companies in relation to off-label and/or pre-approval promotion. The FDA has also requested that certain companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed, curtailed or prohibited or have delayed approval of investigational products due to pre-approval conduct. Inappropriate promotional activities may also subject a company to investigations, prosecutions and litigation by other government entities or private citizens.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the use of our products and product candidates, including risks which may arise from misuse or malfunction of, or design flaws in, such products or product candidates, whether or not such problems directly relate to the products, product candidates and services we have provided. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial and potentially crippling liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product candidates or products that we may develop;

- injury to our reputation and significant negative media attention;
- regulatory investigations, prosecutions or enforcement actions that could require costly recalls or product modifications;
- withdrawal of clinical trial participants;
- regulatory authorities placing ongoing clinical trials on clinical hold;
- significant costs to defend the related litigation;
- increased insurance costs, or an inability to maintain appropriate insurance coverage;
- substantial monetary awards to trial participants or patients, including awards that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available, and would damage our ability to obtain liability insurance at reasonable costs, or at all, in the future;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive and we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. On occasion, large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or a series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our available cash and adversely affect our business including our ability to service our debt and comply with the liquidity and revenue covenants contained therein.

If the FDA or other applicable regulatory authorities approve generic or biosimilar products that compete with our products or any of our product candidates, it could reduce our sales of our products or those product candidates.

In the U.S., after an NDA is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA, or ANDA. The Federal Food, Drug, and Cosmetic Act, or the FD&C Act, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredients, dosage form, strength, route of administration, and conditions of use, or product labeling, as one of our products or product candidates and that the generic product is absorbed in the body at the same rate and to the same extent as, or is bioequivalent to, our product or product candidate. These generic equivalents would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices because they do not need to conduct highly expensive clinical trials to support their ANDA filing. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to our products or product candidates, including Galafold®, would substantially limit our ability to generate revenues or achieve profitability with a negative impact on continued operations. As of the end of 2022, we had received Paragraph 4 certifications from three ANDA filers for Galafold® and had initiated Hatch-Waxman litigation against these ANDA filers. That litigation remains pending. While we strongly believe in our patent protection and will vigorously defend our Galafold® intellectual property rights, there is no guarantee we will prevail in the Hatch-Waxman litigation or any other challenges to our intellectual property. Moreover, we may be compelled to settle this litigation on unfavorable terms with a direct negative impact on our revenue and profitability projections.

The Biologics Price Competition and Innovation Act, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act of 2010. The BPCIA authorizes the FDA to approve "abbreviated" BLAs for products whose sponsors demonstrate they are "biosimilar" to reference products previously approved under BLAs, to which Pombiliti™ is subject. The FDA may also separately determine whether "biosimilar" products are "interchangeable" with their reference products. However, the FDA may not approve an "abbreviated" BLA for a biosimilar product until at least twelve years after the date on which the BLA for the reference product was approved. FDA approval of abbreviated BLAs could be further delayed if the reference products are subject to unexpired and otherwise valid patents.

Accordingly, other manufacturers potentially could develop and seek FDA approval of "biosimilar" products at some point in the future, including a biosimilar of Pombiliti™ or any other product we develop or acquire that is approved under a BLA.

Our competitors may be able to develop and commercialize their products, including products identical to ours, in any ex-U.S. jurisdiction in which we are unable to obtain, maintain, or enforce our patent claims. Furthermore, generic manufacturers may develop, seek approval for and launch generic versions of our products, and may challenge the scope, validity or enforceability of our patents, requiring us to possibly engage in complex, lengthy and costly litigation or other proceedings.

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

As a result of pursuing the development and commercialization of our product and product candidates using our proprietary and licensed technologies, we may fail to develop other products or product candidates, or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success.

Risks Related to our Products and the Regulatory Approval and Clinical Development of our Product Candidates

Our products or product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our products, Galafold® and Pombiliti™ + Opfolda™, or product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA, EMA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our products or product candidates, if approved, and generating revenues from their sale. In addition, if we or others identify undesirable side effects caused by our products or product candidates after receipt of marketing approval:

- regulatory authorities may require the addition of restrictive labeling statements;
- regulatory authorities may withdraw their approval of the product; and
- we may be required to change the way the product is administered, or additional clinical trials are conducted.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or product candidate or could substantially increase the costs and expenses of commercializing the product or product candidate, if approved, which in turn could delay or prevent us from generating significant revenues from its sale and limiting our ability to meet our financial guidance, debt covenants or adversely affect our reputation.

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

Any product or product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA, PMDA and other regulatory authorities. For example, the FDA's requirements include submissions of safety and other post-marketing information and reports, registration requirements, Current Good Manufacturing Practices, or cGMP, requirements relating to manufacturing, quality control, quality assurance and complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to healthcare professionals and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval, including the requirement of a REMS. The FDA also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The labeling, advertising, promotion, marketing and distribution of a drug, biologic, or gene therapy product also must be in compliance with FDA requirements which include, among others, promotional activities, standards and regulations for direct-to-consumer advertising, promotional activities involving the internet, and industry sponsored scientific and educational activities. In general, all product promotion must be consistent with the labeling approved by the FDA for such product, contain a balanced presentation of information on the product's uses, benefits, risks, and important safety information and limitations on use, and otherwise not be false or misleading. The FDA has very broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing a company to correct deviations from regulatory standards and enforcement actions that can include seizures, injunctions and criminal prosecution. Failure to comply with applicable FDA requirements and restrictions also may subject a company to adverse publicity and enforcement action by the FDA, the U.S. Department of Justice ("DOJ") or the Office of the Inspector General of the U.S. Department of Health and Human Services ("HHS") as well as state authorities. This could subject us to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes its products.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- changes to or restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to implement a REMS;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters, untitled letters or Form 483s;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions; or
- the imposition of civil or criminal penalties.

Non-compliance with E.U. and U.K. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the E.U.'s and U.K.'s requirements regarding the protection of personal information can also lead to significant penalties and sanctions and business restrictions.

If we, or our suppliers, third-party contractors, clinical investigators or collaborators are slow to adapt, or are unable to adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, we or our collaborators may lose marketing approval for our products when and if any of them are approved, resulting in decreased revenue from milestones, product sales or royalties.

Our relationships with customers, healthcare providers, patients, patient organizations, charitable foundations and third-party payors are subject to applicable anti-kickback, fraud and abuse, anti-bribery and corruption and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of our products and any product candidates for which we may obtain marketing approval. Increasingly, patients, patient organizations and charitable foundations also can influence selection of and payment for therapies. Our current and future arrangements with payors, healthcare providers, patient organizations, charitable foundations and patients may expose us to broadly applicable fraud and abuse, anti-bribery and corruption, and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products and any product candidates for which we may obtain marketing approval. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal, state and foreign healthcare laws and regulations pertaining to fraud and abuse, anti-bribery and corruption, interaction with patient organizations, charitable foundations, and patients' rights are and will be applicable to our business. Restrictions under applicable federal, state and foreign healthcare laws and regulations may affect our ability to operate and expose us to areas of risk, including:

- U.S. federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Several other countries, including the U.K., have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations;
- U.S. federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. In addition, charitable contributions to foundations for use in supporting patients may expose those foundations and us to additional penalties and prosecution under the False Claims Act. There is also a separate false claims provision imposing criminal penalties. Moreover, the Office of Inspector General ("OIG") issues guidance documents and Advisory Opinions on matters that could give rise to prosecutions, investigations, litigation and/or settlements under the False Claims Act. For example, OIG issued an Advisory Opinion in April 2022 regarding manufacturer support of genetic testing which could form a basis for government scrutiny in certain circumstances. Applicable regulations of both the EMA and E.U. member states also impose liability for failing to comply with fraud and abuse laws or improperly using information obtained in in the course of clinical trials with the EMA or other regulatory authorities;

- U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal liability and amends provisions on the reporting, investigation, enforcement, and penalizing of civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute to defraud any healthcare benefit program or specific intent to violate it in order to have committed a violation. This statute also may impose monetary penalties on any offers or transfers of remuneration to Medicare or Medicaid beneficiaries (patients) which is likely to influence the beneficiary's selection of particular supplier of government payable items. States, such as California have enacted their own privacy regulations and others may enact similar legislation. Similarly, the collection and use of personal health data in the E.U. is governed by the E.U. General Data Protection Regulation (the "GDPR"), with many requirements mandated by the GDPR for the consent of the individuals to whom the personal data relates, the information provided to the individuals, transfer of personal data within and outside of the E.U. and the security and confidentiality of the personal data. Failure to comply with the requirements of the GDPR may result in substantial fines and other administrative penalties. The GDPR increases our 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 the GDPR. This may be onerous and adversely affect our business, financial condition, results of operations and prospects;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- U.S. federal laws requiring drug manufacturers to report annually information related to certain payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists chiropractors, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives) and teaching hospitals, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, commonly known as the Sunshine Act, as well as other state and foreign laws regulating marketing activities and requiring manufacturers to report marketing expenditures, payments and other transfers of value to physicians and other healthcare providers. Similarly, payments made to physicians in certain E.U. 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 and/or the regulatory authorities of the individual E.U. member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the E.U. member states. In addition, 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 prohibited in the E.U. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment;
- U.S. federal government price reporting laws, which require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our marketed drugs. Participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, potential liability for the failure to report such prices in an accurate and timely manner, and potentially limit our ability to offer certain marketplace discounts;

- U.S. Foreign Corrupt Practices Act, which prohibit us and third parties working on our behalf from making payments to foreign government officials to assist in obtaining or retaining business. Specifically, the anti-bribery provisions of the FCPA prohibit the willful use of the mails or any means of instrumentality of interstate commerce corruptly in furtherance of any offer, payment, promise to pay, or authorization of the payment of money or anything of value to any person, while knowing that all or a portion of such money or thing of value will be offered, given or promised, directly or indirectly, to a foreign official to influence the foreign official in his or her official capacity, induce the foreign official to do or omit to do an act in violation of his or her lawful duty, or to secure any improper advantage in order to assist in obtaining or retaining business for or with, or directing business to, any person; enforcement actions may be brought by the Department of Justice or the SEC; legislation has expanded the SEC's power to seek disgorgement in all FCPA cases filed in federal court and extended the statute of limitations in SEC enforcement actions in intent-based claims, such as those under the FCPA, from five years to ten years; and
- state and foreign equivalents of each of the above laws, including foreign anti-bribery and corruption laws and state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers; state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

While we do not submit claims and our customers will make the ultimate decision on how to submit claims, in the U.S. we may provide reimbursement guidance and support regarding Galafold® or Pombiliti™ + Opfolda™, as well as our product candidates for which we receive regulatory approval, to our customers and patients. If a government authority were to conclude that we provided improper advice to our customers and patients and/or encouraged the submission of false claims for reimbursement, we could face action by government authorities. Similarly, if a government authority were to conclude that our patient support efforts or interactions with charitable foundations were improper, we could face action by government authorities. While we have processes and controls to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations, it is nonetheless possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, EMA, PMDA or other foreign regulatory authorities, or do not otherwise produce favorable results, we may experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

In connection with seeking marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. 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 products.

In addition, the regulatory pathways for gene therapies are evolving. In some cases, the FDA will approve gene therapies based on Phase 2 clinical trial data. If, however, the FDA decides we need to complete Phase 3 clinical trial(s), we may need to expend significantly more capital to pursue FDA approval of gene therapies. If we are required to conduct additional clinical trials or other testing of our product candidates or any gene therapies that we develop beyond those tests and trials that we contemplate; if we are unable to successfully complete our clinical trials or other testing; if the results of these trials or tests are not positive or are only modestly positive; or if there are safety concerns, we may:

- choose not to seek regulatory approval in the U.S., E.U., U.K. or other key jurisdictions;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements, safety strategies or restrictions, such as a requirement of a risk evaluation and mitigation strategy, or REMS; or
- have the product removed from the market after obtaining regulatory approval.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential regulatory approval or commercialization of our product candidates, if approved, could be delayed or prevented.

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

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or patients may drop out of these clinical trials at a higher rate than we anticipate;
- we may be unable to enroll a sufficient number of patients in our trials to ensure adequate statistical power to detect any statistically significant treatment effects;
- 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;
- regulators, institutional review boards, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators, institutional review boards, or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the trials.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Each of the diseases that our lead product candidates are intended to treat are characterized by small patient populations, which could result in slow enrollment of clinical trial participants. In addition, our competitors have ongoing clinical trials for product candidates that could be competitive with our product candidates. As a result, potential clinical trial sites may elect to dedicate their limited resources to participation in our competitors' clinical trials and not ours, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the Company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients in any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

Initial results from a clinical trial do not ensure that the trial will be successful and success in preclinical or early stage clinical trials does not ensure success in later-stage clinical trials.

We will only obtain regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable non-U.S. regulatory authority, in well-designed and conducted clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain duration and results. A failure of one or more of our clinical trials may occur at any stage of testing.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Our product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials. For some of our product candidates, we have no safety or efficacy data in humans. There can be no assurance that the results seen in preclinical studies for any product candidates will result in success in clinical trials. When administered in humans, the product candidates may perform differently than in preclinical studies. Product candidates may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies or animal studies, and may interact with human biological systems in unforeseen, ineffective or harmful ways. We may be unable to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials.

Initial results from a clinical trial do not necessarily predict final results. We cannot be assured that these trials will ultimately be successful. In addition, patients may not be compliant with their dosing regimen or trial protocols or they may withdraw from the clinical trial at any time for any reason. In addition, while the clinical trials of our product candidates are designed based on the available relevant information, in view of the uncertainties inherent in drug development, such clinical trials may not be designed with focus on indications, patient populations, dosing regimens, safety or efficacy parameters or other variables that will provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting product candidates. This is particularly the case for emerging gene therapies where we do not yet have a defined regulatory pathway and there can be no assurance that regulators in the U.S., E.U., U.K., Japan or other jurisdictions will accept any gene therapy clinical data sets for approval and without additional clinical trials or that future trials will support approvals. In addition, individual patient responses to the dose administered of a product candidate may vary in a manner that is difficult to predict. Also, the methods we select to assess particular safety or efficacy parameters may not yield statistical precision in estimating our product candidates' effects on study participants. Even if we believe the data collected from clinical trials of our product candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us or our partners, which could delay, limit or prevent regulatory approval.

In addition, certain of our product candidates are based on emerging gene therapy technologies. The FDA may require different endpoints than the endpoints we anticipate using or have used in our clinical trials, or a different analysis of those endpoints, it may be more difficult for us to obtain, or we may be delayed in obtaining, FDA approval of our product candidates. If we are not successful in commercializing any of our products or product candidates, if approved, or are significantly delayed in doing so, our business will be materially harmed.

We may not be able to obtain or maintain orphan drug exclusivity for our products or product candidates. If our competitors are able to obtain orphan drug exclusivity for their products, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the E.U., U.K., and the U.S., may designate drugs for relatively small patient populations as orphan drugs. We obtained orphan drug designations from the FDA for Galafold® for the treatment of Fabry disease in February 2004. We also obtained orphan medicinal product designation in the E.U. and U.K. for Galafold® in May 2006. Pombiliti™ + Opfolda™ has also received this designation from the FDA in 2017, EMA in 2018, and, in 2020, from PMDA. Our competitors have also received orphan designations. However, these orphan designations may be retracted following regulatory review of our or our competitor’s marketing authorization and/or BLA submissions and may not be reflected in the final approval of a product. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which, subject to certain exceptions, precludes the EMA from approving another marketing application for a similar medicinal product or the FDA from approving another marketing application for the same drug for the same indication for that time period. The FDA defines “same drug” as a drug or biologic that contains the same active moiety and is intended for the same use. The applicable market exclusivity period for orphan drugs is ten years in the E.U. and U.K. and seven years in the U.S. The E.U. and U.K. exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified.

In the E.U. and U.K., a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. If a competitor to our product candidates obtains orphan drug exclusivity for and approval of a product with the same indications as our product candidates before we do, and if the competitor's product is the same drug or a similar medicinal product as ours, we could be excluded from the market for a certain period of time.

Even if we obtain orphan drug exclusivity for other product candidates in these indications, we may not be able to maintain it. For example, if a competitive product that is the same drug or a similar medicinal product as our product or product candidate is shown to be clinically superior to our product or product candidate, as applicable, any orphan drug exclusivity we have obtained will not block the approval of such competitive product. In addition, orphan drug exclusivity will not prevent the approval of a product that is the same drug as our product or product candidate if the FDA finds that we cannot assure the availability of sufficient quantities of the drug to meet the needs of the persons with the disease or condition for which the drug was designated.

The FDA Reauthorization Act, signed into law in August 2017, authorizes the FDA to impose additional clinical trial requirements on manufacturers seeking orphan drug designation and/or pediatric indications. Galafold® and Pombiliti™ + Opfolda™ have obtained orphan drug designations from the FDA. The impact, however, of future regulations on other product candidates is uncertain and could result in the need for additional clinical trials.

Failure to obtain or maintain regulatory approval in foreign jurisdictions would prevent us from marketing our products abroad.

In order to market and sell our products in Europe and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, some countries outside the U.S. require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We may not obtain marketing, pricing or reimbursement approvals outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Regulatory approvals in countries outside the U.S. do not ensure pricing approvals in those countries or in any other countries, and regulatory approvals and pricing approvals do not ensure that reimbursement will be obtained. Moreover, our therapy for the treatment of Pompe disease is comprised of two components, an ERT (Pombiliti™) and a small molecule (Opfolda™). Full marketing approval is required for both components in each jurisdiction that we seek to commercialize in and a failure to secure marketing approval for either in a given target geography could materially harm our business and results of operations.

Our gene therapy product candidates are based on novel technologies, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

Only a few gene therapy products have been approved in the U.S., E.U., and U.K. We have acquired the rights to potential gene therapies and have historically focused a substantial amount of our research and development efforts on these gene therapy platforms. There can be no assurance that any development problems we experience in the future related to our gene therapies will not cause significant delays or unanticipated costs, or that such development problems can be solved. In addition, the clinical study requirements of the FDA, the EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as our gene therapies can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. There is no guarantee that our potential gene therapies will ever receive regulatory approval, that we will have the resources to develop these therapies, that we will recoup our investments made in gene therapies, that we will meet any projected timelines for development or that we will continue to pursue these therapies.

Risks Related to the Manufacture and Distribution of our Products and Product Candidates and our Dependence on Third Parties

Use of third parties to manufacture our products or product candidates may increase the risk that we will not have sufficient quantities of our products or product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate manufacturing facilities for clinical or commercial production of our products or product candidates. We currently lack the resources and the capabilities to manufacture ourselves on a clinical or commercial scale. If we choose in the future to manufacture ourselves, we would face all of the risks and uncertainties of third-party manufacturers of our products. We currently outsource all manufacturing and packaging of our products and product candidates to third parties. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. In particular, the manufacture of our biologic product for Pompe is highly complex and we may encounter difficulties in production. These problems include difficulties with production costs and yields and quality control, including stability of the product or product candidate. The occurrence of any of these problems could significantly delay our clinical trials or the commercial availability of our products or product candidates.

We may be unable to enter into agreements for commercial supply with third-party manufacturers or may be unable to do so on acceptable terms. Even if we enter into these agreements, the manufacturers of each product or product candidate will be single source suppliers to us for a significant period of time.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third-party for regulatory compliance and quality assurance, including with their own vendors with which we do not have a contractual relationship;
- limitations on supply availability resulting from capacity, scheduling constraints, and geographic of the third parties;
- inability to manufacture product that meets the regulatory requirements for product approval;
- inability to manufacture batches that meet specifications and quality standards;
- inability to hire and retain the skilled workers necessary to manufacture our products;
- inability to meet environmental sustainability requirements;
- impact on our reputation in the marketplace if manufacturers of our products, once commercialized, fail to meet the demands of our customers;
- the possible breach of the manufacturing agreement by the third-party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the high cost of manufacturing processes and raw materials; and
- the possible termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us.

The failure of any of our contract manufacturers to maintain high manufacturing standards could result in injury or death of clinical trial participants or patients using products. Such failure could also result in product liability claims, product recalls, product seizures or withdrawals, delays or failures in testing or delivery, cost overruns or other problems that could seriously harm our business or profitability.

The FDA and regulatory authorities in other jurisdictions require our contract manufacturers to comply with cGMP regulations. These regulations cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our product candidates and any products that we may commercialize, including Galafold®, Pombiliti™ + Opfolda™, and our gene therapy product candidates. The FDA and other regulatory authorities may, and often will, require the inspection of our contract manufacturers in order to approve, or maintain the approval of, our products or product candidates, including Galafold® and Pombiliti™ + Opfolda™. Different geopolitical situations or other unforeseeable events could impact the FDA, or other regulatory authorities, ability to timely inspect such contract manufacturers and such delays could materially harm our business and accuracy of our financial guidance projections.

Our contract manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the U.S. Our failure or the failure of our third-party manufacturers, to comply with applicable regulations could significantly and adversely affect regulatory approval and supplies of our products and product candidates. Our products and product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing our products and product candidates.

The majority of our preclinical, clinical and commercial products, including Galafold® and Pombiliti™, are manufactured by single source third-party manufacturers. If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us or in a timely fashion. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop and commercialize our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins, our ability to meet our obligations under our credit facility, and our ability to develop product candidates and commercialize any products that receive regulatory approval on a timely and competitive basis.

We rely on third parties to distribute our products, and those third parties may not perform satisfactorily, including failing to deliver products to meet demand.

We do not distribute our products ourselves and rely on third parties for the delivery of clinical and commercial products to our customers and patients. Any of these third parties may experience delays in the delivery of our products, may be unable to deliver the products or may not comply with the appropriate delivery conditions. Failure to deliver our products may adversely affect our future profit margins, our ability to meet our obligations under our credit facility and our ability to develop and commercialize our products.

We rely on third parties to conduct certain preclinical development activities and our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials for our product candidates or certain preclinical development activities of our product candidates. We rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators and collaboration partners to perform these functions. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for certain preclinical and clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. The FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register certain ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within particular timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Similar GCP and transparency requirements apply in the E.U. and U.K. Failure to comply with such requirements, including with respect to clinical trials conducted outside the E.U., U.K. and U.S., can also lead regulatory authorities to refuse to take into account clinical trial data submitted as part of an MAA.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

We also rely on other third parties to obtain, store and distribute drug supplies for our preclinical development activities and clinical trials. In addition, in some instances we are required to purchase clinical supplies from our competitors, who may refuse to allow this purchase or do so at prohibitively high prices. Any performance failure on the part of our distributors or inability to secure supply from our competitors could delay preclinical and clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

Extensions, delays, suspensions or terminations of our preclinical development activities or our clinical trials as a result of the performance of our independent clinical investigators and CROs will delay, and make more costly, regulatory approval for any product candidates that we may develop or acquire. Any change in a CRO during an ongoing preclinical development activity or clinical trial could seriously delay that trial and potentially compromise the results of the activity or trial.

We may not be successful in maintaining or establishing collaborations, which could adversely affect our ability to develop and, particularly in international markets, commercialize products.

We are collaborating with physicians, academic institutions, hospitals, patient advocacy groups, foundations and government agencies in order to assist with the development of our products and each of our product candidates. We plan to pursue similar activities in future programs and plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies. We also may seek to establish collaborations for the sales, marketing and distribution of our products in all or select geographies. If we elect to seek collaborators in the future but are unable to reach agreements with suitable collaborators, we may fail to meet our business objectives for the affected product or program. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts, if any, to establish and implement collaborations or other alternative arrangements. The terms of any collaboration or other arrangements that we establish, if any, may not be favorable to us.

Any collaboration that we enter into may not be successful. The success of our collaboration arrangements, if any, will depend heavily on the efforts and activities of our collaborators. It is likely that any collaborators of ours will have significant discretion in determining the efforts and resources that they will apply to these collaborations. The risks that we may be subject to in possible future collaborations include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our products or product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators 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 liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;
- we may grant rights to our collaborators to be the holder of any marketing authorizations in a jurisdiction;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Such terminations or expirations may adversely affect us financially and could harm our business reputation in the event we elect to pursue collaborations that ultimately expire or are terminated.

Materials necessary to manufacture our products or product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our products or product candidates.

We currently rely on the manufacturers of our products and product candidates to purchase from third-party suppliers the materials necessary to produce the compounds for our preclinical studies, clinical trials, and commercial supply and we rely, or will rely, on these other manufacturers for commercial distribution of our products and, if and when we obtain marketing approval, for any of our product candidates. Suppliers may not sell these materials to our manufacturers at the time we need them or on commercially reasonable terms and all such materials are susceptible to fluctuations in price and availability due to transportation costs, government regulations, price controls, geopolitical risk and changes in economic climate or other foreseen circumstances. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. We may enter into agreements to purchase certain materials and provide them to our manufacturers, with all the risks and uncertainties of supply associated with those purchases. If we or our manufacturers are unable to obtain these materials for our preclinical studies and clinical trials, product testing and potential regulatory approval of our product candidates would be delayed, significantly impacting our ability to develop and commercialize our product candidates. If our manufacturers or we are unable to purchase these materials for commercial distribution of our products or, after regulatory approval has been obtained, our product candidates, the commercial launch of our products and product candidates would be delayed or there would be a shortage in supply, which would materially affect our ability to generate revenues from the sale of our products or product candidates.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.

Manufacturing of our products and product candidates requires us or our manufacturing partners to conduct required stability and comparability testing. We or our partners may encounter product, packaging, equipment and process-related issues that may require refinement or resolution in order to successfully commercialize our products, proceed with planned clinical trials, or obtain regulatory approval for commercial marketing of our product candidates. In the future we may identify impurities which could result in increased scrutiny by regulatory authorities, delays in our clinical programs and regulatory approval, increases in our operating expenses or failure to obtain or maintain approval for our products or product candidates.

We currently rely on WuXi Biologics Co., Ltd., a company based in the People's Republic of China, as the sole supplier of our biologic product, Pombiliti™. Accordingly, there is a risk that supplies of our product may be significantly delayed by, or may become unavailable as a result of, manufacturing, equipment, process, regulatory or business-related issues affecting that company. We may also face additional manufacturing and supply-chain risks due to the regulatory and political structure of the PRC, or as a result of the international relationship between the PRC and the U.S., including but not limited to potential sanctions imposed by the U.S. government on WuXi, or any of the other countries in which our products are marketed. In addition, the out-breaks of illnesses in the PRC could impact operations at WuXi. Although currently there has been no impact on our ability to obtain supply of Pombiliti™., and we and Wuxi have robust mitigation plans in place to the extent feasible based on the risk, there can be no assurance that operations would not be impacted in the future with a negative impact on supply of our product.

We may encounter difficulties manufacturing our gene therapy which could impact timing and availability of clinical and commercial supply.

We may experience delays in developing a sustainable, reproducible and commercial-scale manufacturing process or transferring that process to commercial partners for our gene therapy product candidates. There is intense competition for limited commercial manufacturing capacity in gene therapy and for base materials, such as plasmids, necessary to the manufacturing of gene therapy products. We do not currently have our own gene therapy manufacturing capacity and rely instead on commercial manufacturing partners. These commercial manufacturing partners are expanding rapidly and there can be no assurance that needed capacity will be available or that these partners will continue to meet evolving regulatory standards. Any delay in securing supply of these materials and the manufacturing slots with commercial partners may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all. In addition, FDA and other regulatory bodies are continuing to evolve their guidance for gene therapy manufacturing and could impose rigorous requirements relating to the manufacturing and testing of clinical and commercial products that could add time, complexity and the risk that we or our manufacturing partners will be unable to meet these requirements.

Risks Related to our Financial Position

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

To date, we have focused on developing and commercializing our first product, Galafold® and second therapy, Pombiliti™ + Opfolda™, as well as our pipeline gene therapies. Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. Although the European Commission, PMDA and FDA have granted approval for Galafold®, for the treatment of adults with a confirmed diagnosis of Fabry disease and who have an amenable genetic variant, as well as Pombiliti™ + Opfolda™ for the treatment of adults with Pompe disease, and we are generating product sales, we continue to incur significant research, development, commercialization and other expenses related to our ongoing operations. As a result, we are not profitable, have incurred losses in each period since our inception, and may not be profitable on a non-GAAP or GAAP basis or achieve our year-to-year profitability guidance.

We expect to continue to incur significant costs in the foreseeable future as we:

- continue our development and commercialization of our products and seek regulatory approvals for our product candidates in the U.S., the E.U., U.K., Japan and other foreign countries, as applicable;
- conduct additional clinical trials to support the full approval of Galafold® in the U.S. and post-approval commitments or trials;
- continue communicating with the EMA, as necessary, regarding post-marketing requirements and clinical trials for Galafold®;
- continue to or initiate the regulatory submission process for marketing approval of Galafold® and Pombiliti™ + Opfolda™ outside of the U.S. and E.U. and other foreign jurisdictions where approved, as applicable;
- build and maintain our commercial infrastructure so that it is capable of supporting product sales, marketing and distribution of Galafold® and Pombiliti™ + Opfolda™, as well as our other product candidates in Europe, Japan and the U.S. or other territories in which we have received or may receive regulatory approval;
- continue our next-generation product research; and
- continue our rigorous prosecution and defense of our patent portfolio.

We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If any of our product candidates fails in clinical trials or does not gain regulatory approval, or if approved, fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses and potential future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We may never become profitable even though we currently generate revenue from the sale of products.

We began the commercial launch of our first product, Galafold®, in May 2016, with the U.S. and Japan commercial launches in 2018 and are now approved in over 40 countries. We began the commercial launch of our second therapy for the treatment of Pompe disease, Pombiliti™ + Opfolda™, in June 2023 in the E.U, August 2023 in the U.K. and September 2023 in the U.S. Our ability to generate material revenue and become profitable depends upon our ability to successfully commercialize our existing products and product candidates, or product candidates that we may in-license or acquire in the future. Even if we are able to successfully achieve regulatory approval for our product candidates, we do not know when any of these product candidates will generate revenue for us, if at all and we may not meet our current revenue, operating expense and profitability guidance. Our ability to generate revenue from our current or future products and product candidates depends on a number of factors, including our ability to:

- successfully complete development activities and obtain additional regulatory and pricing and reimbursement approvals for, and continue to successfully commercialize, Galafold® and Pombiliti™ + Opfolda™;
- complete and submit regulatory submissions and obtain regulatory approval in target geographies for Pombiliti™ + Opfolda™;
- develop and maintain a commercial organization capable of sales, marketing, and distribution for Galafold® and Pombiliti™ + Opfolda™, and any product candidates we intend to market if approved, in the countries where we have chosen to commercialize the products ourselves, including the U.S., EU, UK, and Japan;
- manufacture commercial quantities of our products at acceptable cost levels;
- obtain a commercially viable price for our products;
- obtain coverage and adequate reimbursement from third parties, including government payors;
- successfully satisfy post-marketing requirements that the FDA, EMA, or other foreign regulatory authorities may impose for Galafold®, Pombiliti™ + Opfolda™, or any of our other product candidates that may receive regulatory approval, including pediatric trials and patient registries;
- successfully develop or acquire new products and product candidates;
- successfully complete development activities, including the necessary preclinical studies and clinical trials, with respect to product candidates;
- successfully protect our intellectual property rights; and
- successfully navigate the evolving geopolitical landscape and any adverse impacts arising therefrom, including actions by governments, our customers, our suppliers or other third parties.

Even if we are able to generate significant revenues from the sale of our products and accurately predict and control expenses, we may not reach our financial guidance or become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

If we require substantial additional capital to fund our operations and we fail to obtain necessary financing, we may be unable to complete the development and commercialization of our products and development and commercialization of our product candidates.

Our operations have consumed substantial amounts of cash. We expect to continue to spend substantial amounts to advance the preclinical and clinical development of our product candidates, and launch and commercialize our products and product candidates for which we may receive regulatory approval, including continuing to maintain our own commercial organization. We believe that our current cash position, including expected revenues, is sufficient to fund our operations and ongoing research programs for at least the next 12 months. Potential impacts of global pandemics, government sanctions, future business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements. As such, we may require substantial additional capital for the development and commercialization of our products and further development and commercialization of our product candidates.

If additional funding is needed, we cannot be certain that such funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts, when required or on acceptable terms, we could also be required to:

- significantly delay, scale back, or discontinue the development or the commercialization of our products or product candidates or one or more of our other research and development initiatives;
- seek collaborators for Galafold®, Pombiliti™ + Opfolda™, or one or more of our current or future product candidates at an earlier stage than otherwise would be desirable, or on terms that are less favorable than might otherwise be available;
- relinquish or license on unfavorable terms our rights to our technologies, products or product candidates that we otherwise would seek to develop or commercialize ourselves;
- significantly curtail operations; or
- enter into strategic partnerships on unfavorable terms, including a sale of our assets for less than full value.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the costs of commercialization activities, including maintaining sales, marketing, and distribution capabilities for Galafold® and Pombiliti™ + Opfolda™, and any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own;
- the scope, progress, results, and costs of preclinical development, laboratory testing, and clinical trials for our product candidates and any other product candidates that we may in-license or acquire;
- the cost of manufacturing drug supply for our preclinical studies, clinical trials, and commercial supply, including the significant cost of manufacturing Pombiliti™ + Opfolda™ and our gene therapies;
- the outcome, timing, and cost of the regulatory approval process by the FDA, EMA, PMDA and other foreign regulatory authorities, including the potential for regulatory authorities to delay approvals pending site inspections or requiring that we perform more studies than those that we currently anticipate for our products and product candidates;
- the activities of our competitors;
- the cost of filing, prosecuting, defending, and enforcing any patent claims and other intellectual property rights;
- the cost and timing of completion of existing or expanded commercial-scale outsourced manufacturing activities;
- the cost of defending any claims asserted against us or prosecuting any claims we may assert against others;
- the cost of complying with new laws, rules, regulations or executive orders in the geographies in which we or our key manufacturers, suppliers and customers operate;
- the emergence of competing technologies and other adverse market developments;
- the impact of foreign exchange rates on our operating expenses and revenue projections;
- the extent to which we acquire or invest in additional businesses, products, and technologies.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies, Galafold®, Pombiliti™ + Opfolda™, or product candidates.

We may seek additional capital through a combination of private and public equity offerings, debt financings, receivables or royalty financings, strategic collaborations and alliances, restructuring and licensing arrangements. We have an effective "shelf" registration statement on Form S-3 that allows us to issue securities in registered offerings as well as an available at-the-market financing facility that allows us to sell shares of our common stock through a placement agent at market prices. To the extent that we raise additional capital through the sale of equity, warrants or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt, receivables, and royalty financings may be coupled with an equity component, such as warrants to purchase stock, which could also result in dilution of our existing stockholders' ownership. The incurrence of additional indebtedness beyond our existing indebtedness with the Senior Secured Term Loan due 2029 could also result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur further debt, limitations on our ability to acquire or license intellectual property rights, and other operating restrictions that could have a material adverse effect on our ability to conduct our business and may result in liens being placed on our assets and intellectual property. If we were to default on any of our indebtedness, we could lose such assets and intellectual property. If we raise additional funds through strategic collaborations and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to Galafold®, Pombiliti™ + Opfolda™ or our product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market our technologies that we would otherwise prefer to develop and market ourselves.

Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.

In October 2023, we entered into the Senior Secured Term Loan due 2029 for a $400 million credit facility with Blackstone Alternative Credit Advisors LP and Blackstone Life Sciences Advisors L.L.C. (collectively, "Blackstone"), with an interest rate equal to a 3-month adjusted Term SOFR, subject to a 2.5% floor, plus 6.25% per annum that requires interest-only payments until late-2026 and matures in 2029. We received net proceeds of $387.4 million in October 2023, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2029, but Blackstone simultaneously made a $29.8 million investment in our common stock, net of offering costs. The Senior Secured Term Loan due 2029 contains a minimum liquidity covenant tested monthly and in effect at all times, and a minimum consolidated revenue covenant measured as of the previous four consecutive fiscal quarters over the term of the loan.

There can be no assurance that our cash and cash equivalents, together with funds generated by our operations and any future financings, will be sufficient to satisfy our debt payment obligations or that we will have sufficient equity to satisfy these obligations. Our inability to generate funds sufficient to satisfy our debt payment obligations or remain in compliance with the debt covenants may result in such obligations being accelerated by our lenders, which would likely have a material adverse effect on our business, financial condition and results of operations.

Foreign currency exchange rate fluctuations could harm our financial results.

We conduct operations in many countries involving transactions denominated in a variety of currencies other than the U.S. dollar. The majority of our current Galafold® revenue is derived from outside the U.S. Accordingly, changes in the value of currencies relative to the U.S. dollar may impact our consolidated revenues and operating results due to transactional and translational remeasurement that is reflected in our earnings. The current exposures arise primarily from cash, accounts receivable, intercompany receivables and payables, and net product sales denominated in foreign currencies. Fluctuations in currency exchange rates have had, and will continue to have, an impact on our results as expressed in U.S. dollars. We are not currently engaged in any foreign currency hedging activities and there can be no assurance that currency exchange rate fluctuations will not adversely affect our results of operations, financial condition and cash flows. Adverse fluctuations in currency exchange rates from the date of our outlooks could cause our actual results to differ materially from those anticipated in our outlooks and adversely impact our business, results of operations and financial condition.

We also face risks arising from the imposition of exchange controls and currency devaluations. Exchange controls may limit our ability to convert foreign currencies into U.S. dollars or to make payments by our foreign subsidiaries or businesses located in or conducted within a country imposing controls. Currency devaluations result in a diminished value of funds denominated in the currency of the country instituting the devaluation.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2023, we had U.S. federal, U.K. and state net operating loss carry forwards ("NOLs") of approximately $1.2 billion, $28.4 million and $1.0 billion, respectively. The federal carry forward for losses generated prior to 2018 will expire in 2029 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the Tax Act. The U.K. carryforward period is unlimited. Most of the state net operating loss carry forwards generated prior to 2009 have expired through 2016. The remaining state net operating loss carry forwards including those generated in 2009 through 2023 will expire in 2030 through 2042. State research and development credits will expire beginning 2024 through 2033. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended, as well as similar state statutes in the event of an ownership change. Such ownership changes have occurred in the past and could occur again in the future. Under Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income may be limited. We may experience ownership changes in the future as a result of shifts in our stock ownership some of which are outside our control. We completed a detailed study of the NOLs for the tax year 2023 and determined that there was not an ownership change in excess of 50%. Ownership changes in future periods may place additional limits on our ability to utilize net operating loss and tax credit carry forwards. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently decrease the amount of state attributes and increase state taxes owed.

Our executive officers, directors and principal stockholders maintain the ability to exert significant influence and control over matters submitted to our stockholders for approval.

Our executive officers, directors and affiliated stockholders beneficially own shares representing approximately 47% of our common stock as of December 31, 2023. As a result, if these stockholders were to choose to act together, they would be able to exert significant influence and control over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could influence the election of directors and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization. This concentration of voting power could delay or prevent an acquisition of us on terms that other stockholders may desire. The interests of this group of stockholders may not always coincide with the interests of other stockholders, and they may act, whether by meeting or written consent of stockholders, in a manner that advances their best interests and not necessarily those of other stockholders, including obtaining a premium value for their common stock, and might affect the prevailing market price for our common stock.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders sole source of gain for the foreseeable future.

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

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission. We believe that any disclosure 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 reflect the reality that judgments can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Risks Related to our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the U.S. and in certain foreign jurisdictions related to our novel technologies, products and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering this intellectual property. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, including U.S. Hatch-Waxman litigation. 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 technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we or our licensors were the first to make the inventions covered by each of our pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents issued to us or our licensors will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- licenses from other third parties will not be required to commercialize patented products;
- we will develop additional proprietary technologies that are patentable;
- we will file patent applications for new proprietary technologies promptly or at all;
- our patents will not expire prior to or shortly after commencing commercialization of a product;
- the patents of others will not have a negative effect on our ability to do business;
- patent authorities will not identify deficiencies in our patent applications and refuse to grant our patents; or
- outcome of any patent litigation, including Hatch-Waxman litigation involving Galafold®, or any possible future litigation involving Pombiliti™ + Opfolda™, will demonstrate that our patents are valid and enforceable.

In addition, we cannot be assured that any of our pending patent applications will result in issued patents. In particular, we have filed patent applications in the U.S., the European Patent Office and other countries outside the U.S. that have not been issued as patents. These pending applications include, among others, some of the patent applications for Pombiliti™ + Opfolda™, Galafold®, and our gene therapy platforms and product candidates. If patents are not issued in respect of our pending patent applications, we may not be able to stop competitors from marketing similar products in Europe and other countries in which we do not have issued patents.

In addition to patent protection outside of the U.S., we intend to seek orphan medicinal product designation of our product candidates and to rely on statutory data exclusivity provisions in jurisdictions outside the U.S. where such protections are available, including Europe. The patent rights that we own or have licensed relating to our product candidates are limited in ways that may affect our ability to exclude third parties from competing against us if we obtain regulatory approval to market these product candidates. In particular:

- We have multiple composition of matter patents covering Galafold® and multiple method of treatment patents issued and listed in the Orange Book. We have composition of matter, method of treatment, method of manufacture, formulation and other patents issued for Pombiliti™ + Opfolda™. We also have several pending applications covering Galafold®, Pombiliti™ + Opfolda™ and gene therapy. There can be no assurance that these applications will be allowed or that allowed applications will be issued or that the scope of such patents, if they issue, will be sufficient to protect our products. Composition of matter patents can provide protection for pharmaceutical products to the extent that the specifically covered compositions are important. For our product candidates for which we do not hold composition of matter patents, competitors who obtain the requisite regulatory approval can offer products with the same composition as our products so long as the competitors do not infringe any method of use patents that we may hold.
- For some of our product candidates the principal patent protection that covers or those we expect will cover our product candidate is a method of use patent. This type of patent only protects the product when used or sold for the specified method. However, this type of patent does not limit a competitor from making and marketing products that are identical to our products that is labeled for an indication that is outside of the patented method, or for which there is a substantial use in commerce outside the patented method.

Moreover, physicians may prescribe such competitive identical products for indications other than the one for which the products have been approved, or off-label indications, that are covered by the applicable patents. Although such off-label prescriptions may infringe or induce infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Certain foreign jurisdictions may not recognize or enforce any patents granted or patent applications filed in those jurisdictions. In addition, we may not pursue or obtain patent protection in all major markets. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the U.S., the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office or become involved in opposition, derivation, reexamination, *inter partes* review, post grant review, interference proceedings or other patent office proceedings or litigation, in the U.S. or elsewhere, challenging our patent rights or the patent rights of others, including U.S. Hatch-Waxman litigation. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the E.U. and elsewhere may also result in clinical trial data submitted as part of an MAA becoming publicly available. Such developments could enable other companies to circumvent our intellectual property rights and use our clinical trial data to obtain marketing authorizations in the E.U. and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, 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 technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Further, litigation, interferences, oppositions, *inter partes* reviews, administrative challenges or other similar types of proceedings are, have been and may in the future be necessary in some instances to determine the validity and scope of certain of our proprietary rights, and in other instances to determine the validity, scope or non-infringement of certain patent rights claimed by third parties to be pertinent to the manufacture, use or sale of our products. We may also face challenges to our patent and regulatory protections covering our products by third parties, including manufacturers of generics and biosimilars that may choose to launch or attempt to launch their products before the expiration of our patent or regulatory exclusivity. Litigation, interference, oppositions, *inter partes* reviews, administrative challenges or other similar types of proceedings are unpredictable and may be protracted, expensive and distracting to management. The outcome of such proceedings could adversely affect the validity and scope of our patent or other proprietary rights, hinder our ability to manufacture and market our products, require us to seek a license for the infringed product or technology or result in the assessment of significant monetary damages against us that may exceed amounts, if any, accrued in our financial statements. An adverse determination in a judicial or administrative proceeding or a failure to obtain necessary licenses could prevent us from manufacturing or selling our products. Furthermore, payments under any licenses that we are able to obtain would reduce our profits derived from the covered products and services.

Additionally, our products, or the technologies or processes used to formulate or manufacture those products may now, or in the future, infringe the patent rights of third parties. It is also possible that third parties will obtain patent or other proprietary rights that might be necessary or useful for the development, manufacture or sale of our products. We may need to obtain licenses for intellectual property rights from others and may not be able to obtain these licenses on commercially reasonable terms, if at all.

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

There has been, and we expect that there may continue to be, significant litigation in the industry regarding patents and other intellectual property rights. Litigation, arbitrations, administrative proceedings and other legal actions with private parties and governmental authorities concerning patents and other intellectual property rights may be protracted, expensive and distracting to management. Competitors may sue us as a way of delaying the introduction of our drugs or to remove our drugs from the market. Any litigation, including litigation related to Abbreviated New Drug Applications, or ANDA, litigation related to 505(b)(2) applications, interference proceedings to determine priority of inventions, derivations proceedings, *inter partes* review, oppositions to patents in foreign countries, litigation against our collaborators or similar actions, may be costly and time consuming and could harm our business. We expect that litigation may be necessary in some instances to determine the validity and scope of certain of our proprietary rights. Litigation may be necessary in other instances to determine the validity, scope or non-infringement of certain patent rights claimed by third parties to be pertinent to the manufacture, use or sale of our products. Ultimately, the outcome of such litigation could adversely affect the validity and scope of our patent or other proprietary rights, hinder our ability to manufacture and market our products, or result in the assessment of significant monetary damages against us that may exceed amounts, if any, accrued in our financial statements.

To the extent that valid present or future third-party patents or other intellectual property rights cover our drugs, drug candidates or technologies, we or our strategic collaborators may seek licenses or other agreements from the holders of such rights in order to avoid or settle legal claims. Such licenses may not be available on acceptable terms, which may hinder our ability to, or prevent us from being able to, manufacture and market our drugs. Payments under any licenses that we are able to obtain would reduce our profits derived from the covered products.

As part of the approval process for Galafold®, FDA granted us a New Chemical Entity ("NCE") exclusivity period during which other manufacturers' applications for approval of generic versions of our product will not be approved. Generic manufacturers may challenge the patents protecting products that have been granted NCE exclusivity one year prior to the end of the NCE exclusivity period. Generic manufacturers have sought and may continue to seek FDA approval for a similar or identical drug through an abbreviated new drug application ("ANDA"), the application form typically used by manufacturers seeking approval of a generic drug. The sale of generic versions of Galafold® earlier than their patent expiration would have a significant negative effect on our revenues and results of operations. To seek approval for a generic version of a product having NCE status, a generic company may submit its ANDA to FDA four years after the branded product's approval.

Starting in October 2022, we received letters from Aurobindo Pharma Ltd., Lupin Ltd., and Teva Pharmaceutical, Inc. (collectively, "generic manufacturers") indicating that they have submitted ANDAs to FDA requesting permission to market and manufacture generic versions of Galafold®. They have challenged the validity of all or some of the patents listed on the Orange Book associated with Galafold®. We filed lawsuits against the generic manufacturers, and we intend to enforce and defend our intellectual property. Although we cannot predict with certainty the ultimate outcome of the foregoing actions, or any other litigation that we may have with generic manufacturers in the future, an adverse judgment could result in substantial monetary damages, including Galafold®'s lost revenues, and we may spend significant resources enforcing and defending our patents. If we are unsuccessful in these lawsuits, some or all of our original claims in the patents may be narrowed or invalidated, and the patent protection for Galafold® in the United States may be shortened. Further, if all the patents are invalidated, the FDA could approve the requests to manufacture a generic version of Galafold® in the United States prior to the expiration date of those patents. Moreover, we may be forced to settle litigation on terms that are unfavorable and result in sales of generic versions of Galafold® prior to expiration of our patents. The sale of generic version of Galafold® earlier than the patent expiration would have a significant negative effect on our revenues, projections of profitability and results of operations.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, including Galafold® or Pombiliti™ + Opfolda™, may infringe or be accused of infringing one or more claims of an issued patent or may fall within the scope of one or more claims in a published patent application that may subsequently issue and to which we do not hold a license or other rights. Third parties may own or control these patents or patent applications in the U.S. and abroad. These third parties could bring claims against us that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, we or they could be forced to stop or delay research, development, manufacturing or sales of the products or product candidate that is the subject of the suit.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering our product candidates, technology or methods. Because of the number of patents issued and patent applications filed in our field, we believe there is a risk that third parties may allege they have patent rights encompassing our product candidates, technology or methods.

If any of these patents were to be asserted against us, while we do not believe that our product candidates would be found to infringe any valid claim of such patents, there is no assurance that a court would find in our favor. If we were to challenge the validity of any issued U.S. patent in court, we would need to overcome a presumption of validity that attaches to every patent. This burden is high and would require us to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on infringement or validity. Furthermore, during the course of litigation, confidential information may be disclosed in the form of documents or testimony in connection with discovery requests, depositions or trial testimony. Disclosure of our confidential information and our involvement in intellectual property litigation could materially adversely affect our business.

In order to avoid or settle potential claims with respect to any patent rights of third parties, we may choose or be required to seek a license from a third-party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including interference proceedings declared by the U.S. Patent and Trademark Office and opposition proceedings in the European Patent Office, regarding intellectual property rights with respect to our products and technology. Even if we prevail, the cost to us of any patent litigation or other proceeding could be substantial.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from any litigation could significantly limit our ability to continue our operations. Patent litigation and other proceedings may also absorb significant management time.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees 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 employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

As part of our business, we have historically been a party to license agreements pursuant to which we license key intellectual property relating to certain products or product candidates. We expect to enter into additional licenses in the future. Such licenses impose various diligences, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product or product candidate that is covered by the licensed patents.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the U.S. Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Risks Related to Employment, Environmental, Social and Governance Matters

Our future success depends on our ability to retain our Chief Executive Officer and other key personnel and to attract, retain and motivate qualified personnel.

We are highly dependent on Bradley L. Campbell, our President and Chief Executive Officer, and Simon Harford, our Chief Financial Officer, both of whom has significant pharmaceutical industry experience. The loss of the services of either of these individuals might impede the achievement of our research, development and commercialization objectives and materially adversely affect our business and we may not be able to replace them with candidates with similar background and experience in the event of the loss of their services. We do not maintain "key person" insurance on Mr. Campbell or on any of our other key personnel.

Recruiting and retaining qualified scientific, clinical and sales and marketing personnel will also be critical to our success. In addition, maintaining a qualified finance and legal department is key to our ability to meet our regulatory obligations as a public company and important in any potential capital raising activities. Our industry has experienced a high rate of turnover in recent years. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, particularly in New Jersey and Philadelphia and their surrounding areas. Although we believe we offer competitive salaries and benefits, we may have to increase spending in order to retain personnel. If we fail to retain our remaining qualified personnel or replace them when they leave, we may be unable to recruit replacements without increased expense, if at all, or continue our development and commercialization activities.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

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

As of December 31, 2023, we had 517 full-time employees. As our development and commercialization strategies develop, we will need additional managerial, operational, sales, marketing, financial, technical operations and other resources. Our management, personnel and systems currently in place may not be adequate to support this future growth. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our existing or future product candidates, and we may not be able to replace key personnel in the event of turnover. Future growth would impose significant added responsibilities on members of management, including:

- managing the development and commercialization of any products or product candidates approved for marketing;
- overseeing our ongoing preclinical studies and clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees, including any sales and marketing personnel engaged in connection with the commercialization of any approved product;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- managing our collaboration partners and associated joint steering committees;
- managing any clinical or commercial collaborations with third parties;
- improving our managerial, development, operational and financial systems and procedures;
- monitoring and improving diversity, inclusion and pay-equity initiatives;
- developing our compliance infrastructure and processes to ensure compliance with regulations applicable to public companies;
- developing expertise in newly acquired or in-licensed technologies; and
- expanding our facilities.

As our operations expand, we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

Our employees, independent contractors, principal investigators, CROs, consultants, agents and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants, agents and vendors may engage in fraudulent conduct, harassment or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- FDA or similar regulations of foreign regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;
- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations, anti-bribery and corruption laws, anti-discrimination and harassment laws, privacy and similar laws and regulations established and enforced by foreign regulatory authorities;

- laws that require the reporting of financial information or data accurately; or
- laws requiring the timely and accurate disclosure of material information to investors and analysts.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing, bribery and corruption and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, a robust Enterprise Risk Management Program, have extensive Board of Directors oversight, and conduct comprehensive training, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. 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 material adverse effect on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

If our enterprise risk program, global risk committee and other compliance methods are not effective, our business, financial condition and operating results may be adversely affected.

Our ability to identify, manage and respond to the various risks related to our business is largely dependent on our established and maintained compliance, risk, audit and reporting systems and procedures. The Board of Directors has ultimate responsibility for risk oversight of the company and carries out this duty through its various committees. Our Audit and Compliance Committee, Nominating and Corporate Governance Committee, Compensation and Leadership Development Committee and Science and Technology Committee have each been delegated oversight authority by the Board of Directors with respect to issues in their applicable areas of expertise. These committees are responsible for identifying, monitoring and reporting areas of concern to the full Board of Directors. At the company level, our senior management team similarly monitors risk through the Global Risk Committee. Membership of the Global Risk Committee consists primarily of key department heads who are asked to bring to such committee relevant items for discussion that they or their teams have identified at the numerous sub-committees these individuals chair or attend. The Global Risk Committee then uses this information to develop an Enterprise Risk Management Program, which identifies key risks, develops mitigation strategies for these risks, and reports material developments directly to the Audit and Compliance Committee on a quarterly basis, and to the full Board of Directors on a yearly basis. Our international business segment also has its own companion committee which operates in substantially the same way as the Global Risk Committee, reporting key risks to the Global Risk Committee for inclusion in the Enterprise Risk Management Program.

If our policies, procedures, and compliance systems, including our Enterprise Risk Management Program and the Global Risk Committee are not effective, or if we are not successful in monitoring or evaluating the risks to which we are or may be exposed, our business, reputation, financial condition and operating results could be materially adversely affected. We cannot provide assurance that our policies and procedures will always be effective, or that our management, the Enterprise Risk Management Program or the Global Risk Committee would be able to identify any such ineffectiveness. If our compliance and risk management strategies are not effective, our business, financial condition and operating results may be adversely affected.

The increased focus on environmental, social and governance matters and emissions reporting by investors, governmental bodies and other stakeholders, as well as existing and proposed laws related to these topics, may adversely affect our business and reputation.

Companies are being increasingly judged by not just their financial performance, but also by their performance on a variety of ESG matters. These matters include, among others, (i) the company's efforts and contributions to or impacts on climate change and human rights matters, (ii) ethics and compliance with law, (iii) diversity and inclusion, and (iv) the role of the company's board of directors in supervising various sustainability issues. Additionally, in the healthcare, pharmaceutical and life sciences industries, the public's ability to access our medicines is of particular importance.

Investment in funds that specialize in companies that perform well in ESG assessments are increasingly popular, and major institutional investors and advisors have publicly emphasized the importance of ESG measures to their investment decisions and recommendations. Investors who are focused on ESG matters may seek enhanced ESG disclosures or to implement policies adverse to our business, and there can be no assurances that stockholders will not advocate, via proxy contests, media campaigns or other public or private means, for us to make corporate governance changes or engage in certain corporate actions.

Additionally, the SEC has announced a proposal aimed at mandating the disclosure of certain greenhouse gas emissions and climate change-related risks for publicly traded U.S. companies, with similar laws and regulations related to the disclosure of greenhouse gas emissions and/or climate change-related risks enacted or proposed in California, the European Union, and various other jurisdictions. Compliance with any such new laws or regulations will be costly, time consuming, and, as a global commercial organization, require expenditure of our limited resources to be in compliance with the various standards across the jurisdictions in which we operate. Failure to adequately meet these new and upcoming disclosure requirements may affect the manner and locations in which we choose to conduct our business and could adversely affect our profitability and returns to our investors.

There can be no certainty that we will successfully navigate or manage ESG issues or that we will successfully meet society's expectations as to our proper role in the economy at large or as a global citizen or meet the evolving regulatory requirements. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation with investors, governments, customers, employees, other third parties and the communities and industries in which we operate and on our business, share price, financial condition, access to capital or results of operations, including the sustainability of our business over time.

Our business activities involve the use of hazardous materials, which require compliance with environmental and occupational safety laws regulating the use of such materials. If we violate these laws, we could be subject to significant fines, liabilities or other adverse consequences.

Our research and development programs involve the controlled use of hazardous materials, including microbial agents, corrosive, explosive and flammable chemicals and other hazardous compounds in addition to certain biological hazardous waste. Additionally, the activities of our third-party product manufacturers of our product, and of our product candidates if and when they reach commercialization, will also require the use of hazardous materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of these materials comply in all material respects with the standards prescribed by local, state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In addition, although our collaborators have environmental compliance processes in place, and we include oversight of these processes in our business reviews, they may not ultimately comply with these laws. In the event of an accident or failure to comply with environmental laws, we could be held liable for damages that result, and any such liability could exceed our assets and resources or we could be subject to limitations or stoppages related to our use of these materials which may lead to an interruption of our business operations or those of our third-party contractors. While we believe that our existing insurance coverage is generally adequate for our normal handling of these hazardous materials, it may not be sufficient to cover pollution conditions or other extraordinary or unanticipated events. Furthermore, an accident could damage or force us to shut down our operations. Changes in environmental laws may impose costly compliance requirements on us or otherwise subject us to future liabilities and additional laws relating to the management, handling, generation, manufacture, transportation, storage, use and disposal of materials used in or generated by the manufacture of our products or related to our clinical trials. In addition, we cannot predict the effect that these potential requirements may have on us, our suppliers and contractors or our customers.

Our business could be adversely affected by the effects of health pandemics or epidemics, which could cause significant disruptions in our operations.

Health pandemics or epidemics have in the past and could again in the future result in quarantines, stay-at-home orders, remote work policies or other similar events that may disrupt businesses, delay our research and development programs and timelines, negatively impact productivity and increase risks associated with cybersecurity, the future magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations. More specifically, these types of events may negatively impact personnel at third-party manufacturing facilities or the availability or cost of materials, which could disrupt our supply chain. In addition, impact on the operations of the FDA or other regulatory authorities could negatively affect our planned approval processes. Finally, economic conditions and business activity may be negatively impacted and may not

recover as quickly as anticipated. The effects of epidemics and pandemic are highly uncertain and subject to change. If we are not able to respond to and manage the impact of such events effectively, our business, operating results, financial condition and cash flows could be adversely affected.

General Risk Factors

Our business and operations would suffer in the event of computer system failures or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, contract manufacturing organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, ransomware attacks and other security breaches, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. If such an event were to occur and cause interruptions to our operations, it could result in a material disruption to the commercialization of our products and our product candidate development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruptions or security breach were to result in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur significant unexpected losses, expenses and liabilities, we could face litigation or suffer reputational harm and the further development of our product candidates could be delayed.

In addition, cybersecurity threats and reported incidents are increasing in their frequency, sophistication and intensity, including as a result of ongoing military conflicts, certain U.S. foreign relations, and increased remote work arrangements, and are becoming increasingly difficult to detect, particularly when they impact vendors, customers or suppliers, and other companies in our supply chain. Cybersecurity threats or incidents may include the deployment of malware via emails disguised to look legitimate or the use of social engineering to obtain employee access credentials to the company's computer network and systems, as well as various other schemes and approaches designed to breach company cyber defenses. Once access has been obtained, the illegitimate actor can steal sensitive information, install ransomware requiring a large financial outlay to recover company systems and files, or wreak havoc in a variety of different and creative ways. While we have robust detection, mitigation, response and recovery protocols in place, there is no guarantee that these will be effective in preventing disruptions to our operations and adequately safeguard confidential, propriety or sensitive information from misappropriation or corruption. Our key business partners, manufacturers and vendors face these same risks and a successful attack on their systems could have a similar negative impact to our business and operations. Moreover, new SEC reporting requirements now mandate specific disclosures in the event of a material cybersecurity incident. As such, we may have to report certain incidents that could result in reputational harm and loss of investor, customer and patient confidence even if our cybersecurity defenses are ultimately effective in staving off such incidents. To date and to our knowledge, we have not experienced a material cybersecurity incident.

We may use artificial intelligence in our business, and challenges with properly managing its use could adversely affect our business.

We may incorporate artificial intelligence ("AI") solutions into our business, and applications of AI may become important in our operations over time. Our competitors or other third parties may incorporate AI into their businesses more quickly or more successfully than us, which could impair our ability to compete effectively and adversely affect our results of operations. Additionally, if the types of information that AI applications assist in producing are or are alleged to be deficient, inaccurate, or biased, our business, financial condition, and results of operations may be adversely affected. The rapid evolution of AI, including potential government regulation of AI, may require significant resources to develop, test and maintain our implementations of AI.

We may acquire or divest assets or businesses, or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.

As part of our business strategy, we may continue to pursue acquisitions or licenses of assets or businesses, or strategic alliances and collaborations, to expand our existing technologies and operations. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all despite a substantial outlay of resources in pursuing such

transactions, and we may not realize the anticipated benefits of any such transaction, any of which could have a detrimental effect on our financial condition, results of operations, and cash flows. We may not be able to find suitable acquisition or licensing candidates, and if we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business and we may incur additional debt, issue equity, or assume unknown or contingent liabilities in connection therewith. Integration of an acquired company or assets may also disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, especially the acquisition of commercial assets, and require management resources that would otherwise focus on developing our existing business. We may not be able to find suitable collaboration partners or identify other investment opportunities, and we may experience losses related to any such investments.

To finance any acquisitions, licenses or collaborations, we may choose to issue debt or shares of our common stock as consideration. Any such issuance of shares would dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may not be able to acquire other assets or companies or fund a transaction using our stock as consideration. Alternatively, it may be necessary for us to raise additional funds for acquisitions through public or private financings. Additional funds may not be available on terms that are favorable to us, or at all.

In addition, we may divest or license all or a portion of certain businesses and/or facilities, joint venture or minority equity investment interests, subsidiaries, distributorships, or product categories, which could cause a decline in revenue or profitability and may make our financial results more volatile. We may be unable to complete any such divestiture or license on terms favorable to us, within the expected timeframes, or at all despite a substantial outlay of resources in pursuing such divesture or license. We may have continued financial exposure to divested or licensed businesses following the completion of any such transaction, including increased costs due to potential litigation, contingent liabilities and indemnification of the buyer or licensee related to, among other things, lawsuits, regulatory matters or tax liabilities. Such divestitures or licenses may also divert management's attention from our core businesses and lead to potential issues with employees, customers or suppliers.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions:

- establish a classified board of directors, and, as a result, not all directors are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock, without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 67% of the outstanding voting stock to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Unfavorable global economic conditions, whether brought about by material global crises, health epidemics, military conflicts or war, geopolitical and trade disputes or other factors, may adversely affect our business and financial results.

Our business is sensitive to global economic conditions, which can be adversely affected by public health crises and epidemics, political and military conflict, trade and other international disputes, significant natural disasters (including as a result of climate change) or other events that disrupt macroeconomic conditions.

For example, climate change could present risks to our operations, including an adverse impact on global temperatures, weather patterns and the frequency and severity of extreme weather and natural disasters. Natural disasters and extreme weather conditions, such as a hurricane, tornado, earthquake, wildfire or flooding, may pose physical risks to our facilities, employees, customers, patients and disrupt the operation of our supply chain and increase operational costs.

Additionally, trade policies and geopolitical disputes (including as a result of China-Taiwan relations) and other international conflicts can result in tariffs, sanctions and other measures that restrict international trade, and can materially adversely affect our business, particularly if these measures occur in regions where we source our components or raw materials. Tensions between the United States and China have led to a series of tariffs being imposed by the United States on imports from China mainland, as well as other business restrictions. Tariffs increase the costs of the components and raw materials we source. Countries may also adopt other measures, such as controls on imports or exports of goods, technology or data, that could adversely impact our operations and supply chain. As these tensions continue to rise, more targeted approaches by the U.S. or PRC governments on certain products, industries or companies (including WuXi, a sole supplier of one of our products) could significantly impact our ability to effectively manufacture and distribute our products, including Pombiliti™ + Opfolda™, materially impacting our ability to meet patient demands or financial forecasts.

Further, recent global events have adversely affected and are continuing to adversely affect workforces, organizations, economies, and financial markets globally, leading to economic downturns, inflation, and increased market volatility. Military conflicts and wars (such as the ongoing conflicts between Russia and Ukraine, Israel and Hamas, and the Red Sea crisis and its impact on shipping and logistics), terrorist attacks, instability in Venezuela, other geopolitical events, high inflation, increasing interest rates, bank failures and associated financial instability and crises, and supply chain issues can cause exacerbated volatility and disruptions to various aspects of the global economy. The uncertain nature, magnitude, and duration of hostilities stemming from such conflicts, including the potential effects of sanctions and counter-sanctions, or retaliatory cyber-attacks on the world economy and markets, have contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business and operations.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock is highly volatile and may be subject to wide fluctuations in response to numerous factors, some of which are beyond our control. In addition to the factors discussed in this Annual Report on Form 10-K, these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to our products or product candidates or our competitors' products or product candidates;
- actual or anticipated changes in our growth rate relative to our competitors;
- the outcome of any patent infringement or other litigation that may be brought against us or we may bring against others;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;

- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the E.U., U.K., U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product or any of our product candidates or clinical development programs;
- actual or anticipated variations in our quarterly operating results;
- the number and characteristics of our efforts to in-license or acquire additional product candidates or products;
- introduction of new products or services by us or our competitors;
- failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in accounting practices;
- lawsuits and other claims asserted against us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- publication of research reports about us, our competitors or our industry, or positive or negative recommendations or withdrawal of research coverage by securities or industry analysts;
- other events or factors, many of which are beyond our control; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have 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. The realization of any of the above risks or any of a broad range of other risks stated above could have a material adverse effect on the market price of our common stock.

As we operate in the pharmaceutical and biotechnology industry, we are especially vulnerable to these factors to the extent that they affect our industry or our products. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

A significant portion of our total outstanding shares may be sold into the market. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Certain holders of our common stock have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered on Form S-8 registration statements all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. In addition, certain of our employees, executive officers and directors have entered into, or may enter into, Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information. In September 2021, we entered into a securities purchase agreement with an investor for the private placement of, among other things, pre-funded warrants to purchase an aggregate of 8,349,705 shares of common stock, at a purchase price of $10.17 per pre-funded warrant. Each pre-funded warrant, some of which have been exercised, has an initial exercise price of $0.01 per share and is exercisable at any time after its original issuance at the option of each holder, in such holder’s discretion, by (i) payment in full in immediately available funds of the initial exercise price for the number of shares of common stock purchased upon such exercise or (ii) a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. In November 2022, we announced an "at the market offering" under which we may offer and sell shares of our common stock having an aggregate offering amount of up to $250,000,000. Finally, in October 2023, we entered into a securities purchase agreement with Blackstone for the private placement of 2,467,104 shares of our common stock, at a purchase price of $12.16 per share.

We may fail to qualify for continued listing on The NASDAQ Global Market which could make it more difficult for investors to sell their shares.

Our common stock is listed on The NASDAQ Global Market, or NASDAQ. As a NASDAQ listed company, we are required to satisfy the continued listing requirements of NASDAQ for inclusion in the Global Market to maintain such listing, including, among other things, the maintenance of a minimum closing bid price of $1.00 per share and stockholders' equity of at least $10.0 million. There can be no assurance that we will be able to maintain compliance with the continued listing requirements or that our common stock will not be delisted from NASDAQ in the future. If our common stock is delisted by NASDAQ, we could face significant material adverse consequences, including:

- a limited availability of market quotations for our securities;
- reduced liquidity with respect to our securities;
- a determination that our shares are a "penny stock," which will require brokers trading in our shares to adhere to more stringent rules, possibly resulting in a reduced level of trading activity in the secondary trading market for our shares;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

If securities or industry analysts do not publish research or reports or publish unfavorable research about our business, the price of our common stock and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If securities or industry analysts do not initiate or continue coverage of us, the trading price for our common stock would be negatively affected. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our common stock, the price of our common stock would likely decline. If one or more of these analysts ceases to cover us or fails to publish regular reports on us, interest in the purchase of our common stock could decrease, which could cause the price of our common stock or trading volume to decline.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

We have broad discretion in the use of our cash and cash equivalents, and investors must rely on the judgment of our management regarding the use of our cash and cash equivalents. Our management may not use cash and cash equivalents in ways that ultimately increase the value of your investment. Our failure to use our cash and cash equivalents effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our products and product candidates. Pending their use, we may invest our cash and cash equivalents in short-term or long-term, investment-grade, interest-bearing securities. These investments may not yield favorable returns. If we do not invest or apply our cash and cash equivalents in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause the price of our common stock to decline.

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 some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. 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 U.S. 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, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be obtained or independently developed by a competitor, our competitive position would be harmed.

Litigation may adversely affect our business, financial condition, results of operations or liquidity.

Our business is subject to the risk of litigation by employees, consumers, vendors, competitors, intellectual property rights holders, stockholders, government agencies and others through private actions, class actions, administrative proceedings, regulatory actions, Hatch-Waxman or other litigation. For example, we and certain of our current and former officers have previously been parties to securities class action lawsuits against us, all of which have been settled or dismissed, and we are currently involved in Hatch-Waxman litigation. The outcome of litigation, particularly class action lawsuits, regulatory actions and intellectual property claims, is difficult to assess or quantify. Plaintiffs in these types of lawsuits may seek recovery of very large or indeterminate amounts, and the magnitude of the potential loss relating to these lawsuits may remain unknown for substantial periods of time. In addition, certain of these lawsuits, if decided against us or settled by us, may result in liability material to our Consolidated Financial Statements as a whole or may negatively affect our operating results if changes to our business operation are required. The cost to prosecute or defend litigation may be significant. There also may be adverse publicity associated with litigation that could negatively affect customer perception of our business, regardless of whether the allegations are valid or whether we are ultimately found liable. As a result, litigation may adversely affect our business, financial condition, results of operations or liquidity.

We may be exposed to employment-related claims and losses which could have an adverse effect on our business.

As we continue to increase the size of our workforce, the risk of potential employment-related claims will also increase. As such, we may be subject to claims, allegations or legal proceedings related to employment matters including, but not limited to, discrimination, harassment (sexual or otherwise), wrongful termination or retaliation, local, state or federal labor law violations, injury, and wage violations. In the event we are subject to one or more employment-related claims, allegations or legal proceedings, we may incur substantial costs, losses or other liabilities in the defense, investigation, settlement or other disposition of such claims. In addition to the economic impact, we may also suffer reputational harm as a result of such claims, allegations and legal proceedings and the investigation, defense and prosecution of such claims, allegations and legal proceedings could cause substantial disruption in our business and operations. While we do have policies and procedures in

place to reduce our exposure to these risks, there can be no assurance that such policies and procedures will be effective or that we will not be exposed to such claims, allegations or legal proceedings.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 1C. CYBERSECURITY

The Company's Board of Directors (the "Board") recognizes the critical importance of maintaining the trust and confidence of our customers, clients, business partners and employees. The Board is actively involved in oversight of the Company's Enterprise Risk Management Program ("ERMP"), and cybersecurity represents an important component of the Company's overall approach to enterprise risk management. The Company's cybersecurity policies, standards, processes and practices are integrated into the Company's ERMP and are based on recognized frameworks established by the National Institute of Standards and Technology and other applicable industry standards. In general, the Company seeks to address cybersecurity risks through a systematic, cross-functional approach that is focused on preserving the confidentiality, security and availability of the information that the Company collects and stores by identifying, preventing and mitigating cybersecurity threats and responding to cybersecurity incidents if they should occur.

Risk Management and Strategy

As one of the critical elements of the Company's overall enterprise risk management approach, the Company's cybersecurity program is focused on the following key areas:

- *Governance:* As discussed in more detail under the heading "Governance," the Board's oversight of cybersecurity is delegated to the Audit and Compliance Committee of the Board, which oversees the Company's entire ERMP, reporting up to the full board on a periodic basis. The Company's Chief Information Officer ("CIO"), the Chief Compliance Officer and other members of management regularly report to the Audit and Compliance Committee, with cybersecurity representing a standing meeting agenda topic.
- *Collaborative Approach:* The Company has implemented a systematic, cross-functional approach to identifying, preventing and mitigating cybersecurity threats and incidents, while also implementing controls and procedures that provide for the prompt escalation of certain cybersecurity incidents so that decisions regarding the public disclosure and reporting of such incidents can be made by management in a timely manner.

Technical Safeguards: The Company deploys technical safeguards that are designed to protect the Company's information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, anti-malware functionality and access controls, 24x7 security monitoring, and other controls which are evaluated and improved through vulnerability assessments and cybersecurity threat intelligence.

- *Incident Response and Recovery Planning:* The Company has established and maintains systematic incident response and recovery plans that address the Company's response to a cybersecurity incident, and such plans are tested and evaluated on a periodic basis.
- *Third-Party Risk Management:* The Company maintains a systematic, risk-based approach to identifying and overseeing cybersecurity risks presented by third parties, including vendors, service providers and other external users of the Company's systems, as well as the systems of third parties that could adversely impact our business in the event of a cybersecurity incident affecting those third-party systems.
- *Education and Awareness:* The Company provides regular, mandatory cybersecurity training for all personnel as a means to equip the Company's workforce with effective tools to recognize, address and communicate potential or actual threats to the Company's cybersecurity systems. Moreover, these trainings also allow Company personnel to remain up-to-date with evolving information security policies, standards, processes and best practices.

The Company engages in the periodic assessment and testing of the Company's policies, standards, processes and practices that are designed to address cybersecurity threats and incidents. These efforts include a wide range of activities, including audits, assessments, tabletop exercises, threat modeling, vulnerability testing and other exercises focused on evaluating the

effectiveness of our cybersecurity measures and planning. The Company has also engaged third parties to perform assessments on our cybersecurity measures, including information security maturity assessments, audits and independent reviews of our information security control environment and operating effectiveness. The results and findings of these exercises are reported to the Audit and Compliance Committee, who in turn updates the Board as appropriate. Management will then evaluate such findings and, with input from the Audit and Compliance Committee, take the appropriate steps to adjust the Company's cybersecurity policies, standards, processes and practices, as may be applicable, to strengthen or address any weaknesses, gaps or findings as the case may be.

As of the date of this Annual Report on Form 10-K, we are not aware of any risks from the cybersecurity threats that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations and financial condition.

Governance

The Board has delegated their oversight of cybersecurity to the Company's Audit and Compliance Committee which oversees the entire ERMP process. As detailed above, cybersecurity is a standing agenda topic for the Audit and Compliance Committee which receives regular presentations and reports from the Company's CIO on cybersecurity risks, detection protocols, disaster recovery readiness, the threat environment, recent developments in the cybersecurity space (including known incidents affecting the Company or key Company suppliers), evolving standards, vulnerability assessments, third-party and independent reviews, technological trends and information security considerations arising with respect to the Company's peers and third parties. Under the current cybersecurity framework, the Audit and Compliance Committee receives prompt and timely information regarding any cybersecurity incident that meets established reporting thresholds, as well as ongoing updates regarding any such incident. The Audit and Compliance Committee will keep the full board informed, as may be appropriate, until any such threat has been addressed to their satisfaction. Additionally, cybersecurity is also a standing agenda topic for the Global Risk Committee, with periodic updates to the Executive Committee and Senior Leadership Team.

The CIO, in coordination with the Chief Executive Officer, Chief Financial Officer, Chief Compliance Officer, Chief Legal Officer, and Chief People Officer works collaboratively across the Company to implement a program designed to protect the Company's information systems from cybersecurity threats and to promptly respond to any cybersecurity incidents in accordance with the Company's incident response and recovery plans. To facilitate the success of the Company's cybersecurity risk management program, multidisciplinary teams throughout the Company are deployed to address cybersecurity threats and to respond to cybersecurity incidents. The CIO has served in various leadership roles in information technology and information security for over 24 years, including serving as the vice president of information technology, with direct responsibility over the cyber security program, for a large publicly-traded company and as the chief information security officer of several large healthcare organizations. The CIO holds a Certified Information Systems Security Professional certification, an undergraduate degree in engineering, an MBA and a PhD in engineering.

Item 2. PROPERTIES

The following table contains information about our current significant leased properties as of December 31, 2023.

Location	Approximate Square Feet	Use	Lease expiry date [1]
Philadelphia, Pennsylvania, U.S.	50,816	Office and laboratory	September 2034
Marlow, United Kingdom	36,796	Office	August 2028
Princeton, New Jersey, U.S.	29,972	Office	January 2034

[1] Includes renewal options on leases which we are reasonably certain to exercise.

In addition to the above, we also maintain offices in other U.S. and international jurisdictions in which we operate. We believe that our current office and laboratory facilities are adequate and suitable for our current and anticipated needs. We believe that, to the extent required, we will be able to lease or buy additional facilities at commercially reasonable rates.

Item 3. LEGAL PROCEEDINGS

The information called for by this item is incorporated herein by reference to the information set forth in Note 15 "Legal Proceedings" of the Notes to Consolidated Financial Statements included in Item 8 of this Report.

Item 4. MINE SAFETY DISCLOSURES

None.

PART II

Item 5. MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES

Market for Our Common Stock

Our common stock has been traded on the NASDAQ Global Market under the symbol "FOLD" since May 31, 2007. Prior to that time, there was no public market for our common stock. The closing price for our common stock as reported by the NASDAQ Global Market on February 13, 2024 was $12.80 per share. As of February 13, 2024, there were 17 holders of record of our common stock.

Dividends

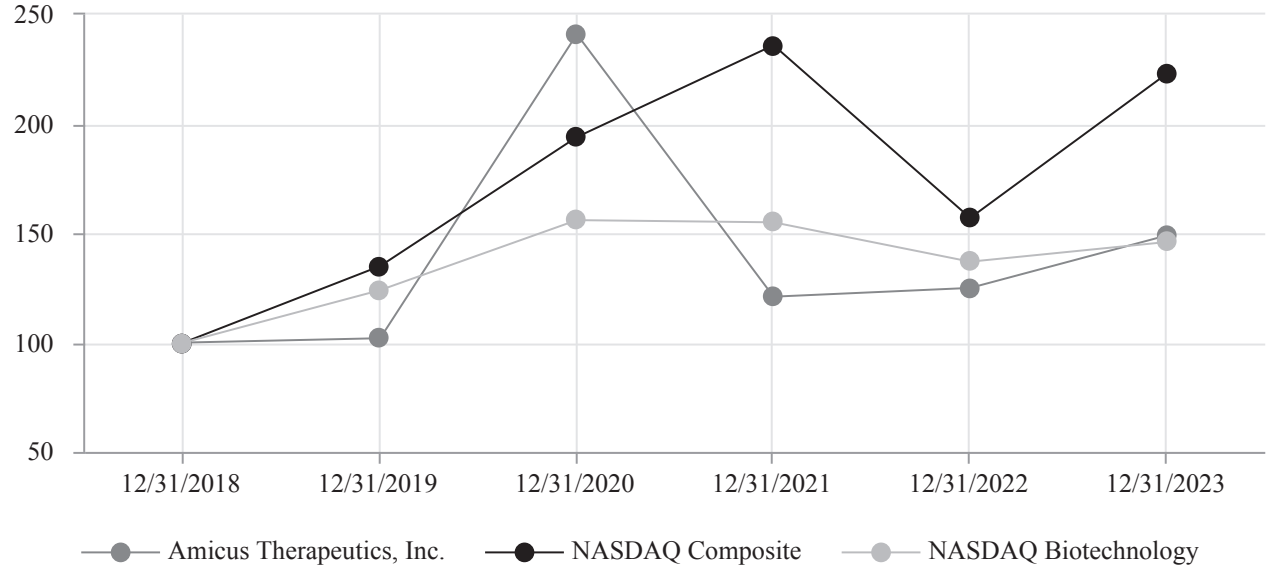
We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance the development and growth of our business. We do not intend to declare or pay cash dividends to our stockholders in the foreseeable future.

Recent Sales of Unregistered Securities

None.

Performance Graph

The following performance graph compares the cumulative total return on our common stock during the last five fiscal years with the NASDAQ Composite Index (U.S.) and the NASDAQ Biotechnology Index during the same period. The graph shows the value at the end of each of the last five fiscal years, of $100 invested in our common stock. Pursuant to applicable SEC rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder return shown on the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



	12/31/2018	12/31/2019	12/31/2020	12/31/2021	12/31/2022	12/31/2023
Amicus Therapeutics, Inc.	$100	$102	$241	$121	$125	$149
NASDAQ Composite	$100	$135	$194	$236	$157	$223
NASDAQ Biotechnology	$100	$124	$156	$155	$137	$146

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Issuer Purchases of Equity Securities

The following table provides certain information with respect to purchase of our common stock during the three months ended December 31, 2023:

Period	Total Number of Shares Purchased [1]	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares That May Yet Be Purchased Under the Plans or Programs
October 1, 2023 through October 31, 2023	47,887	$ 10.46	—	—
November 1, 2023 through November 30, 2023	12,420	$ 10.66	—	—
December 1, 2023 through December 31, 2023	38,804	$ 13.61	—	—
Total	99,111	$ 11.72	—	—

[1] Represents shares of common stock withheld to satisfy taxes associated with the vesting of restricted stock awards.

Item 6. [RESERVED]

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We seek to deliver the highest quality therapies that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. Our two marketed therapies are Galafold®, the first oral monotherapy for people living with Fabry disease who have amenable genetic variants, and Pombiliti™ + Opfolda™, a novel treatment designed to improve uptake of active enzyme into key disease relevant tissues for adults living with late-onset Pompe disease.

Galafold® (also referred to as "migalastat") is approved in over 40 countries around the world, including the United States ("U.S."), European Union ("E.U."), United Kingdom ("U.K."), and Japan. Additionally, Galafold® has been granted orphan drug designation in the U.S., E.U., U.K., Japan and several other countries.

Pombiliti™ + Opfolda™ (also referred to as "cipaglucosidase alfa-atga/miglustat") was approved in 2023 in the three largest Pompe markets: the U.S., the E.U., and the U.K. Multiple regulatory submissions and reimbursement processes with global health authorities are currently underway. Additionally, Pombiliti™ + Opfolda™ has been granted orphan drug designation in the U.S., E.U., U.K., Japan and several other countries.

Consolidated Results of Operations

The following discussion should be read in conjunction with the Consolidated Financial Statements and related notes included elsewhere in this report. The following section generally discusses 2023 and 2022 items and year-to-year comparisons between 2023 and 2022. Discussions of 2021 items and year-to-year comparisons between 2022 and 2021 that are not included in this Form 10-K can be found in Part II, Item 7 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, which comparisons are hereby incorporated by reference.

Year Ended December 31, 2023 Compared to Year Ended December 31, 2022

The following table provides selected financial information of our operations:

	Years Ended December 31,		
(in thousands)	**2023**	**2022**	**Change**
Net product sales	$ 399,356	$ 329,233	$ 70,123
Cost of goods sold	37,326	38,599	(1,273)
Cost of goods sold as a percentage of net product sales	9.3 %	11.7 %	(2.4)%
Operating expenses:			
Research and development	152,381	276,677	(124,296)
Selling, general, and administrative	275,270	213,041	62,229
Changes in fair value of contingent consideration payable	2,583	1,078	1,505
Loss on impairment of assets	1,134	6,616	(5,482)
Depreciation and amortization	7,873	5,342	2,531
Other (expense) income:			
Interest income	7,078	3,024	4,054
Interest expense	(50,149)	(37,119)	(13,030)
Loss on extinguishment of debt	(13,933)	—	(13,933)
Other (expense) income	(15,886)	4,176	(20,062)
Income tax (expense) benefit	(1,483)	5,471	(6,954)
Net loss attributable to common stockholders	$ (151,584)	$ (236,568)	$ 84,984

Net Product Sales. Net product sales increased $70.1 million during the year ended December 31, 2023 compared to the prior year. The increase was primarily due to continued growth of Galafold® in the U.S., Europe, and Japan markets as well as our commercial launch of Pombiliti™ + Opfolda™ in Europe and the U.S.

Cost of goods sold. Cost of goods sold includes manufacturing costs for our commercial products as well as royalties associated with net product sales of Galafold®. Cost of goods sold as a percentage of net product sales decreased 2.4% primarily due to inventory write-offs in the prior year. A portion of inventory available for sale was expensed as research and development costs prior to regulatory approval and as such, the cost of goods sold and related gross margins are not necessarily indicative of future costs of goods sold and gross margin.

Research and Development Expense. The following table summarizes our principal product development programs for each product candidate in development, and the out-of-pocket, third-party expenses incurred with respect to each product candidate:

(in thousands)	Years Ended December 31,	
Projects	**2023**	**2022**
Third-party direct project expenses		
Galafold® (Fabry Disease)	$ 12,928	$ 15,012
Pombiliti™ + Opfolda™ (Pompe Disease)	58,826	99,584
Gene therapy programs	872	48,948
Pre-clinical and other programs	1,681	124
Total third-party direct project expenses	74,307	163,668
Other project costs		
Personnel costs	62,492	82,386
Other costs	15,582	30,623
Total other project costs	78,074	113,009
Total research and development costs	$ 152,381	$ 276,677

The $124.3 million decrease in research and development costs was primarily driven by the strategic deprioritization of our gene therapy portfolio, which resulted in the recognition of contract exit costs in the prior year. Additionally, Pompe disease program spend decreased due to reduced clinical manufacturing costs. Personnel and other costs decreased in connection with the reallocation of resources to support our Pombiliti™ + Opfolda™ commercial launch and continued growth of Galafold®.

Selling, General, and Administrative Expense. Selling, general, and administrative expense increased $62.2 million, primarily driven by personnel costs in connection with the reallocation of resources to support our Pombiliti™ + Opfolda™ commercial launch and third-party professional fees.

Loss on Impairment of Assets. The $5.5 million decrease was primarily in connection with the strategic deprioritization of our gene therapy portfolio in the prior year, which resulted in us recognizing a loss on impairment of assets.

Loss on Extinguishment of Debt. In October 2023, the Company voluntarily prepaid the outstanding principal amount, accrued interest and prepayment premiums of the Senior Secured Term Loan due 2026. As a result of this early extinguishment, a loss on extinguishment of debt of $13.9 million was recognized in the Consolidated Statements of Operations.

Interest Expense. Interest expense increased $13.0 million during the year ended December 31, 2023. The increase was due to a higher variable interest rate on debt year over year.

Other (Expense) Income. The $20.1 million variance was primarily related to movement in foreign exchange rates caused by remeasurement of foreign-denominated balances.

Income Tax Expense. The income tax expense for the year ended December 31, 2023 was $1.5 million. We are subject to income taxes in various jurisdictions. Our tax liabilities are largely dependent on the distributions of pre-tax earnings among the many jurisdictions in which we operate.

Critical Accounting Policies and Significant Judgments and Estimates

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the following discussion represents our critical accounting policies.

Revenue Recognition

Our net product sales consist of sales of Galafold® for the treatment of Fabry disease and Pombiliti™ + Opfolda™ for the treatment of Pompe disease. We have recorded revenue on sales where our products are available either on a commercial basis or through a reimbursed early access program. Orders for our products are generally received from distributors and pharmacies with the ultimate payor often a government authority.

We recognize revenue when our performance obligations with our customers have been satisfied, which occurs at a point in time when the pharmacies or distributors obtain control of our products. The transaction price is determined based on fixed consideration in our customer contracts net of estimates for variable consideration. Variable consideration, which primarily consists of discounts and rebates due to foreign and U.S. government programs, is estimated based on contractual arrangements or statutory obligations, which may vary by product and payer and is recorded in the same period the related sales occur.

Estimation requires evaluation of our actual historical experience, customer mix, current contractual and statutory obligations, and inventory channel levels. We evaluate our customer mix to estimate which sales will be subject to which revenue dilutive items and consider changes to government program guidelines or contractual obligations that would impact the actual rebate or discount and/or our estimates of which sales qualify for such rebate or discount. We recognize revenue to the extent that it is probable that a significant revenue reversal will not occur in a future period. These estimates may differ from actual consideration received. We evaluate these estimates each reporting period to reflect known changes.

Liquidity and Capital Resources

As a result of our significant research and development expenditures, as well as expenditures to build a commercial organization to support the launch of Galafold® and Pombiliti™ + Opfolda™, we have not been profitable and have generated operating losses since we were incorporated in 2002. We have historically funded our operations through stock offerings, product revenues, debt issuance, collaborations, and other financing arrangements.

Sources of Liquidity

In November 2022, we entered into a Sales Agreement with The Goldman Sachs & Co. LLC to create an at-the-market equity program ("ATM program"), pursuant to which we may offer to sell shares of our common stock having aggregate offering gross proceeds of up to $250.0 million. During the year ended December 31, 2023, we issued and sold an aggregate of 5,244,936 shares through our ATM program at a weighted-average public offering price of $12.50 per share, resulting in net proceeds of $63.1 million. As of December 31, 2023, an aggregate of $184.4 million worth of shares remain available to be issued and sold under the ATM program.

In October 2023, we entered into the Senior Secured Term Loan due 2029. This transaction resulted in net proceeds of $387.4 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2029. Simultaneously, we also entered into a securities purchase agreement with funds managed by Blackstone, for the private placement of an aggregate of 2,467,104 shares of our common stock, at a purchase price of $12.16 per share. Proceeds from the private placement, net of offering costs, were $29.8 million. We used proceeds from the Senior Secured Term Loan due 2029 and the private placement to prepay the Senior Secured Term Loan due 2026, inclusive of the outstanding principal amount, accrued interest and prepayment premium.

In September 2021, we entered into securities purchase agreements with certain investors for the private placement of an aggregate of 11,296,660 shares of our common stock, at a purchase price of $10.18 per share, and pre-funded warrants to purchase an aggregate of 8,349,705 shares of common stock, at a purchase price of $10.17 per pre-funded warrant. The net proceeds from these private placements were approximately $199.8 million.

Cash Flow Discussion

As of December 31, 2023, we had cash, cash equivalents, and marketable securities of $286.2 million. We invest cash in excess of our immediate requirements in regard to liquidity and capital preservation in a variety of interest-bearing instruments, including obligations of U.S. government agencies and money market accounts. Wherever possible, we seek to minimize the potential effects of concentration and degrees of risk. Although we maintain cash balances with financial institutions in excess of insured limits, we do not anticipate any losses with respect to such cash balances. For more details on the cash, cash equivalents, and marketable securities, refer to "— Note 4. Cash, Cash Equivalents, Marketable Securities, and Restricted Cash," in our Notes to Consolidated Financial Statements.

Net Cash Used in Operating Activities

Net cash used in operations for the year ended December 31, 2023 was $69.1 million. The components of net cash used in operations included the net loss for the year ended December 31, 2023 of $151.6 million and the net change in operating assets and liabilities of $48.0 million offset by $86.1 million of stock compensation and $44.4 million of other non-cash adjustments. The change in operating assets was primarily due to an increase in inventory of $44.6 million, an increase in accounts receivable of $20.1 million associated with increased commercial sales, and an increase in prepaid and other current assets of $8.1 million primarily associated with tax prepayments. The net cash used in operations was also impacted by an increase in accounts payable and accrued expenses of $49.2 million, associated with accrued interest due to timing, inventory purchases to support our continued commercial growth, personnel costs, and an increases in sales rebates associated with increased commercial sales.

Net cash used in operations for the year ended December 31, 2022 was $166.6 million. The components of net cash used in operations included the net loss for the year ended December 31, 2022 of $236.6 million and the net change in operating assets and liabilities of $39.9 million offset by $76.5 million of stock compensation and $33.4 million of other non-cash adjustments. The change in operating assets was primarily due to increases in accounts receivable of $17.3 million due to increased commercial sales of Galafold®, an increase in prepaid and other current assets of $6.2 million to support commercial activities for Galafold®, and an increase in inventory of $5.3 million. The net cash used in operations was also impacted by a decrease in accounts payable and accrued expenses of $6.4 million, associated with payments of contract manufacturing and third-party development services partially offset by increases in sales rebates and royalties associated with increased commercial sales of Galafold®.

Net Cash Provided by Investing Activities

Net cash provided by investing activities for the year ended December 31, 2023 was $98.1 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash provided by investing activities reflects $197.2 million for the sale and redemption of marketable securities, partially offset by $91.7 million for the purchase of marketable securities and $7.4 million for capital expenditures.

Net cash provided by investing activities for the year ended December 31, 2022 was $92.3 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash provided by investing activities reflects $335.9 million for the sale and redemption of marketable securities and $3.4 million of proceeds from the sale of our property and equipment, partially offset by $243.3 million for the purchase of marketable securities and $3.8 million for capital expenditures.

Net Cash Provided by (Used in) Financing Activities

Net cash provided by financing activities for the year ended December 31, 2023 was $61.7 million. Net cash provided by financing activities primarily reflects $387.4 million of net proceeds from the Senior Secured Loan due in 2029, $63.1 million of net proceeds from the issuance of shares in connection with our ATM program, $29.8 million of net proceeds from our private placement with Blackstone, and $10.3 million in proceeds from the exercise of stock options. Net cash provided by financing activities was partially offset by the $408.0 million repayment of our Senior Secured Loan due in 2026, and $17.9 million for payments of employee withholding taxes related to restricted stock unit vesting.

Net cash used in financing activities for the year ended December 31, 2022 was $7.5 million. Net cash used in financing activities primarily reflects $11.5 million from payments of employee withholding taxes related to restricted stock unit vesting, partially offset by $4.3 million from the exercise of stock options.

Funding Requirements

We expect to continue to incur significant costs in the foreseeable future primarily due to research and development expenses, including expenses related to conducting clinical trials. Our future capital requirements will depend on a number of factors, including:

- the scope, progress, results and costs of clinical trials for our drug candidates;
- the cost of manufacturing drug supply for our commercial, clinical and preclinical studies, including the cost of manufacturing Pombiliti™ (also referred to as "ATB200" or "cipaglucosidase alfa");
- the future results of preclinical research and subsequent clinical trials for pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates;
- any changes in regulatory standards relating to the review of our product candidates;
- any changes in laws, rules or regulations affecting our ability to manufacture, transport, test, develop, or commercialize our products, including Galafold®, Pombiliti™ + Opfolda™, or our product candidates;
- the costs of commercialization activities, including product marketing, sales, and distribution;
- the emergence of competing technologies and other adverse market developments;
- the estimates regarding the potential market opportunity for our products and product candidates;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl");
- our ability to successfully commercialize Pombiliti™ + Opfolda™ (together, also referred to as "AT-GAA") in the E.U., U.K., and U.S., and elsewhere, if regulatory applications are approved;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and Pombiliti™ + Opfolda™;
- our ability to obtain reimbursement for Galafold® and Pombiliti™ + Opfolda™;

- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold® and Pombiliti™ + Opfolda™;
- our ability to obtain market acceptance of Galafold® and Pombiliti™ + Opfolda™ or any other product developed or acquired that has received regulatory approval;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims, including Hatch-Waxman litigation;
- the impact of litigation that has been or may be brought against us or of litigation that we are pursuing or may pursue against others, including Hatch-Waxman litigation;
- the extent to which we acquire or invest in businesses, products, and technologies;
- our ability to successfully integrate acquired products and technologies into our business, or successfully divest or license existing products and technologies from our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish licensing agreements, collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other economic benefits from any such collaborators;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards, including climate reporting requirements at the local, state and national levels;
- our ability to successfully protect our information technology systems and maintain our global operations and supply chain without interruption;
- our ability to accurately forecast revenue, operating expenditures, or other metrics impacting profitability;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

We may seek additional funding through public or private financings of debt or equity. Based on our current operating model, we believe that the current cash position, which includes expected revenues, is sufficient to fund our operations and ongoing research programs for at least the next 12 months. Potential impacts of business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our long-term capital requirements.

Contractual Obligations and Commitments

As of December 31, 2023, remaining maturities, including expected interest payments through maturity, on our Senior Secured Term Loan due 2029 were $623.4 million. Refer to "— Note 11. Debt," to the Consolidated Financial Statements for more information.

We are lessees to various operating leases for facilities and equipment. As of December 31, 2023, our undiscounted cash liabilities for operating leases were $89.8 million, with maturities ranging up through fiscal 2034. Refer to "— Note 12. Leases," to the Consolidated Financial Statements for more information.

In connection with our collaboration agreement with GlaxoSmithKline ("GSK"), pursuant to which we obtained global rights to develop and commercialize Galafold® as a monotherapy and in combination with ERT for Fabry disease, GSK is eligible to receive post-approval and sales-based milestones up to $40 million, as well as tiered royalties in the mid-teens in eight major markets outside the U.S. As of December 31, 2023, remaining milestones under this agreement were $9.8 million. Refer to "— Note 14. Collaborative Agreements," to the Consolidated Financial Statements for more information.

We have a number of binding minimum purchase and manufacturing commitments due to our third-party manufacturers. As of December 31, 2023, these purchase and manufacturing obligations totaled $126.2 million, of which $83.9 million and $42.3 million are expected in 2024 and 2025, respectively. Contracts for which our commitment is variable, based on volumes, with no fixed minimum quantities, and contracts that can be canceled without payment penalties have been excluded. These purchase obligations are in addition to amounts recorded on our December 31, 2023 Consolidated Balance Sheets.

We have no off-balance sheet arrangements as of December 31, 2023 and 2022.

Recent Accounting Pronouncements

Please refer to "— Note 2. Summary of Significant Accounting Policies," in our Notes to the Consolidated Financial Statements.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Market risk is the risk of change in fair value of a financial instrument due to changes in interest rates, equity prices, creditworthiness, financing, exchange rates or other factors. Our primary market risk exposure relates to changes in interest rates in our cash, cash equivalents, and marketable securities. We place our investments in high-quality financial instruments, primarily money market funds, asset backed securities, and U.S. government agency notes with maturities of less than one year, which we believe are subject to limited interest rate and credit risk. The securities in our investment portfolio are not leveraged, are classified as available-for-sale and, due to the short-term nature, are subject to minimal interest rate risk. We believe that a 1% (100 basis points) change in average interest rates would either increase or decrease the market value of our investment portfolio by $0.1 million as of December 31, 2023. We currently do not hedge interest rate exposure and consistent with our investment policy, we do not use derivative financial instruments in our investment portfolio.

We are exposed to interest rate risk with respect to variable rate debt. At December 31, 2023, we had a $400 million Senior Secured Term Loan due 2029 that bears interest at a rate equal to the 3-month Term Secured Overnight Financing Rate ("SOFR"), subject to a 2.5% floor, plus a Term SOFR adjustment of 0.26161% and a margin of 6.25% per year. We entered into this loan in October of 2023, and simultaneously used proceeds from the Senior Secured Term Loan due 2029 and the private placement to prepay the Senior Secured Term Loan due 2026. We do not currently hedge our variable interest rate debt. The annual average variable interest rate for our variable rate debts during the year ended December 31, 2023 was 11.7%. A hypothetical 100 basis point increase or decrease in the average interest rate on our variable rate debts would result in $4.1 million change in the interest expense as of December 31, 2023.

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars. We are not currently engaged in any foreign currency hedging activities. The current exposures arise primarily from cash, accounts receivable, intercompany receivables and payables, and net product sales denominated in foreign currencies. Both positive and negative impacts to our international product sales from movements in foreign currency exchange rates may be partially mitigated by the natural, opposite impact that foreign currency exchange rates have on our international operating expenses. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our Consolidated Financial Statements.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Management's Report on Consolidated Financial Statements and Internal Control over Financial Reporting

The management of Amicus Therapeutics, Inc. has prepared, and is responsible for the Company's Consolidated Financial Statements and related footnotes. These Consolidated Financial Statements have been prepared in conformity with U.S. generally accepted accounting principles ("U.S. GAAP").

We are responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of the Company's principal executive and principal financial officers and effected by the Company's board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of Amicus Therapeutics, Inc.;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of Amicus therapeutics, Inc. are being made only in accordance with authorizations of management and directors of Amicus therapeutics, Inc.; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the assets of Amicus Therapeutics, Inc. that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

We assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, we used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) ("COSO") in Internal Control — Integrated Framework. Based on our assessment we believe that, as of December 31, 2023, our internal control over financial reporting is effective based on those criteria.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2023 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report. This report appears on the following page.

Dated February 28, 2024

/s/ BRADLEY L. CAMPBELL	/s/ SIMON HARFORD
President and Chief Executive Officer	Chief Financial Officer

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Amicus Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Amicus Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Amicus Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2023 and 2022, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes and our report dated February 28, 2024 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Consolidated Financial Statements and Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Iselin, New Jersey
February 28, 2024

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Amicus Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Amicus Therapeutics, Inc. (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity and cash flows for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2024 expressed an unqualified opinion thereon.

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 PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue recognition – Measurement of variable consideration for Ex-U.S. third-party discounts and rebates

Description of the Matter

As described in Note 2 to the consolidated financial statements, the Company recognizes revenue net of estimates for variable consideration, which are primarily third-party discounts and rebates. The sales discounts and rebates are recorded as a reduction of revenue at the time revenue from the sale of the Company's products is recognized, which occurs at a point in time when the customer obtains control of the product.

Auditing the Ex-U.S. sales discounts and rebates was complex because of the volume of sales discounts and rebates and the different contractual product price, discount and/or rebate rate for each country.

How We Addressed the Matter in Our Audit

We identified, evaluated, and tested controls over management's calculations of the discounts and rebates as well as the data input utilized in the calculations.

To test the revenue adjustments related to sales discounts and rebates our procedures included, among others, assessing the terms of the arrangement, evaluating the methodology used, testing the significant inputs, and the completeness, accuracy and relevance of the underlying data used by management in its calculations. We inspected significant sales contracts and agreements that include the contractual rights to discounts and rebates and tested credit memos issued during the year and subsequent to year end. In addition, we assessed the historical accuracy of management's estimates against actual results.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2003.

Iselin, New Jersey
February 28, 2024

Amicus Therapeutics, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2023	**2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 246,994	$ 148,813
Investments in marketable securities	39,206	144,782
Accounts receivable	87,632	66,196
Inventories	59,696	23,816
Prepaid expenses and other current assets	49,533	40,209
Total current assets	483,061	423,816
Operating lease right-of-use assets, net	26,312	29,534
Property and equipment, less accumulated depreciation of $25,429 and $22,281 at December 31, 2023 and 2022, respectively	31,667	30,778
Intangible assets, less accumulated amortization of $2,510 and $0 at December 31, 2023 and December 31, 2022, respectively	20,490	23,000
Goodwill	197,797	197,797
Other non-current assets	18,553	19,242
Total Assets	$ 777,880	$ 724,167
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 15,120	$ 15,413
Accrued expenses and other current liabilities	144,245	93,636
Contingent consideration payable	—	21,417
Operating lease liabilities	8,324	8,552
Total current liabilities	167,689	139,018
Long-term debt	387,858	391,990
Operating lease liabilities	48,877	51,578
Other non-current liabilities	13,282	18,534
Total liabilities	617,706	601,120
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.01 par value, 500,000,000 shares authorized, 293,594,209 and 281,108,273 shares issued and outstanding at December 31, 2023 and 2022, respectively	2,918	2,815
Additional paid-in capital	2,836,018	2,664,744
Accumulated other comprehensive gain (loss):		
Foreign currency translation adjustment	5,429	(11,989)
Unrealized loss on available-for-sale securities	(188)	(116)
Warrants	71	83
Accumulated deficit	(2,684,074)	(2,532,490)
Total stockholders' equity	160,174	123,047
Total Liabilities and Stockholders' Equity	$ 777,880	$ 724,167

See accompanying Notes to Consolidated Financial Statements

Amicus Therapeutics, Inc.
Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2023	**2022**	**2021**
Net product sales	$ 399,356	$ 329,233	$ 305,514
Cost of goods sold	37,326	38,599	34,466
Gross profit	362,030	290,634	271,048
Operating expenses:			
Research and development	152,381	276,677	272,049
Selling, general, and administrative	275,270	213,041	192,710
Changes in fair value of contingent consideration payable	2,583	1,078	6,514
Loss on impairment of assets	1,134	6,616	—
Depreciation and amortization	7,873	5,342	6,209
Total operating expenses	439,241	502,754	477,482
Loss from operations	(77,211)	(212,120)	(206,434)
Other (expense) income:			
Interest income	7,078	3,024	509
Interest expense	(50,149)	(37,119)	(32,471)
Loss on extinguishment of debt	(13,933)	—	(257)
Other (expense) income	(15,886)	4,176	(2,901)
Loss before income tax	(150,101)	(242,039)	(241,554)
Income tax (expense) benefit	(1,483)	5,471	(8,906)
Net loss attributable to common stockholders	$ (151,584)	$ (236,568)	$ (250,460)
Net loss attributable to common stockholders per common share — basic and diluted	$ (0.51)	$ (0.82)	$ (0.92)
Weighted-average common shares outstanding — basic and diluted	295,164,515	289,057,198	271,421,986

See accompanying Notes to Consolidated Financial Statements

Amicus Therapeutics, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Years Ended December 31,		
	2023	2022	2021
Net loss	$ (151,584)	$ (236,568)	$ (250,460)
Other comprehensive gain (loss), net of tax:			
Foreign currency translation adjustment gain (loss)	17,418	(17,240)	(3,161)
Unrealized (loss) gain on available-for-sale securities	(72)	154	(85)
Other comprehensive gain (loss)	17,346	(17,086)	(3,246)
Comprehensive loss	$ (134,238)	$ (253,654)	$ (253,706)

See accompanying Notes to Consolidated Financial Statements

Amicus Therapeutics, Inc.
Consolidated Statements of Changes in Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Warrants	Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
Balance at December 31, 2020	262,063,461	$ 2,650	$ 2,308,578	$ 12,387	$ 8,227	$ (2,045,462)	$ 286,380
Stock options exercised, net	1,461,189	15	10,213	—	—	—	10,228
Common stock issued from equity financing and pre-funded warrants, net of offering costs	11,296,660	112	199,552	83	—	—	199,747
Vesting of restricted stock units, net of taxes	1,064,135	—	(15,009)	—	—	—	(15,009)
Stock-based compensation	—	—	57,838	—	—	—	57,838
Warrants exercised	2,554,999	26	31,591	(12,387)	—	—	19,230
Equity component of the convertible notes	472,356	5	2,656	—	—	—	2,661
Unrealized loss on available-for-sale securities	—	—	—	—	(85)	—	(85)
Foreign currency translation adjustment	—	—	—	—	(3,161)	—	(3,161)
Net loss	—	—	—	—	—	(250,460)	(250,460)
Balance at December 31, 2021	278,912,800	2,808	2,595,419	83	4,981	(2,295,922)	307,369
Stock options exercised, net	656,377	7	4,303	—	—	—	4,310
Vesting of restricted stock units, net of taxes	1,539,096	—	(11,490)	—	—	—	(11,490)
Stock-based compensation	—	—	76,512	—	—	—	76,512
Unrealized gain on available-for-sale securities	—	—	—	—	154	—	154
Foreign currency translation adjustment	—	—	—	—	(17,240)	—	(17,240)
Net loss	—	—	—	—	—	(236,568)	(236,568)
Balance at December 31, 2022	281,108,273	2,815	2,664,744	83	(12,105)	(2,532,490)	123,047
Stock options exercised, net	1,357,945	14	10,247	—	—	—	10,261
Issuance of shares in connection with at-the-market offering, net of issuance costs	5,244,936	52	63,056	—	—	—	63,108
Common stock issued from private placement, net of offering costs	2,467,104	25	29,802	—	—	—	29,827
Vesting of restricted stock units, net of taxes	2,195,851	—	(17,920)	—	—	—	(17,920)
Stock-based compensation	—	—	86,077	—	—	—	86,077
Warrants exercised	1,220,100	12	12	(12)	—	—	12
Unrealized loss on available-for-sale securities	—	—	—	—	(72)	—	(72)
Foreign currency translation adjustment	—	—	—	—	17,418	—	17,418
Net loss	—	—	—	—	—	(151,584)	(151,584)
Balance at December 31, 2023	293,594,209	$ 2,918	$ 2,836,018	$ 71	$ 5,241	$ (2,684,074)	$ 160,174

See accompanying Notes to Consolidated Financial Statements

Amicus Therapeutics, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2023	**2022**	**2021**
Operating activities			
Net loss	$ (151,584)	$ (236,568)	$ (250,460)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of debt discount and deferred financing	2,616	2,634	2,490
Depreciation and amortization	7,873	5,342	6,209
Stock-based compensation	86,077	76,512	57,838
Loss on extinguishment of debt	13,933	—	257
Non-cash changes in the fair value of contingent consideration payable	2,583	1,078	6,514
Foreign currency remeasurement loss	19,613	6,121	3,565
Non-cash deferred taxes	(4,939)	9	34
Asset impairment charges and other asset write-offs	2,727	18,177	—
Changes in operating assets and liabilities:			
Accounts receivable	(20,108)	(17,330)	(8,189)
Inventories	(44,614)	(5,343)	(7,790)
Prepaid expenses and other current assets	(8,062)	(6,194)	(5,919)
Accounts payable, accrued expenses, and other current liabilities	49,195	(6,377)	7,430
Other non-current assets and liabilities	(3,054)	(4,636)	(4,117)
Payment of contingent consideration	(21,347)	—	(10,353)
Net cash used in operating activities	$ (69,091)	$ (166,575)	$ (202,491)
Investing activities			
Sale and redemption of marketable securities	197,227	335,926	424,043
Purchases of marketable securities	(91,723)	(243,255)	(341,398)
Capital expenditures	(7,440)	(3,766)	(3,884)
Proceeds from sale of assets	—	3,411	—
Net cash provided by investing activities	$ 98,064	$ 92,316	$ 78,761
Financing activities			
Proceeds from the issuance of shares in connection with at-the-market offering, net of issuance costs	63,108	—	—
Proceeds from equity financing, net of issuance costs	29,827	—	199,750
Withholding taxes paid on vested restricted stock units	(17,920)	(11,490)	(15,009)
Proceeds from stock options exercised, net	10,261	4,310	10,228
Proceeds from warrants exercised, net	12	—	19,230
Payment of long-term debt	(408,043)	—	—
Proceeds from long-term debt, net of issuance costs	387,360	—	—
Payment of contingent consideration	(2,653)	—	(1,647)
Payment of finance leases	(275)	(283)	(479)
Net cash provided by (used in) financing activities	$ 61,677	$ (7,463)	$ 212,073
Effect of exchange rate changes on cash, cash equivalents, and restricted cash	$ 6,312	$ (14,619)	$ (5,049)
Net increase (decrease) in cash, cash equivalents, and restricted cash	96,962	(96,341)	83,294
Cash, cash equivalents, and restricted cash at the beginning of the year	153,115	249,456	166,162
Cash, cash equivalents, and restricted cash at the end of the year	$ 250,077	$ 153,115	$ 249,456

	Years Ended December 31,		
	2023	2022	2021
Supplemental disclosures of cash flow information			
Tenant improvements paid through lease incentive	$ 105	$ —	$ 300
Cash paid during the period for interest	$ 36,090	$ 34,358	$ 30,468
Capital expenditures unpaid at the end of period	$ 868	$ 1,141	$ 1,448
Cash paid for income taxes	$ 8,525	$ 1,609	$ 20,032

See accompanying Notes to Consolidated Financial Statements

1. Description of Business

Amicus Therapeutics, Inc. (the "Company") is a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. The Company seeks to deliver the highest quality therapies that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. The Company's two marketed therapies are Galafold®, the first oral monotherapy for people living with Fabry disease who have amenable genetic variants, and Pombiliti™ + Opfolda™, a novel treatment designed to improve uptake of active enzyme into key disease relevant tissues for adults living with late-onset Pompe disease.

Galafold® (also referred to as "migalastat"), is approved in over 40 countries around the world, including the United States ("U.S."), European Union ("E.U."), United Kingdom ("U.K."), and Japan. Additionally, Galafold® has been granted orphan drug designation in the U.S., E.U., U.K., Japan and several other countries.

Pombiliti™ + Opfolda™ (also referred to as "cipaglucosidase alfa-atga/miglustat"), was approved in 2023 in the three largest Pompe markets: the U.S., the E.U., and the U.K. Multiple regulatory submissions and reimbursement processes with global health authorities are currently underway. Additionally, Pombiliti™ + Opfolda™ has been granted orphan drug designation in the U.S., E.U., U.K., Japan and several other countries.

The Company had an accumulated deficit of $2.7 billion as of December 31, 2023 and anticipates incurring losses through the fiscal year ending December 31, 2024. The Company has historically funded its operations through stock offerings, product revenues, debt issuances, collaborations, and other financing arrangements.

Based on its current operating model, the Company believes the current cash position, which includes expected revenues, is sufficient to fund the Company's operations and ongoing research programs for at least the next 12 months. Potential business development opportunities, pipeline expansion, and investment in manufacturing capabilities could impact the Company's long-term capital requirements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company has prepared the accompanying Consolidated Financial Statements in accordance with U.S. generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. Certain prior year amounts have been reclassified for comparative purposes. The reclassifications did not affect results of operations, net assets or cash flows.

Consolidation

The Consolidated Financial Statements include the accounts of the Company and its subsidiaries. Intercompany accounts and transactions are eliminated in consolidation.

Foreign Currency Transactions

The functional currency for most of the Company's foreign subsidiaries is their local currency. For non-U.S. subsidiaries that transact in a functional currency other than the U.S. dollar, assets and liabilities are translated at current rates of exchange at the balance sheet date. Income and expense items are translated at the weighted average foreign exchange rates for the period. Adjustments resulting from the translation of the financial statements of the Company's foreign operations into U.S. dollars are excluded from the determination of net income and are recorded in accumulated other comprehensive income, a separate component of stockholders' equity. Transactions which are not in the functional currency of the entity are remeasured into the functional currency with gains or losses resulting from the remeasurement recorded in other (expense) income.

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, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

Cash, Cash Equivalents, Marketable Securities, and Restricted Cash

The Company considers all highly liquid investments purchased with a maturity of three months or less at the date of acquisition to be cash equivalents. Marketable securities consist of fixed income investments with a maturity of greater than three months and other highly liquid investments that can be readily purchased or sold using established markets. These investments are classified as available-for-sale and are reported at fair value on the Company's Consolidated Balance Sheets. Unrealized holding gains and losses are reported within other comprehensive gain (loss) in the Company's Consolidated Statements of Comprehensive Loss. Fair value is based on available market information including quoted market prices, broker or dealer quotations, or other observable inputs.

Restricted cash consists primarily of funds held to satisfy the requirements of certain agreements that are restricted in their use and is included as a component of other non-current assets on the Company's Consolidated Balance Sheets.

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash, cash equivalents, and marketable securities. The Company maintains its cash and cash equivalents in bank accounts, which, at times, exceed federally insured limits. The Company invests its marketable securities in high-quality commercial financial instruments. The Company has not recognized any losses from credit risks on such accounts during any of the periods presented. The Company believes it is not exposed to significant credit risk on its cash, cash equivalents, or marketable securities.

The Company is subject to credit risk from its accounts receivable primarily related to its product sales of Galafold®. The Company's accounts receivable at December 31, 2023 have arisen from product sales primarily in Europe, the U.S., and Japan. The Company will periodically assess the financial strength of its customers to establish allowances for anticipated losses, if any. For accounts receivable that have arisen from named patient sales, the payment terms are predetermined, and the Company evaluates the creditworthiness of each customer on a regular basis. As of December 31, 2023, the Company's allowance for doubtful accounts was $0.2 million.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated over the estimated useful lives of the respective assets, which range from three to five years, or the lesser of the related initial term of the lease or useful life for leasehold improvements.

The initial cost of property and equipment consists of its purchase price and any directly attributable costs of bringing the asset to its working condition and location for its intended use. Expenditures incurred after the fixed assets have been put into operation, such as repairs and maintenance, are expensed as incurred. Major replacements, improvements, and additions are capitalized in accordance with Company policy.

The Company evaluates long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset group may not be recoverable. If indications of impairment exist, projected future undiscounted cash flows associated with the asset or asset group are compared to the carrying value of the asset to determine whether the asset or asset group's value is recoverable. If impairment is determined, the Company writes down the asset to its estimated fair value and records an impairment loss equal to the excess of the carrying value of the long-lived asset over its estimated fair value in the period at which such a determination is made.

Revenue Recognition

The Company has recorded revenue on sales where its products are available either on a commercial basis or through a reimbursed early access program. Product orders are generally received from distributors and pharmacies, with the ultimate payor often a government authority. In 2023, one customer accounted for 28% of net product sales and 16% of accounts receivable from product sales while another customer accounted for 17% of accounts receivable from product sales. In 2022, one customer accounted for 27% of net product sales and 14% of accounts receivable from product sales.

The Company recognizes revenue when its performance obligations to its customers have been satisfied, which occurs at a point in time when the pharmacies or distributors obtain control of the products. The transaction price is determined based on fixed consideration in the Company's customer contracts and is recorded net of estimates for variable consideration, which primarily consist of third-party discounts and rebates. The identified variable consideration is recorded as a reduction of revenue at the time revenue from the sale is recognized. The Company recognizes revenue to the extent that it is probable that a significant revenue reversal will not occur in a future period. These estimates may differ from actual consideration received. The Company evaluates these estimates each reporting period to reflect known changes.

The following table summarizes the Company's net product sales disaggregated by product:

	For the Year		
(in thousands)	**2023**	**2022**	**2021**
Galafold®	$ 387,777	$ 329,046	$ 305,514
Pombiliti™ + Opfolda™	11,579	187	—
Total net product sales	$ 399,356	$ 329,233	$ 305,514

The following table summarizes the Company's net product sales disaggregated by geographic area:

	For the Year		
(in thousands)	**2023**	**2022**	**2021**
U.S.	$ 146,937	$ 115,946	$ 95,387
Ex-U.S.	252,419	213,287	210,127
Total net product sales	$ 399,356	$ 329,233	$ 305,514

Inventories and Cost of Goods Sold

Until regulatory approval of Pombiliti™ + Opfolda™, the Company expensed all manufacturing costs as research and development expense. Upon regulatory approval, the Company began capitalizing costs related to the purchase and manufacture of Pombiliti™ + Opfolda™.

Inventories are stated at the lower of cost and net realizable value, determined by the first-in, first-out method. Inventories are reviewed periodically to identify slow-moving or obsolete inventory based on projected sales activity as well as product shelf-life. In evaluating the recoverability of inventories produced, the probability that revenue will be obtained from the future sale of the related inventory is considered and inventory value is written down for inventory quantities in excess of expected requirements. Expired inventory is disposed of and the related costs are recognized as cost of goods sold in the Company's Consolidated Statements of Operations.

Cost of goods sold includes the cost of inventory sold, manufacturing and supply chain costs, product shipping and handling costs, provisions for excess and obsolete inventory, as well as royalties payable. A portion of inventory available for sale was expensed as research and development costs prior to regulatory approval and, as such, the cost of goods sold and related gross margins are not necessarily indicative of future costs of goods sold and gross margin.

Fair Value Measurements

The Company records certain asset and liability balances under the fair value measurements as defined by the Financial Accounting Standard Board ("FASB") guidance. Current FASB fair value guidance emphasizes that fair value is a market-based measurement, not an entity-specific measurement. Therefore, a fair value measurement should be determined based on the assumptions that market participants would use in pricing the asset or liability. As a basis for considering market participant assumptions in fair value measurements, current FASB guidance establishes a fair value hierarchy that distinguishes between market participant assumptions based on market data obtained from sources independent of the reporting entity (observable inputs that are classified within Levels 1 and 2 of the hierarchy) and the reporting entity's own assumptions that market participant's assumptions would use in pricing assets or liabilities (unobservable inputs classified within Level 3 of the hierarchy).

Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access at measurement date. Level 2 inputs are inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs may include quoted prices for similar assets and liabilities in active markets, as well as inputs that are observable for the asset or liability (other than quoted prices), such as interest rates, foreign exchange rates, and yield curves that are observable at commonly quoted intervals. Level 3 inputs are unobservable inputs for the asset or liability, which is typically based on an entity's own assumptions, as there is little, if any, related market activity. In instances where the determination of the fair value measurement is based on inputs from different levels of the fair value hierarchy, the level in the fair value hierarchy within which the entire fair value measurement falls is based on the lowest level input that is significant to the fair value measurement in its entirety. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires judgment and considers factors specific to the asset or liability.

Contingent Liabilities

On an ongoing basis, the Company may be involved in various claims and legal proceedings. On a quarterly basis, the Company reviews the status of each significant matter and assesses its potential financial exposure. If the potential loss from any claim, asserted or unasserted, or legal proceeding is considered probable and the amount can be reasonably estimated, the Company will accrue a liability for the estimated loss. Because of uncertainties related to claims and litigation, accruals will be based on the Company's best estimates based on available information. On a periodic basis, as additional information becomes available, or based on specific events such as the outcome of litigation or settlement of claims, the Company may reassess the potential liability related to these matters and may revise these estimates, which could result in material adverse adjustments to the Company's operating results.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expense consist primarily of costs related to personnel, including salaries and other personnel related expenses, consulting fees, and the cost of facilities and support services used in drug development. Assets acquired that are used for research and development and have no future alternative use are expensed as in-process research and development.

Interest Income and Interest Expense

Interest income consists of interest earned on the Company's cash, cash equivalents, and marketable securities. Interest expense consists of interest incurred on debt and finance leases.

Income Taxes

The Company accounts for income taxes under the liability method. Under this method deferred income tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax basis of assets and liabilities and for operating losses and tax credit carry forwards, using enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance is recorded if it is "more likely than not" that a portion or all of a deferred tax asset will not be realized.

The Company's tax returns are subject to examination by U.S. Federal, state, and foreign taxing jurisdictions. The impact of an uncertain tax position taken or expected to be taken on an income tax return must be recognized in the financial statements at the largest amount that is more likely than not to be sustained. An uncertain income tax position will not be recognized in the financial statements unless it is more likely than not to be sustained.

Other Comprehensive Gain (Loss)

Components of other comprehensive gain (loss) include unrealized gains and losses on available-for-sale securities and gains and losses on foreign currency transactions, and are included in the Consolidated Statements of Comprehensive Loss.

Leases

The Company primarily enters into lease agreements for office space, equipment, and vehicles. The leases have varying terms, some of which could include options to renew, extend, and early terminate. The Company determines if an arrangement is a lease at contract inception. Operating leases are included in right-of-use ("ROU") assets and lease liabilities on the Consolidated Balance Sheets.

ROU assets represent the Company's right to control the use of an explicitly or implicitly identified fixed asset for a period of time and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Control of an underlying asset is conveyed if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

Lease payments included in the measurement of the lease liability are comprised of fixed payments. Variable lease payments are excluded from the ROU asset and lease liability and are recognized in the period in which the obligation for those payments is incurred. Variable lease payments are presented in the Consolidated Statements of Operations in the same line item as expenses arising from fixed lease payments for operating leases. The Company has lease agreements that include lease and non-lease components, which the Company accounts for as a single lease component for all underlying asset categories.

The lease term for all of the Company's leases includes the non-cancellable period of the lease plus any additional periods covered by either a Company option to extend (or not to terminate) the lease that the Company is reasonably certain to exercise, or an option to extend (or not to terminate) the lease controlled by the lessor.

Leases with an initial term of 12 months or less are not recorded on the Consolidated Balance Sheets. The Company recognizes lease expense for these leases on a straight-line basis over the lease term. The Company applies this policy to all underlying asset categories.

Nonqualified Cash Deferral Plan

The Company's Cash Deferral Plan (the "Deferral Plan") provides certain key employees and members of the Board of Directors as selected by the Compensation Committee of the Board of Directors of the Company (the "Compensation Committee"), with an opportunity to defer the receipt of such participant's base salary, bonus, and director's fees, as applicable. The Deferral Plan is intended to be a nonqualified deferred compensation plan that complies with the provisions of Section 409A of the Internal Revenue Code. All of the investments held in the Deferral Plan are classified as trading securities and recorded at fair value with changes in the investments' fair value recognized as earnings in the period they occur. The corresponding liability for the Deferral Plan is included in other non-current liability in the Consolidated Balance Sheets.

Equity-based Compensation

At December 31, 2023, the Company had one equity-based employee compensation plan, which is described more fully in "— Note 8. Stockholders' Equity." The Company applies the fair value method of measuring equity-based compensation, which requires a public entity to measure the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award.

Loss per Common Share

The Company calculates net loss per share as a measurement of the Company's performance while giving effect to all dilutive potential common shares that were outstanding during the reporting period. The Company had a net loss for all periods presented; accordingly, the inclusion of common stock options and unvested restricted stock units would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same.

Segment Information

The Company currently operates in one business segment focused on the discovery, development, and commercialization of advanced therapies to treat a range of devastating rare and orphan diseases. The Company is not organized by market and is managed and operated as one business. A single management team reports to the chief operating decision maker, its Chief Executive Officer, who comprehensively manages the entire business. The Company does not operate any separate lines of business or separate business entities with respect to its products. Accordingly, the Company does not accumulate discrete financial information with respect to separate service lines, and thus there is one reporting unit.

Business Combinations

The Company assigns fair value to the tangible and intangible assets acquired and liabilities assumed based upon their estimated fair values on the acquisition date from acquired businesses. The purchase price allocation process requires management to make significant estimates and assumptions, especially at the acquisition date with respect to intangible assets and in-process research and development ("IPR&D"). In connection with the purchase price allocations for acquisitions, the Company estimates the fair value of contingent payments utilizing a probability-based income approach inclusive of an estimated discount rate.

Contingent Consideration Payable

Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved and the consideration is paid or becomes payable. This does not apply in circumstances when the contingent consideration meets the definition of a derivative, in which case the amount becomes part of the basis in the asset acquired. Upon recognition of the contingent consideration payable, the amount is included in the cost of the acquired asset or group of assets. For contingent consideration payments in business combinations, the Company determines the fair value of contingent acquisition consideration payable on the acquisition date using a probability-based income approach utilizing an appropriate discount rate, with changes in fair value recorded on the Consolidated Statements of Operations. The payments made related to the settlement of the contingent consideration payable recognized at fair value as of the acquisition date (including measurement-period adjustments) were disclosed as cash outflows for financing activities, whereas the payments related to the change in fair value of the contingent consideration payable were disclosed as cash outflows for operating activities in the Consolidated Statement of Cash Flows.

Intangible Assets and Goodwill

The Company records goodwill in a business combination when the total consideration exceeds the fair value of the net tangible and identifiable intangible assets acquired. Goodwill is assessed annually for impairment on October 1 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. The Company first assesses the qualitative factors to determine if a quantitative test is necessary. If required, or if the Company elects to bypass the qualitative assessment, a quantitative goodwill impairment test is concluded. If it is determined the Company's single reporting unit's carrying value, including goodwill, exceeds its fair value, an impairment loss is recorded for the difference.

Finite-lived intangible assets are recorded at cost, net of accumulated amortization, and, if applicable, impairment charges. Amortization of finite-lived intangible assets is recorded over the assets' estimated useful lives on a straight-line basis or based on the pattern in which economic benefits are consumed, if reliably determinable. The Company reviews finite-lived intangible assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. If impairment is determined, the Company writes down the asset to its estimated fair value and records an impairment loss equal to the excess of the carrying value of the asset over its estimated fair value in the period at which such a determination is made.

No indicators of impairment were noted during the years ended December 31, 2023 and 2022.

Recent Accounting Developments - Guidance Not Yet Adopted

In November 2023, the FASB issued the Accounting Standards Update ("ASU") No. 2023-07, Segment Reporting (Topic 280): *Improvements to Reportable Segment Disclosures*. The amendments expand reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses. The amendments require, among other things, disclosure of the title and position of the chief operating decision maker and require that public entities with a single reportable segment provide all disclosures required by this update and existing segment disclosures in Topic 280. Annual disclosures are required for fiscal years beginning after December 15, 2023 and interim disclosures are required for periods within fiscal years beginning after December 15, 2024. Retrospective application is required unless it is impracticable, and early adoption is permitted. The adoption of this guidance is not expected to have a significant impact on the Company's consolidated financial statements.

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740): I*mprovements to Income Tax Disclosures*. The ASU requires disclosure of disaggregated income taxes paid, prescribes standard categories for the components of the effective tax rate reconciliation, and modifies other income tax-related disclosures. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024, must be applied prospectively with an option to apply retrospectively, and early adoption is permitted. The adoption of this guidance is not expected to have a significant impact on the Company's consolidated financial statements.

3. Goodwill and Intangible Assets

Finite-lived Intangible Assets

As of December 31, 2023, the Company had intangible assets of $20.5 million. Intangible assets consist of lead enzyme replacement therapy assets acquired with the Callidus Biopharma, Inc. ("Callidus") acquisition in 2013, previously accounted for as in-process research and development. In March 2023, as a result of the European Commission's ("EC") approval of Pombiliti™, the Company began amortizing the assets over the initial regulatory exclusivity period of 7 years. The Company completed an impairment assessment before changing the classification to finite-lived intangible asset noting no impairment. Amortization expense for finite-lived intangible assets was $2.5 million for the year ended December 31, 2023. There was no amortization expense for finite-lived intangible asset for the year ended December 31, 2022. Total estimated amortization expense for the finite-lived intangible assets for each of the next 5 years is approximately $3.3 million and has a remaining amortization period of 6.2 years.

Goodwill

As of December 31, 2023, in connection with the acquisition of Callidus in 2013 and Scioderm, Inc. in 2015, the Company had goodwill of $197.8 million. There has been no change to the balance of goodwill since the dates of acquisition.

4. Cash, Cash Equivalents, Marketable Securities, and Restricted Cash

As of December 31, 2023, the Company held $247.0 million in cash and cash equivalents and $39.2 million of marketable securities which are reported at fair value on the Company's Consolidated Balance Sheets. Unrealized holding gains and losses are generally reported within other comprehensive gain (loss) in the Consolidated Statements of Comprehensive Loss. If a decline in the fair value of a marketable security below the Company's cost basis is determined to be other-than-temporary or if an available-for-sale debt security's fair value is determined to be less than the amortized cost and the Company intends or is more than likely to sell the security before recovery and it is not considered a credit loss, such security is written down to its estimated fair value as a new cost basis and the amount of the write-down is included in the Consolidated Statements of Operations as an impairment charge. If the unrealized loss of an available-for-sale debt security is determined to be a result of credit loss the Company would recognize an allowance and the corresponding credit loss would be included in the Consolidated Statements of Operations.

The Company regularly invests excess operating cash in deposits with major financial institutions, money market funds, notes issued by the U.S. government, as well as fixed income investments and U.S. bond funds, both of which can be readily purchased and sold using established markets. The Company believes that the market risk arising from its holdings of these financial instruments is mitigated as, in accordance with Company policy, securities are of high credit rating. Investments that have original maturities greater than three months but less than one year are classified as current.

Cash, cash equivalents, and marketable securities are classified as current unless mentioned otherwise below and consisted of the following:

	As of December 31, 2023			
(in thousands)	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Cash and cash equivalents	$ 246,994	$ —	$ —	$ 246,994
Commercial paper	14,651	12	—	14,663
Treasury bill	12,944	2	—	12,946
U.S. government agency bonds	11,450	—	(4)	11,446
Money market	100	—	—	100
Certificates of deposit	51	—	—	51
	$ 286,190	$ 14	$ (4)	$ 286,200
Included in cash and cash equivalents	$ 246,994	$ —	$ —	$ 246,994
Included in marketable securities	39,196	14	(4)	39,206
Total cash, cash equivalents, and marketable securities	$ 286,190	$ 14	$ (4)	$ 286,200

	As of December 31, 2022			
(in thousands)	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Cash and cash equivalents	$ 148,813	$ —	$ —	$ 148,813
Commercial paper	144,299	82	—	144,381
Money market	350	—	—	350
Certificates of deposit	51	—	—	51
	$ 293,513	$ 82	$ —	$ 293,595
Included in cash and cash equivalents	$ 148,813	$ —	$ —	$ 148,813
Included in marketable securities	144,700	82	—	144,782
Total cash, cash equivalents, and marketable securities	$ 293,513	$ 82	$ —	$ 293,595

For the year ended December 31, 2023 and 2022, there were no realized gains or losses. The cost of securities sold is based on the specific identification method.

Unrealized loss positions in the marketable securities as of December 31, 2023 reflect temporary impairments and are not a result of credit loss. Additionally, as these positions have been in a loss position for less than twelve months and the Company does not intend to sell these securities before recovery, the losses are recognized in other comprehensive gain (loss) . The fair value of these marketable securities in unrealized loss positions are $11.4 million as of December 31, 2023. The Company had no marketable securities in an unrealized loss position as of December 31, 2022.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the Consolidated Balance Sheets that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows.

(in thousands)	December 31, 2023	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 246,994	$ 148,813	$ 245,197
Restricted cash	3,083	4,302	4,259
Cash, cash equivalents, and restricted cash shown in the Consolidated Statements of Cash Flows	$ 250,077	$ 153,115	$ 249,456

5. Inventories

Inventories as of December 31, 2023 and December 31, 2022 consisted of the following:

(in thousands)	December 31, 2023	December 31, 2022
Raw materials	$ 30,230	$ 10,054
Work-in-process	22,597	9,615
Finished goods	6,869	4,147
Total inventories	$ 59,696	$ 23,816

The Company's reserve for inventory was $0.5 million and $0.4 million as of December 31, 2023 and 2022, respectively. The Company has a number of binding minimum purchase and manufacturing commitments due to the third-party manufacturers. As of December 31, 2023, these purchase and manufacturing obligations totaled $126.2 million, of which $83.9 million and $42.3 million are expected in 2024 and 2025, respectively.

6. Property and Equipment

Property and equipment consist of the following:

(in thousands)	December 31, 2023	December 31, 2022
Leasehold improvements	$ 28,032	$ 24,162
Research equipment	16,220	16,345
Computer equipment	4,934	4,486
Construction in progress	3,810	4,160
Furniture and fixtures	2,928	2,734
Computer software	1,106	1,106
Vehicles	66	66
Gross property and equipment	57,096	53,059
Less accumulated depreciation	(25,429)	(22,281)
Net property and equipment	$ 31,667	$ 30,778

For both the years ended December 31, 2023 and 2022, depreciation expense was $4.8 million. Additionally, during the year ended December 31, 2022, in connection with the strategic deprioritization of its gene therapy portfolio, the Company performed an assessment of its fixed assets. As a result, the Company recognized an impairment charge of $6.6 million.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

(in thousands)	December 31, 2023	December 31, 2022
Accrued compensation and benefits	$ 38,305	$ 25,701
Accrued sales rebates and discounts	31,190	21,886
Accrued program fees	13,607	10,515
Accrued contract manufacturing & contract research costs	13,380	8,230
Accrued taxes	12,434	5,938
Accrued interest on debt	11,661	125
Accrued royalties	8,238	6,908
Accrued professional fees	5,059	6,868
Other	10,371	7,465
	$ 144,245	$ 93,636

8. Stockholders' Equity

Common Stock and Warrants

As of December 31, 2023, the Company was authorized to issue 500 million shares of common stock. Dividends on common stock will be paid when, and if, declared by the Board of Directors. Each holder of common stock is entitled to vote on all matters that are appropriate for stockholder voting and is entitled to one vote for each share held.

In November 2022, the Company entered into a Sales Agreement with The Goldman Sachs & Co. LLC to create an at-the-market equity program ("ATM program"), pursuant to which the Company may offer to sell shares of its common stock having an aggregate offering gross proceeds of up to $250.0 million. During the year ended December 31, 2023, the Company issued and sold an aggregate of 5,244,936 shares through its ATM program at a weighted-average public offering price of $12.50 per share, resulting in net proceeds of $63.1 million. During the year ended December 31, 2022, no shares were sold under this ATM program. As of December 31, 2023, an aggregate of $184.4 million worth of shares remain available to be issued and sold under the ATM program.

In October 2023, the Company entered into a securities purchase agreement with funds managed by Blackstone Alternative Credit Advisors LP and Blackstone Life Sciences Advisors L.L.C. (collectively, “Blackstone”), for the private placement of an aggregate of 2,467,104 shares of the Company’s common stock, at a purchase price of $12.16 per share. Proceeds from the private placement, net of offering costs, were $29.8 million.

In September 2021, the Company entered into a securities purchase agreement with certain entities, the (“Purchase Agreements”) for the private placement of an aggregate of 11,296,660 shares of the Company’s common stock, at a purchase price of $10.18 per share, and pre-funded warrants to purchase an aggregate of 8,349,705 shares of common stock, at a purchase price of $10.17 per pre-funded warrant. Proceeds from the private placement, net of offering costs, were $199.8 million. Each pre-funded warrant has an initial exercise price of $0.01 per share and is exercisable at any time after its original issuance, subject generally to the lock-up period, at the option of each holder, in such holder’s discretion, by (i) payment in full in immediately available funds of the initial exercise price for the number of shares of common stock purchased upon such exercise or (ii) a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Certain of the Purchase Agreements provide for a lock-up period of either 60 days or nine months based on the individual agreements. As of December 31, 2023, 1,220,100 pre-funded warrants have been exercised.

During the first quarter of 2021, 1,294,999 and 1,260,000 warrants were exercised at $7.98 and $7.06 per share of common stock, respectively, resulting in gross cash proceeds of $19.2 million.

Nonqualified Cash Deferral Plan

The Company's Deferral Plan provides certain key employees and members of the Board of Directors, as selected by the Compensation Committee, with an opportunity to defer the receipt of such participant's base salary, bonus, and director's fees, as applicable. The Deferral Plan is intended to be a nonqualified deferred compensation plan that complies with the provisions of Section 409A of the Internal Revenue Code of 1986 as amended.

The Company had a deferred compensation investment balance of $7.5 million and $5.5 million as of December 31, 2023 and 2022, respectively, with corresponding approximate amounts of liability.

Deferral Plan investment assets are classified as trading securities and recorded at fair value with changes in the investments' fair value recognized as earnings in the period they occur. Deferred compensation liability amounts under the Deferral Plan are included in other long-term liabilities.

Equity Incentive Plan

The Company's Amended and Restated 2007 Equity Incentive Plan (the "Plan") provides for the granting of restricted stock units and options to purchase common stock in the Company to employees, directors, advisors, and consultants at a price to be determined by the Company's Board of Directors. The Plan is intended to encourage ownership of stock by employees and consultants of the Company and to provide additional incentives for them to promote the success of the Company's business. Under the provisions of the Plan, no option will have a term in excess of 10 years. The Board of Directors, or its committee, is responsible for determining the individuals to be granted options, the number of options each individual will receive, the option price per share, and the exercise period of each option. Options granted pursuant to the Plan generally vest 25% on the first year anniversary date of grant plus an additional 1/48th for each month thereafter and may be exercised in whole or in part for 100% of the shares vested at any time after the date of grant. As of December 31, 2023, the Company has reserved up to 12,413,532 shares for issuance under the Plan.

9. Stock-based Compensation

The Plan provides for the granting of restricted stock units and options to purchase common stock in the Company to employees, directors, advisors, and consultants at a price to be determined by the Company's Board of Directors. The Plan is intended to encourage ownership of stock by employees and consultants of the Company and to provide additional incentives for them to promote the success of the Company's business. The Board of Directors, or its committee, is responsible for determining the individuals to be granted options, the number of options each individual will receive, the option price per share, and the exercise period of each option.

The Plan provides for certain benefits to qualifying Plan participants who separate from service with the Company due to death, disability or "retirement" (as such term is defined under the Plan) ("Qualified Participants"). Options granted under the Plan to a Qualified Participant shall continue to vest until the 2nd anniversary of the Qualified Participant's separation and all vested options held by such Qualified Participant shall remain exercisable until the earlier of the 4th anniversary of the Qualified Participant's separation or the original expiration date of the option. Options that are not exercised during this exercise period shall be forfeited. Time-based restricted stock units and restricted stock granted to a Qualified Participant under the Plan that was scheduled to vest within the two year period following the Qualified Participant's separation shall accelerate and be delivered upon such separation. Any time-based restricted stock units or restricted stock that would have vested after such two year period will be forfeited upon the Qualified Participant's separation. Also, per the Amendment, any performance-based restricted stock units under the Plan ("PRSUs") received by the Qualified Participant, shall remain eligible to vest after the Qualified Participant's separation based on the actual performance of the Company through the end of the performance period applicable to any such PRSUs.

Stock Option Grants

The Company uses the fair value method of measuring share-based compensation, using the fair value of each equity award granted. The Company chose the ''straight-line'' attribution method for allocating compensation costs and recognized the fair value of each stock option on a straight-line basis over the vesting period of the related awards.

The Company uses the Black-Scholes option pricing model when estimating the grant date fair value for share-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility is based on the historical volatility of the Company's common stock over the look-back period corresponding to the expected life of the options. The average expected life is determined using the Company's actual historical data. The risk-free interest rate is based on U.S. Treasury, zero-coupon issues with a remaining term equal to the expected life assumed at the date of grant. Forfeitures are estimated based on a historical analysis of actual option forfeitures.

The fair value of the stock options granted were estimated on the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions:

	Years Ended December 31,		
	2023	2022	2021
Expected stock price volatility	59.2 %	62.1 %	65.4 %
Risk free interest rate	3.9 %	1.7 %	0.6 %
Expected life of options (years)	5.47	5.34	5.40
Expected annual dividend per share	$ —	$ —	$ —

The weighted average grant-date fair value per share of options granted during 2023, 2022, and 2021 were $6.75, $6.11, and $9.08, respectively.

A summary of the Company's stock options for the year ended December 31, 2023 were as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Years	Aggregate Intrinsic Value
	(in thousands)			(in millions)
Options outstanding, December 31, 2020	14,032	$ 9.54		
Granted	3,262	$ 16.53		
Exercised	(1,483)	$ 7.05		
Forfeited	(844)	$ 12.97		
Expired	(236)	$ 13.28		
Options outstanding, December 31, 2021	14,731	$ 11.08		
Granted	5,733	$ 11.53		
Exercised	(660)	$ 6.58		
Forfeited	(495)	$ 12.57		
Expired	(245)	$ 12.84		
Options outstanding, December 31, 2022	19,064	$ 11.31		
Granted	5,733	$ 11.99		
Exercised	(1,361)	$ 7.54		
Forfeited	(356)	$ 11.59		
Expired	(78)	$ 15.09		
Options outstanding, December 31, 2023	23,002	$ 11.69	6.5	$ 70.8
Vested and unvested expected to vest, December 31, 2023	21,215	$ 11.64	6.3	$ 66.5
Exercisable at December 31, 2023	13,431	$ 11.26	5.0	$ 49.0

The aggregate intrinsic value of options exercised during the years ended December 31, 2023, 2022 and 2021 was $7.1 million, $2.5 million, and $8.5 million, respectively. Cash proceeds from stock options exercised during the years ended December 31, 2023, 2022, and 2021 were $10.3 million, $4.3 million, and $10.2 million, respectively. As of December 31, 2023, the total unrecognized compensation cost related to non-vested stock options granted was $35.0 million and is expected to be recognized over a weighted average period of three years.

Restricted Stock Units and Performance-Based Restricted Stock Units (collectively "RSUs")

RSUs awarded under the Plan are generally subject to graded vesting and are contingent on an employee's continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. The Company expenses the cost of the RSUs, which is determined to be the fair market value of the shares of common stock underlying the RSUs at the date of grant, ratably over the period during which the vesting restrictions lapse. A summary of non-vested RSU activity under the Plan for the year ended December 31, 2023 is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value	Weighted Average Remaining Years	Aggregate Intrinsic Value
	(in thousands)			(in millions)
Non-vested units as of December 31, 2020	7,080	$ 11.35		
Granted	3,191	$ 16.94		
Vested	(1,863)	$ 15.77		
Forfeited	(1,067)	$ 12.82		
Non-vested units as of December 31, 2021	7,341	$ 13.90		
Granted	5,048	$ 11.93		
Vested	(2,251)	$ 12.48		
Forfeited	(421)	$ 12.06		
Non-vested units as of December 31, 2022	9,717	$ 13.07		
Granted	4,762	$ 13.02		
Vested	(3,610)	$ 12.21		
Forfeited	(836)	$ 11.63		
Non-vested units as of December 31, 2023	10,033	$ 13.37	2.1	$ 142.4

As of December 31, 2023, there was $53.6 million of total unrecognized compensation cost related to unvested RSUs with service-based vesting conditions. These costs are expected to be recognized over a weighted average period of two years.

Compensation Expense Related to Equity Awards

The following table summarizes information related to compensation expense recognized in the Company's Consolidated Statements of Operations related to the equity awards:

	Years Ended December 31,		
(in thousands)	2023	2022	2021
Research and development expense	$ 21,470	$ 25,089	$ 17,340
Selling, general, and administrative expense	64,607	51,423	40,498
Total equity compensation expense	$ 86,077	$ 76,512	$ 57,838

10. Assets and Liabilities Measured at Fair Value

The Company's financial assets and liabilities are measured at fair value and classified within the fair value hierarchy which is defined as follows:

Level 1 — Quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 — Inputs other than quoted prices in active markets that are observable for the asset or liability, either directly or indirectly.

Level 3 — Inputs that are unobservable for the asset or liability.

A summary of the fair value of the Company's recurring assets and liabilities aggregated by the level in the fair value hierarchy within which those measurements fall as of December 31, 2023 are identified in the following tables:

(in thousands)	Level 1	Level 2	Total
Assets:			
Commercial paper	$ —	$ 14,663	$ 14,663
Treasury bill	—	12,946	12,946
U.S. government agency bonds	—	11,446	11,446
Money market	7,631	—	7,631
	$ 7,631	$ 39,055	$ 46,686

(in thousands)	Level 1	Level 2	Total
Liabilities:			
Deferred compensation plan liability	$ 7,531	$ —	$ 7,531
	$ 7,531	$ —	$ 7,531

A summary of the fair value of the Company's recurring assets and liabilities aggregated by the level in the fair value hierarchy within which those measurements fall as of December 31, 2022 are identified in the following tables:

(in thousands)	Level 2	Total
Assets:		
Commercial paper	$ 144,381	$ 144,381
Money market	5,808	5,808
	$ 150,189	$ 150,189

(in thousands)	Level 2	Level 3	Total
Liabilities:			
Contingent consideration payable	$ —	$ 21,417	$ 21,417
Deferred compensation plan liability	5,458	—	5,458
	$ 5,458	$ 21,417	$ 26,875

The Company's Senior Secured Term Loan due 2029 falls into the Level 2 category within the fair value level hierarchy and the fair value was determined using a discounted cash flow analysis that factors in current market yields for comparable borrowing arrangements under the Company's credit profile. The carrying value of the Senior Secured Term Loan due 2029 approximates the fair value. Deferred compensation plan liability is recorded as a component of other non-current liabilities on the Company's Consolidated Balance Sheets.

The Company did not have any Level 3 assets as of December 31, 2023 or 2022.

Cash, Money Market Funds and Marketable Securities

The Company classifies its cash and cash equivalents within the fair value hierarchy as Level 1 as these assets are valued using quoted prices in an active market for identical assets at the measurement date. The Company considers its investments in marketable securities as available-for-sale and classifies these assets within the fair value hierarchy as Level 2 primarily utilizing broker quotes in a non-active market for valuation of these securities. No changes in valuation techniques or inputs occurred during the year ended December 31, 2023. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2023.

Contingent Consideration Payable

The contingent consideration payable resulted from the acquisition of Callidus in November 2013. The Company reached regulatory milestones of $9.0 million in March 2023 and $15.0 million in September 2023 associated with the approval of Pombiliti™ by the EC and U.S. Food and Drug Administration ("FDA"), respectively. The $9.0 million and $15.0 million payments were paid in the second and fourth quarter of 2023, respectively.

The following table shows the change in the balance of contingent consideration payable for the year ended December 31, 2023 and 2022, respectively:

	Years ended December 31,	
(in thousands)	**2023**	**2022**
Balance, beginning of the period	$ 21,417	$ 20,339
Changes in fair value during the period, included in the Consolidated Statements of Operations	2,583	1,078
Payment of contingent consideration in cash	(24,000)	—
Balance, end of the period	$ —	$ 21,417

11. Debt

The Company's debt consists of the following:

	As of December 31,	
(in thousands)	**2023**	**2022**
Senior Secured Term Loan due 2029:		
Principal	$ 400,000	$ —
Less: debt discount [(1)]	(9,652)	—
Less: deferred financing [(1)]	(2,490)	—
Net carrying value of Long-term debt	$ 387,858	$ —
Senior Secured Term Loan due 2026[(2)]:		
Principal	$ —	$ 400,000
Less: debt discount [(1)]	—	(4,571)
Less: deferred financing [(1)]	—	(3,439)
Net carrying value of Long-term debt	$ —	$ 391,990
Net carrying value of Long-term debt	$ 387,858	$ 391,990

[(1)] Included in the Consolidated Balance Sheets within long-term debt and amortized to interest expense over the remaining life of the corresponding Senior Secured Term Loan using the effective interest rate method.

[(2)] The principal, accrued interest and prepayment premiums associated with the Senior Secured Term Loan due 2026 were fully paid in October 2023.

Senior Secured Term Loan due 2029

In October 2023, the Company entered into a $400 million loan agreement (the “Senior Secured Term Loan due 2029”) with Blackstone Alternative Credit Advisors LP and Blackstone Life Sciences Advisors L.L.C. (collectively, “Blackstone”) with an interest rate equal to 3-month Term SOFR, subject to a 2.5% floor, plus a Term SOFR adjustment of 0.26161% and a margin of 6.25% that requires interest-only payments until early-2027. The Senior Secured Term Loan due 2029 will be repaid in twelve quarterly payments of $33.3 million, starting on January 2027 with the final balance due on the maturity date in October 2029. This transaction resulted in net proceeds of $387.4 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2029.

The Senior Secured Term Loan due 2029 is subject to mandatory prepayment provisions that require prepayment upon a change of control, the incurrence of certain additional indebtedness, asset sale, or an event of loss, subject to certain conditions set forth in the Senior Secured Term Loan due 2029. The Company may prepay the Senior Secured Term Loan due 2029 in whole or in part, at its option at any time. Any prepayment of the Senior Secured Term Loan due 2029 is subject to certain make-whole premiums and prepayment premiums, the latter of which decrease until the fifth anniversary of the transaction date at which point no prepayment penalty shall exist. The obligations under the Senior Secured Term Loan due 2029 are secured by a first lien security interest in certain assets of the Company. The Senior Secured Term Loan due 2029 contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to the Company. If an event of default occurs and is continuing, Blackstone may declare all amounts outstanding under the Senior Secured Term Loan due 2029 to be immediately due and payable.

Senior Secured Term Loan due 2026

In July 2020, the Company entered into a definitive agreement for a $400 million credit facility with Hayfin Capital Management ("Senior Secured Term Loan due 2026") with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum and requires interest-only payments until mid-2024. The Senior Secured Term Loan due 2026 was to be repaid in nine quarterly payments of $44.4 million, starting on July 2024 with the final balance due on the maturity date in July 2026. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026.

In October of 2023, the Company used $408.9 million of the net proceeds from the Senior Secured Term Loan due 2029 and the private placement to prepay the Senior Secured Term Loan due 2026, inclusive of the outstanding principal amount, $0.8 million in accrued interest and $8.0 million as a prepayment premium. In connection with the prepayment, the Company recorded a loss from early extinguishment of debt of $13.9 million in the Company's Consolidated Statements of Operations.

Interest Expense

The following table sets forth interest expense recognized related to the Company's debt for the years ended December 31, 2023 and 2022, respectively:

(in thousands, except interest rate amounts)	December 31, 2023	December 31, 2022
Contractual interest expense	$ 47,626	$ 34,446
Amortization of debt discount	$ 1,605	$ 1,503
Amortization of deferred financing	$ 1,011	$ 1,131
Effective interest rate of the liability component, Senior Secured Term Loan due 2029	12.8 %	— %
Effective interest rate of the liability component, Senior Secured Term Loan due 2026	— %	12.1 %

12. Leases

The Company currently has operating leases for office and research laboratory space, equipment, and vehicles under agreements expiring at various dates through 2034, which include renewal options on leases which the Company is reasonably certain to exercise.

For the years ended December 31, 2023 and 2022, operating lease expense was $9.5 million and $9.8 million and variable lease expense was $2.1 million and $1.7 million, respectively. For the years ended December 31, 2023 and 2022, the Company paid $9.5 million and $8.3 million, respectively, for amounts included in the measurement of operating lease liabilities and recorded right-of-use assets of $0.6 million and $8.9 million, respectively.

Commitments under finance leases are not significant for the year ended December 31, 2023.

Supplemental balance sheet information related to operating leases were as follows:

(in thousands, except year and discount rate amounts)	December 31, 2023	December 31, 2022
Operating lease ROU assets, net	$ 26,312	$ 29,534
Current portion of the operating lease liabilities	$ 8,324	$ 8,552
Non-current portion of the operating lease liabilities	48,877	51,578
Total operating lease liability	$ 57,201	$ 60,130
Weighted-average remaining lease terms (years)	9.4	17.0
Weighted-average discount rate	9.7 %	12.2 %

At December 31, 2023, the future minimum operating lease payments were as follows:

(in thousands)	Operating Lease
2024	$ 9,236
2025	9,157
2026	9,213
2027	9,351
2028	9,144
Thereafter	43,715
Total lease payments	89,816
Less lease incentives	(22,299)
Less imputed interest	(10,316)
Total operating lease liability	$ 57,201

13. Income Taxes

For financial reporting purposes, income (loss) before income taxes includes the following components:

	Years Ended December 31,		
(in thousands)	2023	2022	2021
United States	$ (234,482)	$ (343,424)	$ (333,571)
Foreign	84,381	101,385	92,017
Total	$ (150,101)	$ (242,039)	$ (241,554)

Following were the components of income tax expense (benefit) for the years ended December 31, 2023, 2022, and 2021:

	Years Ended December 31,		
(in thousands)	2023	2022	2021
Current			
Federal	$ —	$ —	$ —
State	14	6	15
Foreign	6,408	(5,760)	8,857
Deferred			
Federal	(4,801)	274	—
State	(138)	9	34
Foreign	—	—	—
Total	$ 1,483	$ (5,471)	$ 8,906

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2023, 2022, and 2021 are as follows:

	Years Ended December 31,		
	2023	2022	2021
Statutory rate	(21)%	(21)%	(21)%
Tax credits	(8)	(11)	(9)
Impact of foreign operations	(9)	18	3
Other	8	3	3
Valuation allowance	31	9	28
Net	1 %	(2)%	4 %

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act ("Tax Act"). The Tax Act significantly revised U.S. tax law by, among other provisions, lowering the U.S. federal statutory income tax rate to 21%, imposing a mandatory one-time transition tax on previously deferred foreign earnings, and eliminating or reducing certain income tax deductions. The Tax Act also introduced an additional U.S. tax on certain non-U.S. subsidiaries' earnings which are considered to be Global Intangible Low Taxed Income (referred to as "GILTI"). After consideration of the relevant guidance and completing the accounting for the tax effects of the Tax Act, the Company has elected to treat GILTI as a period cost.

Beginning in 2022, the Tax Act eliminated the right to deduct research and development expenditures for tax purposes in the period the expenses were incurred and instead requires all U.S. and foreign research and development expenditures to be amortized over five and fifteen tax years, respectively.

Tax returns for years 2017 through 2022 are open to examination by tax authorities. The Company is also subject to examination in any period for which it has net operating losses.

Deferred income taxes reflect the net effect of temporary difference between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The significant components of the deferred tax assets and liabilities are as follows:

	Years Ended December 31,	
(in thousands)	**2023**	**2022**
Deferred tax assets		
Intellectual property	$ —	$ 68,567
Research tax credit	235,532	223,366
Capitalized research and development costs	34,425	29,317
Net operating loss carry forwards	321,004	315,444
Share-based compensation	17,314	16,417
Interest carry forward limitation	17,627	12,558
Lease liability	10,567	11,428
Inventory	1,931	10,400
Other	20,858	20,109
Gross deferred tax assets	659,258	707,606
Deferred tax liabilities		
Royalty payable	—	(68,567)
Other	(10,004)	(11,745)
Total net deferred tax assets	649,254	627,294
Less: valuation allowance	(649,254)	(632,233)
Net deferred tax liability	$ —	$ (4,939)

The Company records a valuation allowance for temporary differences for which it is more likely than not that the Company will not receive future tax benefits. At December 31, 2023 and 2022, the Company recorded valuation allowances of $649.3 million and $632.2 million, respectively, representing an increase in the valuation allowance of $17.0 million in 2023, due to the uncertainty regarding the realization of such deferred tax assets, to offset the benefits of net operating losses generated during those years. The deferred tax liability related to business acquisitions pertains to the basis difference in intangible assets acquired by the Company. The Company's policy is to record a deferred tax liability related to acquired intangible assets that may eventually be realized either upon amortization of the asset when the research is completed, and a product is successfully launched or the write-off of the asset if it is abandoned or unsuccessful.

As of December 31, 2023, the Company had U.S. federal, U.K. and state net operating loss carry forwards ("NOLs") of approximately $1.2 billion, $28.4 million and $1.0 billion, respectively. The federal carry forward for losses generated prior to 2018 will expire in 2029 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the Tax Act. The U.K. carryforward period is unlimited. Most of the state net operating loss carry forwards generated prior to 2009 have expired through 2016. The remaining state net operating loss carry forwards including those generated in 2009 through 2023 will expire in 2030 through 2042. State research and development credits will expire beginning 2024 through 2033. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended, as well as similar state statutes in the event of an ownership change. Such ownership changes have occurred in the past and could occur again in the future. Under Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income may be limited. The Company may experience ownership changes in the future as a result of shifts in the stock ownership some of which are outside the Company's control. The Company completed a detailed study of the NOLs for the tax year 2023 and determined that there was not an ownership change in excess of 50%. Ownership changes in future periods may place additional limits on the Company's ability to utilize net operating loss and tax credit carry forwards. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently decrease the amount of state attributes and increase state taxes owed.

The Company also has U.S. federal research and experimentation and orphan drug credit carryforwards of approximately $18.4 million and $203.1 million, respectively, which will expire in the years 2030 through 2043. The Company also has state research and development tax credit carryforwards of $14.1 million. Deferred tax assets for these carryforwards are subject to a full valuation allowance.

The Organization Economic Co-operation and Development (“OECD”) introduced Base Erosion and Profit Shifting (“BEPS”) Pillar 2 rules that impose a global minimum tax rate of 15%. Numerous countries, including European Union member states, have enacted or are expected to enact legislation to be effective as early as January 1, 2024, with general implementation of a global minimum tax by January 1, 2025. The Company does not expect this new rule to apply until the Company meets the minimum global revenue threshold.

14. Collaborative Agreements

University of Pennsylvania

In October 2018, as amended, the Company entered into a collaboration agreement with the University of Pennsylvania ("Penn") to pursue research and development of novel gene therapies. The Company's gene therapy portfolio pipeline expanded to include Pompe disease, Fabry disease and other rare diseases.

In December 2022, the Company entered into a mutual termination agreement (the "Termination Agreement") pursuant to which the Company and Penn mutually agreed to terminate the collaboration agreement, as amended. In connection with the Termination Agreement, the Company agreed to pay Penn an aggregate of $23.7 million in connection with an unpaid portion of the discovery support payments, research program wind-down activities, and outstanding patent costs which was recorded as a component of research and development expense within the Consolidated Statements of Operations.

Concurrently, the Company entered into a license agreement with Penn pursuant to which it obtained a license with respect to the pre-clinical research and development of next-generation parvovirus gene therapy products for the treatment of Pompe disease and Fabry disease. Under the agreement, the Company will be responsible for clinical development and commercialization of the licensed products for the indications and Penn is eligible to receive certain milestone and royalty payments with respect to licensed products for each indication, up to an aggregate of $86.5 million per indication. Royalty payments are based on net sales of licensed products on a licensed product-by-licensed product and country-by-country basis.

GlaxoSmithKline

In July 2012, as amended in November 2013, the Company entered into an agreement with GlaxoSmithKline ("GSK"), pursuant to which Amicus obtained global rights to develop and commercialize Galafold® as a monotherapy and in combination with ERT for Fabry disease ("Collaboration Agreement"). Under the terms of the Collaboration Agreement, GSK is eligible to receive post-approval and sales-based milestones up to $40 million, as well as tiered royalties in the mid-teens in eight major markets outside the U.S.

As of December 31, 2023, the contingent milestone payments due to GSK were $5.9 million and are recorded within the other current and other non-current liabilities accounts on the Consolidated Balance Sheets. Sales based tiered royalties due to GSK are recorded within the cost of goods sold within the Consolidated Statements of Operations.

For the year ended December 31, 2023, under the GSK collaboration agreement, the Company incurred approximately $27.7 million of royalty expenses, of which $8.2 million is recorded within accrued expenses in the Consolidated Balance Sheets.

15. Legal Proceedings

In the fourth quarter of 2022, the Company received Paragraph IV Certification Notice Letters from Teva Pharmaceuticals USA, Inc. ("Teva"), Aurobindo Pharma Limited ("Aurobindo"), and Lupin Limited ("Lupin") in connection with Abbreviated New Drug Applications ("ANDA") filed with the FDA requesting approval to market generic Galafold®. In November 2022, the Company filed four lawsuits against Teva, Lupin, and Aurobindo in the U.S. District Court for the District of Delaware for infringement of its Orange Book-listed patents. In the fourth quarter of 2023, a stipulation order to stay litigation with respect to Lupin was ordered. Additionally, in the first quarter of 2024, a stipulation was filed with the court and approved by the presiding judge, whereby the parties agreed to accept the Company's definition of the terms that were in dispute. As such, the scheduled Markman hearing was deemed unneeded and cancelled. The Company has, and will continue to, vigorously enforce its Galafold® intellectual property rights.

16. Basic and Diluted Net Loss per Common Share

The following table provides a reconciliation of the numerator and denominator used in computing basic and diluted net loss attributable to common stockholders per common share:

	Years Ended December 31,		
(in thousands, except per share amounts)	**2023**	**2022**	**2021**
Numerator:			
Net loss attributable to common stockholders	$ (151,584)	$ (236,568)	$ (250,460)
Denominator:			
Weighted average common shares outstanding — basic and diluted	295,164,515	289,057,198	271,421,986

Dilutive common stock equivalents would include the dilutive effect of outstanding common stock options and unvested RSUs. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect. Weighted average common shares outstanding includes outstanding pre-funded warrants with an exercise price of $0.01.

The table below presents potential shares of common stock that were excluded from the computation as they were anti-dilutive using the treasury stock method:

	Years ended December 31,		
(in thousands)	2023	2022	2021
Options to purchase common stock	23,002	19,064	14,731
Unvested restricted stock units	10,033	9,717	7,341
Total number of potentially issuable shares	33,035	28,781	22,072

Item 9. ***CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.***

None.

Item 9A. ***CONTROLS AND PROCEDURES.***

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2023, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

There have been no changes in our internal controls over financial reporting during the fourth quarter of the year ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Management's Report on Internal Control Over Financial Reporting

The information required by this section which includes the "Management's Report on Consolidated Financial Statements and Internal Control over Financial Reporting" and the "Report of Independent Registered Public Accounting Firm" are incorporated by reference from "Item 8. Financial Statements and Supplementary Data."

Item 9B. ***OTHER INFORMATION.***

Rule 10b5-1 Trading Plans

The following table describes, for the quarterly period covered by this report, each director and officer (as defined in Rule 16a-1(f) under the Exchange Act who has adopted, modified, or terminated a trading plan intended to satisfy the affirmative defense of Rule 10b5-1(c) under the Exchange Act (each plan, a "Rule 10b5-1 Trading Plan"). Each Rule 10b5-1 Trading Plan described below was adopted during an open insider trading window and in accordance with the Company's policies regarding both insider trading and transactions relating to Company securities.

Name (Title)	Action Taken (Date of Action)	Rule 10b5-1 Trading Plan Provides for Purchase/Sale	Duration of the Trading Plan[(1)]	Aggregate Number of Securities
Margaret G. McGlynn (Director)	Adoption (November 10, 2023)	Sale	June 12, 2024	15,000[(2)]

[(1)] The dates in this column represent the scheduled expiration date of each director or officer's Rule 10b5-1 Trading Plan. Each Rule 10b5-1 Trading Plan may terminate earlier than the date provided should all transactions contemplated thereunder occur prior to such date.

[(2)] Ms. McGlynn's Rule 10b5-1 Trading Plan provides for the exercise of up to 15,000 stock options and the sale of up to 15,000 underlying shares of common stock.

Item 9C. ***DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.***

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K as we intend to file our definitive proxy statement for our 2024 annual meeting of stockholders, pursuant to Regulation 14A of the Securities Exchange Act, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and certain information to be included in the proxy statement is incorporated herein by reference.

Item 10. *DIRECTORS, EXECUTIVE OFFICERS OF THE REGISTRANT AND CORPORATE GOVERNANCE.*

The information required by this item is incorporated by reference from the Proxy Statement under the caption "Executive Officers," "Section 16(a) Reports," "Proposal No. 1 — Election of Directors," "Committees of the Board and Meetings."

We have adopted a Code of Business Ethics and Conduct for Employees, Executive Officers and Directors that applies to our employees, officers and directors, including the principal executive officer, principal financial officer, and principal accounting officer, and incorporates guidelines designed to deter wrongdoing and to promote the honest and ethical conduct and compliance with applicable laws and regulations. In addition, the code of ethics incorporates our guidelines pertaining to topics such as conflicts of interest and workplace behavior. We have posted the text of our code on our website, where it is accessible for free, at *www.amicusrx.com* in connection with "Investors/Corporate Governance" materials. In addition, we intend to promptly disclose (1) the nature of any amendment to our code of ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date the waiver on our website in the future.

Item 11. *EXECUTIVE COMPENSATION.*

The information required by this item is incorporated by reference from the Proxy Statement under the caption "Compensation Discussion and Analysis," "Compensation and Leadership Development Committee Report," and "Compensation and Leadership Development Committee Interlocks and Insider Participation."

Item 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.*

The information required by this item is incorporated by reference from the Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" and "Securities Authorized for Issuance under our Equity Compensation Plan."

Item 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE.*

The information required by this item is incorporated by reference from the Proxy Statement under the captions "Policies and Procedures for Related Party Transactions," and "Director Independence."

Item 14. *PRINCIPAL ACCOUNTING FEES AND SERVICES.*

The information required by this item is incorporated by reference from the Proxy Statement.

PART IV

Item 15. ***EXHIBITS, FINANCIAL STATEMENT SCHEDULE***

1. *Index to Consolidated Financial Statements*

The following Consolidated Financial Statements are filed as part of this report:

2. Consolidated Financial Statement Schedules

All schedules are omitted because they are not required or because the required information is included in the Consolidated Financial Statements or notes thereto.

3. Exhibits

		Incorporated by Reference to SEC Filing			
Exhibit No.	**Filed Exhibit Description**	**Form**	**Date**	**Exhibit No.**	**Filed with this Form 10-K**
1.1	Equity Distribution Agreement, dated November 7, 2022, by and between Amicus Therapeutics, Inc. and Goldman Sachs & Co. LLC	Form 8-K	11/7/2022	1.1	
2.1	Agreement and Plan of Merger, dated November 19, 2013, by and among Amicus Therapeutics, Inc., CB Acquisition Corp., Callidus BioPharma, Inc., and Cuong Do	Form 8-K	2/12/2014	2.1	
+2.2	Agreement and Plan of Merger, dated July 5, 2016, by and among MiaMed, Inc., the Registrant and Minervas Merger Sub, Inc.	Form 8-K	7/6/2016	2.1	
+2.3	Agreement and Plan of Merger, dated as of September 19, 2018, by and among Amicus Therapeutics, Inc., Columbus Merger Sub Corp., Celenex, Inc. and Shareholder Representative Services LLC, solely in its capacity as the Shareholders' Representative	Form 8-K	9/25/2018	2.1	
3.1	Restated Certificate of Incorporation of the Registrant	Form 10-K	2/28/2012	3.1	
3.2	Second Amended and Restated By-laws of the Registrant.	Form 10-Q	8/8/2023	3.2	
3.3	Certificate of Amendment to the Registrant's Restated Certificate of Incorporation.	Form 8-K	6/10/2015	3.1	
3.4	Certificate of Amendment to the Restated Certificate of Incorporation	Form 8-K	6/8/2018	3.1	
3.5	Certificate of Amendment to the Restated Certificate of Incorporation	Form 8-K	6/13/2023	3.1	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1/A (333-141700)	5/17/2007	4.1	
4.2	Form of Indenture	Form S-3ASR	4/24/2016	4.7	
4.3	Description of the Registrant's securities	Form 10-K	3/2/2020	4.8	
4.4	Form of Pre-Funded Warrant	Form 8-K	9/29/2021	4.1	
4.5	Securities Purchase Agreement, dated September 29, 2021, by and between the Company and Redmile Group LLC	Form 8-K	9/29/2021	10.3	
10.1	Form of Director and Officer Indemnification Agreement	8-K	12/28/2022	10.1	
*10.2	Amended and Restated 2007 Director Option Plan and form of option agreement	Form 8-K	6/18/2010	10.2	
10.3	Securities Purchase Agreement, dated November 20, 2013 by and among the Company and the purchasers identified therein	Form 8-K	11/20/2013	10.1	
**10.4	Second Restated Agreement, dated November 19, 2013 by and between the Registrant and Glaxo Group Limited				X
*10.5	Amicus Therapeutics, Inc. Amended and Restated Restricted Stock Unit Deferral Plan	Form 8-K	12/28/2017	10.1	
*10.6	Amended and Restated 2007 Equity Incentive Plan	DEF 14A	4/26/2023	A	
*10.7	Amicus Therapeutics, Inc. Cash Deferral Plan	Form 8-K	10/28/2016	10.1	
10.8	Form of Performance-Based Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 8-K	12/30/2016	10.1	
10.9	Amendment #1 to the Amicus Therapeutics, Inc. Cash Deferral Plan.	Form 8-K	10/26/2014	10.1	
10.10	Amendment #2 to the Amicus Therapeutics, Inc. Cash Deferral Plan.	Form 8-K	12/19/2019	10.1	
*10.11	Employment Agreement, dated August 1, 2022, by and between the Registrant and Bradley L. Campbell.	Form 8-K	8/1/2022	10.1	
*10.12	Employment Agreement, dated February 23, 2022, by and between the Registrant and John F. Crowley.	Form 8-K	2/24/2022	10.2	
*10.13	Employment Agreement dated February 18, 2020 between the Registrant and Ellen S. Rosenberg	Form 10-K	3/2/2020	10.45	
*10.14	Employment Agreement dated February 18, 2020, between the Registrant and Daphne Quimi	Form 10-K	3/2/2020	10.48	
*10.15	Employment Agreement, dated August 21, 2023, by and between Amicus Therapeutics, Inc. and Simon Harford	Form 10-Q	11/8/2023	10.3	
*10.16	Employment Agreement dated February 18, 2020 between the Registrant and David Clark	Form 10-K	3/2/2020	10.18	
*10.17	Employment Agreement dated February 18, 2020 between the Registrant and Jeffrey Castelli	Form 10-K	3/2/2020	10.19	
*10.18	Form of Board Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 10-K	3/1/2021	10.39	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
*10.19	Form of Board Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 10-K	3/1/2021	10.41	
*10.20	Form of Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 10-K	3/1/2021	10.42	
*10.21	Form of Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 10-K	2/24/2022	10.25	
**10.22	License Agreement dated December 22, 2022, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania	Form 10-K	3/1/2023	10.25	
**10.23	Mutual Termination Agreement dated December 22, 2022, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania.	Form 10-K	3/1/2023	10.26	
10.24	Loan Agreement, dated October 2, 2023 by and among Amicus Therapeutics, Inc., certain subsidiaries of Amicus Therapeutics, Inc. from time to time party thereto as Guarantors, Blackstone Alternative Credit Advisors LP, Blackstone Life Sciences Advisors L.L.C., certain lenders from time to time party thereto and Wilmington Trust, National Association, as Agent for the lenders.	Form 8-K	10/2/2023	10.1	
10.25	Securities Purchase Agreement, dated October 2, 2023, by and among Amicus Therapeutics, Inc. and the Purchasers identified on the signature pages thereto.	Form 8-K	10/2/2023	10.2	
**10.26	Supply and Manufacturing Services Agreement, dated as of March 31, 2023, by and among the Company, WuXi Biologics (Hong Kong) Limited, WuXi Biologics Ireland Limited and WuXi Biologics Germany GmbH	Form 10-Q	8/8/2023	10.2	
21.1	List of Subsidiaries				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
31.1	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				X
31.2	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				X
32.1	Certificate of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2	Certificate of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				X
97.1	Amicus Therapeutics, Inc. Clawback Policy				X

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
101	The following financial information from this Annual Report on Form 10-K for the year ended December 31, 2023, formatted in Inline XBRL (Extensible Business Reporting Language) and filed electronically herewith: (i) the Consolidated Balance Sheets; (ii) the Consolidated Statements of Operations; (iii) the Consolidated Statements of Comprehensive Loss; (iv) the Consolidated Statements of Cash Flows; (v) and the Notes to the Consolidated Financial Statements.				X
104	The cover page from the Annual Report on Form 10-K for the year ended December 31, 2023 formatted in Inline XBRL (included in Exhibit 101).				X

+ Confidential treatment has been granted as to certain portions of the document, which portions have been omitted and filed separately with the Securities and Exchange Commission.

* Indicates management contract or compensatory plan.

** Portions of the exhibit have been omitted in accordance with 17 CFR § 229.601(b)(10)(iv).

The information required by this item is incorporated by reference from the Proxy Statement under the captions "Certain Relationships and Related Transactions," "Director Independence," "Committee Compensation and Meetings of the Board of Directors," and "Compensation Committee Interlock and Insider Participation."

Item 16. ***FORM 10-K SUMMARY.***

Registrants may voluntarily include a summary of information required by Form 10-K under this Item 16. The Company has elected not to include such 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 on February 28, 2024.

AMICUS THERAPEUTICS, INC.
(Registrant)

By: /s/ Bradley L. Campbell
Bradley L. Campbell
Chief Executive Officer

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/ Bradley L. Campbell (Bradley L. Campbell)	President and Chief Executive Officer (Principal Executive Officer)	February 28, 2024
/s/ Simon Harford (Simon Harford)	Chief Financial Officer (Principal Financial Officer)	February 28, 2024
/s/ Samantha L. Prout (Samantha L. Prout)	Chief Accounting Officer and Controller (Principal Accounting Officer)	February 28, 2024
/s/ John F. Crowley (John F. Crowley)	Executive Chairman	February 28, 2024
/s/ Margaret G. McGlynn (Margaret G. McGlynn)	Director	February 28, 2024
/s/ Michael G. Raab (Michael G. Raab)	Director	February 28, 2024
/s/ Glenn Sblendorio (Glenn Sblendorio)	Director	February 28, 2024
/s/ Craig Wheeler (Craig Wheeler)	Director	February 28, 2024

Signature	Title	Date
/s/ Lynn Bleil (Lynn Bleil)	Director	February 28, 2024
/s/ Burke Whitman (Burke Whitman)	Director	February 28, 2024
/s/ Michael A. Kelly (Michael A. Kelly)	Director	February 28, 2024
/s/ Eiry W. Roberts, M.D. (Eiry W. Roberts, M.D.)	Director	February 28, 2024

Company Information

Headquarters

Amicus Therapeutics, Inc.
47 Hulfish Street
Princeton, NJ 08542

Transfer Agent

Equiniti Trust Company, LLC ("EQ")

48 Wall Street, Floor 23
New York, NY 10005
800 937 5449

Independent Registered Public Accounting Firm

Ernst & Young LLP

Stockholder Inquiries

All stockholder inquiries related to the Company's stock should be directed to:

Amicus Therapeutics, Inc.
Investor Relations
ir@amicusrx.com

Common Stock

NASDAQ Symbol: FOLD

SEC Form 10-K

A copy of the Company's annual report to the Securities and Exchange Commission on Form 10-K will be available without charge upon written request to Amicus Therapeutics, Inc., 47 Hulfish St, Princeton, NJ, 08542 or via the Company's website at www.amicusrx.com.

Annual Meeting

Amicus will hold its 2024 Annual Meeting of Stockholders in virtual format only. Our virtual meeting will be structured in a manner intended to provide our stockholders with a participation experience similar to an in-person meeting. The virtual annual meeting will be held at 9:00 a.m. on Thursday, June 6, 2024. Stockholders can access the meeting via the Internet at www.virtualshareholdermeeting.com/FOLD2024

Safe Harbor

This annual report contains certain forward-looking statements. For a discussion of forward-looking statements, please see Part 1, Item 1 of our annual report on Form 10-K for 2023.

Executive Committee

BRADLEY CAMPBELL
President and Chief Executive Officer

SIMON HARFORD
Chief Financial Officer

ELLEN ROSENBERG
Chief Legal Officer and Corporate Secretary

DAVID CLARK
Chief People Officer

JEFFREY CASTELLI, PH.D.
Chief Development Officer

STEPHEN ARNOLD
Chief, Global Head of Rare Diseases

JAYNE GERSHKOWITZ
Chief Patient Advocate

MITCHELL GOLDMAN, M.D., PH.D.
Chief Medical Officer

PATRIK FLORENCIO
Global Chief Compliance & Risk Officer

SÉBASTIEN MARTEL
Chief Business Officer

PAT O'SULLIVAN
Chief Technical Operations Officer

JILL WEIMER, PH.D.
Chief Science Officer

JULIE YU, PH.D.
Chief Program Officer

Board of Directors

MICHAEL G. RAAB
President and Chief Executive Officer, Ardelyx, Inc.
Chairman of the Board

LYNN D. BLEIL
Former Senior Partner, McKinesey & Co.
Nominating and Governance (Chair)

BRADLEY CAMPBELL
President and Chief Executive Officer

MICHAEL A. KELLY
Founder and President, Sentry Hill Partners, LLC

MARGARET G. MCGLYNN
Former President, Global Vaccines and Anti-Infectives, Merck
Compensation and Leadership Development (Chair)

EIRY W. ROBERTS
Chief Medical Officer, Neurocrine Biosciences, Inc.

GLENN P. SBLENDORIO
Former Chief Executive Officer, IVERIC Bio, Inc.
Audit and Compliance (Chair)

CRAIG A. WHEELER
Chief Executive Officer, Headwaters Biotech Advisors
Science and Technology (Chair)

BURKE W. WHITMAN
Chief Executive Officer, Colmar Holdings; Retired Major General, U.S. Marine Corps

Amicus Therapeutics®

AMICUS THERAPEUTICS, INC.

47 HULFISH STREET

PRINCETON, NJ 08542

609-662-2000

WWW.AMICUSRX.COM