# 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, 2022**

**OR**

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

**For the transition period from to**

**Commission file number 001-33497**

# 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) |
| **3675 Market Street, Philadelphia, PA** | **19104** |
| (Address of Principal Executive Offices) | (Zip Code) |

**(215) 921-7600**

(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 277,450,967 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, 2022) was $2,979,823,386. 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, 2023 was 282,714,738 shares.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2022 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**


| | | |
|---|---|---|
| Item 1. | BUSINESS | 5 |
| Item 1A. | RISK FACTORS | 28 |
| Item 1B. | UNRESOLVED STAFF COMMENTS | 71 |
| Item 2. | PROPERTIES | 71 |
| Item 3. | LEGAL PROCEEDINGS | 71 |
| Item 4. | MINE SAFETY DISCLOSURES | 71 |


**PART II**


| | | |
|---|---|---|
| Item 5. | MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES | 72 |
| Item 6. | [RESERVED] | 73 |
| Item 7. | MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS | 73 |
| Item 7A. | QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK | 82 |
| Item 8. | FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA | 83 |
| Item 9. | CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE | 116 |
| Item 9A. | CONTROLS AND PROCEDURES | 117 |
| Item 9B. | OTHER INFORMATION | 117 |
| Item 9C. | DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS | 117 |


**PART III**


| | | |
|---|---|---|
| Item 10. | DIRECTORS, EXECUTIVE OFFICERS, AND CORPORATE GOVERNANCE | 118 |
| Item 11. | EXECUTIVE COMPENSATION | 118 |
| Item 12. | SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS | 118 |
| Item 13. | CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE | 118 |
| Item 14. | PRINCIPAL ACCOUNTING FEES AND SERVICES | 118 |


**PART IV**


| | | |
|---|---|---|
| Item 15. | EXHIBITS, FINANCIAL STATEMENT SCHEDULES | 119 |
| Item 16. | FORM 10-K SUMMARY | 123 |
| SIGNATURES | | 124 |


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, and Galafold® 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 Pompe Enzyme Replacement Therapy ("ERT" or "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 these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates, including AT-GAA;
- the number and development requirements of other product candidates that we pursue;
- 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 product and product candidates, including AT-GAA;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl") and, if our regulatory applications are approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and AT-GAA;
- our ability to obtain reimbursement for Galafold® and, if our regulatory applications are approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®, and, if approved and applicable, AT-GAA;
- our ability to obtain market acceptance of Galafold® and, if our regulatory applications are approved, AT-GAA;
- 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 our 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 payments from any such collaborators;

- the extent to which our business could be adversely impacted by the effects of the novel coronavirus ("COVID-19") outbreak, including actions by us, governments, our customers, our suppliers, or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards;
- 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 product 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 product or, if approved, product candidates, their commercialization may suffer.
- If the market opportunities for our product or product candidates are smaller than we believe they are, then our revenues may be adversely affected, and our business may suffer.
- Galafold® 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 could adversely affect our business.
- Our product 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 product 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 product or product candidates may cause undesirable side effects or have other properties that could delay or prevent 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 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.
- 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 patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- 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.
- If our competitors obtain orphan drug exclusivity for their products and we do not, we may not 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 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.

- If we are unable to obtain marketing approval, or if approved unable to successfully commercialize AT-GAA, our business could be materially harmed.
- 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.
- Use of third parties to manufacture our product or product candidates may increase the risk that we will not have sufficient quantities of our product 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 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 product 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 product 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® 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 with third parties, we could lose license rights that are important to our business.
- Failure to secure trademark registrations could adversely affect our business.
- Our rights to develop and commercialize our gene therapy product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.
- The novel coronavirus ("COVID-19") pandemic may negatively impact our business and operations.
- 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.
- Our business and reputation may be adversely affected by environmental, social and governance matters.

# 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 have a portfolio including the first, oral monotherapy for Fabry disease that has achieved widespread global approval and a differentiated biologic for Pompe disease that is under review with the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA"), and the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA"). We are committed to discovering and developing next generation therapies in Fabry and Pompe diseases.

The cornerstone of our portfolio is Galafold® (also referred to as "migalastat"), the first and only approved oral precision medicine for people living with Fabry disease who have amenable genetic variants. Migalastat is currently approved under the trade name Galafold® in the United States ("U.S."), European Union ("E.U."), U.K., and Japan, with multiple additional approvals granted and applications pending in several geographies around the world.

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, two-component, potential best-in-class treatment for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. In September 2021, the FDA set the Prescription Drug User Fee Act ("PDUFA") target action date of May 29, 2022 for the New Drug Application ("NDA") for miglustat and July 29, 2022 for the Biologics License Application ("BLA") for cipaglucosidase alfa. The EMA validated the Marketing Authorization Application (“MAA”) in the fourth quarter of 2021. In May 2022, the FDA extended the review period for the NDA for miglustat and the BLA for cipaglucosidase alfa resulting in revised PDUFA action dates of August 29, 2022 and October 29, 2022, respectively. In October 2022, the FDA deferred action on the BLA for cipaglucosidase alfa, citing the inability to complete the manufacturing facility inspection prior to the PDUFA action date. We are actively engaged with the FDA and an inspection has been scheduled. In December 2022, the Committee for Medicinal Products for Human Use ("CHMP") of the EMA adopted a positive opinion recommending market authorization of cipaglucosidase alfa, or Pombiliti™. The regulatory submission process for AT-GAA in the U.K. was initiated in December 2022.

### 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 that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. We are leveraging our global capabilities to develop and broaden our lead franchises in Fabry and Pompe disease, with focused discovery work on next generation therapies and novel platform technologies.

We continue to monitor the novel coronavirus ("COVID-19") pandemic. Our commercial operations have not been significantly impacted by the COVID-19 pandemic and we gradually continue to see an improvement in patient identification and Galafold® initiation. We have been able to continue to meet required commercial demand for Galafold® as well as supply our ongoing Pompe disease clinical studies and access programs including the Early Access to Medicines Scheme ("EAMS") without interruption. In regard to our regulatory operations, the FDA deferred action on the pending BLA for cipaglucosidase alfa, as a facility inspection was necessary, however, could not be completed by the PDUFA action date due to COVID-19 related travel restrictions. The facility inspection has subsequently been scheduled. Per FDA guidance relating to pre-approval inspections during the COVID-19 pandemic, receipt of a deferral action indicates no deficiencies have been identified and the application otherwise satisfies the requirements for approval.

Highlights of our progress include:

- *Commercial and regulatory success in Fabry disease*. For the year ended December 31, 2022, Galafold® revenue was $329.0 million of consolidated revenue, which represented an increase of $23.5 million compared to the prior year. We continue to see strong commercial momentum and expansion into additional geographies. In countries where we have been operating the longest, we see an increasing proportion of previously untreated patients come onto Galafold® as compared to treatment experienced patients. In the U.S., we continue to see a significant increase in patients from a growing and very wide prescriber base. Across all markets, we see a high rate of compliance and adherence to this oral treatment option.
- *Pompe disease program milestones*. AT-GAA is under regulatory reviews in the U.S., E.U. and U.K., respectively. In December 2022, the CHMP of the EMA adopted a positive opinion recommending marketing authorization of Pombiliti™ (cipaglucosidase alfa), a long-term enzyme replacement therapy ("ERT") used in combination with miglustat for adults with late-onset Pompe disease ("LOPD"). Additionally, multiple expanded access mechanisms are in place around the globe, including in the U.S., U.K., Germany, France, Japan, and others.
- *Pipeline advancement and growth.* We are leveraging our global capabilities to develop and broaden our lead franchises in Fabry and Pompe disease, with focused discovery work on next generation therapies and novel platform technologies.
- *Financial strength.* Total cash, cash equivalents, and marketable securities as of December 31, 2022 was $293.6 million. Based on the 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 the COVID-19 pandemic, business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

**Our Commercial Product and Product Candidates**

***Galafold® (migalastat HCl) for Fabry Disease***

Our oral precision medicine Galafold® was granted accelerated approval by the FDA in August 2018 under the brand name Galafold® 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. The FDA has approved Galafold® for 350 amenable GLA variants. 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). The approved E.U. and U.K. labels include 1,384 mutations amenable to Galafold® treatment, which represent up to half of all patients with Fabry disease. In countries where mutations are provided only on the amenability website, these 1,384 amenable mutations are now available. Marketing authorization approvals have been granted in over 40 countries around the world. In July 2021, Galafold® was approved in the E.U. for adolescents aged 12 years and older weighing 45 kg or more. Throughout 2022, Galafold® was approved in 7 additional countries, including the U.K. and Japan, for adolescents aged 12 years and older weighing 45 kg or more. We plan to continue to launch Galafold® in additional countries during 2023, 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. Galafold® is an oral precision medicine intended to treat Fabry disease in patients who have amenable genetic variants, and at this time, it is not intended for concomitant use with ERT.

***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 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 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 JAMA 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, two other products, both ERTs, are approved for the treatment of Fabry disease: agalsidase beta by Sanofi Aventis and agalsidase alfa by Takeda, the latter of which is not approved in the U.S.

***Novel ERT for Pompe Disease***

We are leveraging our biologics capabilities to develop AT-GAA, a novel treatment paradigm for Pompe disease. AT-GAA consists of a uniquely engineered rhGAA enzyme, ATB200, or cipaglucosidase alfa, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with AT2221, or miglustat, that functions as an enzyme stabilizer. Miglustat binds to and stabilizes ATB200 preventing inactivation of rhGAA in circulation to improve the uptake of active enzyme in key disease-relevant tissues, resulting in increased clearance of accumulated substrate, ("glycogen"). Miglustat is not an active ingredient that contributes directly to glycogen reduction.

We initiated ATB200-03 (or "PROPEL"), a global Phase 3 clinical study of AT-GAA in adult patients with late onset Pompe disease in December 2018 and completed last patient, last visit in December 2020. In February 2021, we reported topline results from the Phase 3 PROPEL study. Patients in PROPEL were randomized 2:1 so that for every two patients randomized to be treated with AT-GAA, one was randomized to be treated with alglucosidase alfa. Of the Pompe disease patients enrolled, 77% were being treated with alglucosidase alfa (n=95) immediately prior to enrollment (“Switch”) and 23% had never been treated with any ERT (n=28) (“Naïve”). 117 patients completed the PROPEL study and all 117 voluntarily enrolled in the long-term extension study. The primary endpoint of the study was the mean change in 6-minute walk distance as compared with baseline measurements at 52 weeks across the combined ERT Switch and ERT Naïve patient populations. In this combined population patients taking AT-GAA (n=85) walked on average 21 meters farther at 52 weeks compared to 7 meters with those treated with alglucosidase alfa (n=37). This primary endpoint in the combined population was assessed for superiority and while numerically greater, statistical significance for superiority on this combined population was not achieved for the AT-GAA arm as compared to the alglucosidase alfa arm (p=0.072).

Per the hierarchy of the statistical analysis plan, the first key secondary endpoint of the study was the mean change in percent-predicted Forced Vital Capacity (“FVC”) at 52 weeks across the combined population. In this combined population patients taking AT-GAA demonstrated a nominally statistically significant and clinically meaningful difference for superiority over those treated with alglucosidase alfa. AT-GAA significantly slowed the rate of respiratory decline in patients after 52 weeks. Patients treated with AT-GAA showed a 0.9% absolute decline in percent-predicted FVC, compared to a 4.0% absolute decline in the alglucosidase alfa arm (p=0.023). Patients within the combined study population demonstrated statistically significant improvements on the Gait, Stairs, Gower’s Chair ("GSGC") key secondary endpoint, which captures strength, coordination and mobility, compared to a worsening for alglucosidase alfa treated patients in the overall population ($p<0.05$). Additionally, lower Manual Muscle Testing ("MMT"), Patient-Reported Outcomes Measurement Information System (“PROMIS”) physical function and PROMIS fatigue secondary endpoints favored AT-GAA treated patients over alglucosidase alfa treated patients. Results also showed improvements in the two important biomarker endpoints of Pompe disease (Hex-4 and CK), which significantly favored AT-GAA compared to alglucosidase alfa ($p<0.001$). AT-GAA demonstrated a similar safety profile to alglucosidase alfa.

The PROPEL Switch patients entered the study having been treated with alglucosidase alfa for a minimum of two years. More than two thirds (67%+) of those patients had been on ERT treatment for more than five years prior to entering the PROPEL study (mean of 7.4 years). A pre-specified analysis of the patients switching from alglucosidase alfa on 6-minute walk distance showed that after 52 weeks from switching, AT-GAA treated patients (n=65) walked 16.9 meters farther than their baseline, compared to 0.0 meters for those patients who were randomized to remain on alglucosidase alfa (n=30) (p=0.046). A pre-specified analysis of the patients switching from alglucosidase alfa on percent-predicted FVC showed that AT-GAA treated patients stabilized and slightly improved their respiratory function on this important measure while those patients remaining on alglucosidase alfa continued to significantly decline in respiratory muscle function. AT-GAA patients showed a 0.1% absolute increase in percent-predicted FVC while the alglucosidase alfa patients showed a 4.0% absolute decline over the course of the year (p=0.006).

The PROPEL Naïve patients treated with AT-GAA for 52 weeks (n=20) walked 33 meters farther than their baseline, on the 6-minute walk distance endpoint. The Naïve patients treated with alglucosidase alfa (n=7) walked 38 meters further than their baseline. The difference between the two groups was not statistically significant (p=0.60). Additionally, patients never previously treated with any ERT showed similar declines in percent-predicted FVC at 52 weeks of –4.1% for AT-GAA treated patients and –3.6% for alglucosidase alpha treated patients. The difference between the two groups was not statistically significant (p=0.57).

In October 2022 and February 2023, we reported positive long-term data from our ongoing phase 1/2 clinical study and Phase 3 open-label extension study, respectively. Phase 1/2 and 3 study participants treated with AT-GAA for up to 48 months and up to 2 years, respectively, demonstrated persistent and durable effects on six-minute walk test distance and measures of motor function and muscle strength, stability, or increase in forced vital capacity, and reductions in biomarkers of muscle damage and disease substrate.

In December 2022 the CHMP of the EMA adopted a positive opinion recommending marketing authorization of cipaglucosidase alfa or Pombiliti™. Additionally, we initiated the regulatory submission process with the U.K. MHRA in December 2022.

In addition, we are conducting ongoing clinical studies in pediatric patients for both 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 disorder ("LD") 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.

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

***Additional Development and Next Generation Programs***

We are researching potential therapies for CDKL5 deficiency disorder ("CDD"). We are collaborating with the LouLou Foundation to assess the natural history of the disease to identify endpoints for potential use in future studies. We also have a number of additional gene therapies in clinical and preclinical development, including potential gene therapies in multiple forms of Batten disease.

***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 necessary to develop and market technologies or products with a focus on rare and orphan diseases. We are exploring potential collaborations, alliances, and 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.

**Acquisitions**

***Celenex, Inc.***

In connection with our acquisition of Celenex, Inc. ("Celenex"), we may be obligated to pay up to an additional $10 million in connection with the achievement of certain development milestones, $220 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to $75 million in tiered sales milestone payments. Celenex has an exclusive license agreement with Nationwide Children's Hospital ("Nationwide Children's"). Under this license agreement, Nationwide Children's is eligible to receive development and sales-based milestones of up to $7.8 million for each product.

***MiaMed, Inc.***

In connection with our acquisition of MiaMed, Inc., ("MiaMed"), we may be obligated to pay up to an additional $83 million in connection with the achievement of certain clinical, regulatory, and commercial milestones, for a potential aggregate deal value of $89.5 million.

***Callidus Biopharma, Inc.***

In connection with our acquisition of Callidus Biopharma, Inc. ("Callidus"), we may be obligated to make additional payments to the former stockholders of Callidus upon the achievement of certain clinical milestones of up to $35 million and regulatory milestones of up to $80 million set forth in the merger agreement, provided that the aggregate merger consideration shall not exceed $130 million.

**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 ingredients in Galafold®, in the treatment of Fabry disease, which expire between 2027 and 2039 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 covering various aspects of Galafold®, including composition-of-matter methods of treating a patient diagnosed with Fabry disease with migalastat and their foreign counterparts. 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 our investigational new treatment for Pompe disease, AT-GAA (ATB200/AT2221, an ERT/pharmacological chaperone combination) as well as foreign counterparts to the issued patents, some of which are still pending. Issued U.S. patents cover ATB200 compositions-of-matter, formulations, methods of manufacturing and methods of treatment and will expire between 2033 and 2037. We also have pending U.S. patent applications covering compositions, methods of treatment, methods of manufacture, and formulations with anticipated expiry between 2033 and 2043.
- From the Celenex acquisition, we acquired an exclusive license to composition-of-matter and intrathecal method of treatment patent applications covering the gene therapy for treating Batten disease that are pending in the U.S., Europe, Japan, and other jurisdictions. Any patents issued from these applications will expire in 2033 or 2040. The patent covering an intrathecal method of treatment, which expires in 2033, has issued in Europe and Japan.
- From our agreement with Penn, we have a license to Penn’s patent portfolio pertaining to vector and other platform technologies for treating Pompe disease and Fabry disease. Any patents issued from these applications will expire in 2039.

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:

- Gene therapy protein engineering technology;
- Gene therapy (e.g., Pompe, Fabry) and ERT (e.g., CDKL5) programs and the 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 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.

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

*Nationwide Children's Hospital*

In September 2018, we expanded our pipeline by acquiring the rights and related intellectual property of ten gene therapy programs through our acquisition of Celenex. Celenex has an exclusive license agreement with Nationwide Children’s. Under this license agreement, Nationwide Children’s is eligible to receive development and sales-based milestones of up to $7.8 million for each product.

*University of Pennsylvania*

In October 2018, as amended, we entered into a collaboration agreement with Penn to pursue research and development of novel gene therapies. Our gene therapy portfolio pipeline expanded to include Pompe disease, Fabry disease and other rare diseases.

In December 2022, we entered into a mutual termination agreement (the "Termination Agreement") pursuant to which we and Penn mutually agreed to terminate the collaboration agreement, as amended. In connection with the Termination Agreement, we 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.

Concurrently, 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 LDs. 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 | 2022 Sales (in millions) |
|---|---|---|---|---|---|
| **Sanofi Aventis** | Fabry Disease | Fabrazyme® | ERT | Marketed | €938 |
| | Pompe Disease | Myozyme®/ Lumizyme® | ERT | Marketed | €958 |
| | Pompe Disease | Nexviazyme®/ Nexviadyme® | ERT | Marketed | €196 |
| | Fabry Disease | Venglustat | Oral glucosylceramide synthase ("GCS") Inhibitor | Phase 3 | N/A |
| **Takeda** [2] | Fabry Disease | Replagal® | ERT | Marketed | ¥62,700 |
| **Idorsia** | Fabry Disease | Lucerastat | Oral GCS Inhibitor | Phase 3 | N/A |
| **Protalix Biotherapeutics / Chiesi Farmaceutici S.p.A** | Fabry Disease | PRX-102 | ERT | Regulatory | N/A |
| **Freeline** | Fabry Disease | FLT-190 | Gene Therapy | 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 | AT-845 | Gene Therapy | Phase 1/2 | N/A |
| **Roche** | Pompe Disease | SPK-3006 | Gene Therapy | Phase 1/2 | N/A |
| **Maze Therapeutics** | Pompe Disease | GYS1 | 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, 2022, as Takeda's fiscal year ends on March 31, 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 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 EMA, to be assessed by the 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 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. In September 2020, AT-GTX-501 was granted PRIME designation.

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 ("grand fathered") 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 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.

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 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 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 Securities and Exchanges Commission ("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 product 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. 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 product 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. 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 globally diverse employees 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 the advancement of Diversity, Equity and Inclusion ("DEI") in the workplace. DEI creates a work environment 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 regardless of identities and differences, which is evidenced through our most recent engagement survey where we came within 2% of the global benchmark for DEI.

As of December 31, 2022, we had 484 full-time employees. As of December 31, 2022, 57% of our global workforce, 45% of our executive management team and 30% of our board of directors were women. In addition, we have made a strong commitment to overall diversity, as 97% of all hiring slates included diverse candidates, where diversity is defined as maintaining/increasing gender diversity and increasing representation of minority race, veteran, disabled, and LGBTQ employees. We also saw the impact of this diversity in hiring and promoting, where 61% of all those hired or promoted to Director and above roles were diverse and 83% of all those hired or promoted to Associate Director and below roles were diverse.

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, 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 3675 Market Street, Philadelphia, PA 19104 and our telephone number is 215-921-7600. 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 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 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;
- obtaining and maintaining a commercially viable price for our product and product candidates, if approved; and
- continuing to successfully mitigate the impact of the COVID-19 pandemic.

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.

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

Our product and product candidates, including Galafold® and AT-GAA 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 product and product candidates will prevent us from commercializing our product 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, including AT-GAA, 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, including AT-GAA, 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, including AT-GAA 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 product or product candidates, we may not be successful in commercializing Galafold®, or any product candidate, including AT-GAA, 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 anticipate using these capabilities to support other product candidates, including AT-GAA, when 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 product 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 product 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®, or our product candidates, including AT-GAA, if and when they are approved by regulatory authorities, including the FDA, PMDA and EMA, 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 product or product candidates 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 product 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 product 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 product 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 and may not ever become profitable.

***If the market opportunities for our product 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 product and most advanced product candidates are being developed to address is rare. 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 product 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 product or product candidates prove to be incorrect, the market opportunities for our product 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® 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 any of our other products or 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 product 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® and any of our product candidates that receive marketing approval and we may fail to meet our revenue targets.

***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 product, Galafold®, and product candidates, including AT-GAA, and 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. These products include Sanofi Aventis' Fabrazyme® and Takeda's Replagal®, as well as other Fabry treatment products in development. 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 product 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®, and any of our other product candidates, including AT-GAA, 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 (such as COVID-19), or natural disasters (including earthquakes, typhoons, floods and fires).

In addition, 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.

***Following the receipt of marketing approval of our product 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 commercialize Galafold® or any product candidate, including AT-GAA, if approved, successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and 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® or any product candidate such as AT-GAA, if approved, that we commercialize, and in particular gene therapies, and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, Galafold® and 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 orphan 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. 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. For example, the Tax Cuts and Jobs 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 (the “Code”), commonly referred to as the individual mandate. 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. In 2020 and 2021, during the COVID-19 pandemic, Congress passed several laws including the Coronavirus Aid, Relief, and Economic Security Act and Consolidated Appropriations Act of 2021, that temporarily suspended the 2% sequestration. At the end of 2021, Congress passed the Protecting Medicare and American Farmers from Sequester Cuts Act, which extended the suspension on the 2% sequestration through March 31, 2022, and adjusted the sequester to 1% for the period between April 1, 2022 and June 30, 2022. 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. 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 product 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. 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 product 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® or any of our other product candidates, including AT-GAA, may include restrictions on use, use limited to specific populations or 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 REMS plan. Physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label. 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 testing of our product candidates in human clinical trials and will face an even greater risk when we commercially sell any products that we develop, including those which may arise from misuse or malfunction of, or design flaws in, such products, whether or not such problems directly relate to the products 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 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. We have increased our insurance coverage for the commercialization of Galafold® and may increase insurance coverage when, and if, we begin commercializing any other product candidate that receives marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. 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.

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

In the U.S., after an NDA is approved, such as Galafold®, 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 our product or product candidate 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. 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 product 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 received Para. 4 certifications from three ANDA filers for Galafold® and have initiated Hatch-Waxman litigation against these ANDA filers and will continue to vigorously defend our Galafold® intellectual property rights.

The Biologics Price Competition and Innovation Act, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act of 2010, or the ACA, Pub. L. No. 111-148 (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, including AT-GAA, if approved. 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.

Prior to the enactment of the BPCIA, information in approved BLAs could not be relied upon by other manufacturers to establish the safety and efficacy of their products for which they were seeking FDA approval. Accordingly, if our products such as AT-GAA are approved under a BLA, other manufacturers potentially could develop and seek FDA approval of "biosimilar" products at some point in the future, including a biosimilar of AT-GAA.

***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.

We have historically been focused on the development and commercialization of Galafold®, a small molecule for Fabry disease and a next generation ERT treatment for Pompe disease, ATB-200. In 2018, we also made a significant investment in potential gene therapies for Fabry, Pompe, and other LDs. Notwithstanding our large investment in gene therapies and Pompe ERT to date and anticipated future expenditures in related proprietary technologies, we have not yet developed, and may never successfully develop, any marketed drugs using ERT and gene therapy approaches. 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 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. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates yet fail to yield product candidates for clinical development.

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

***Our product 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 product, Galafold® or product candidates including AT-GAA, 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 product 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 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 product 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, which are effective as of May 25, 2018, 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 product 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 product 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:

- the 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;

- the 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. 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;
- The 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. Enforcement of the GDPR began on May 25, 2018, and 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®, and our other 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. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Nonetheless, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental 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, including AT-GAA, 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. This is particularly the case with AT-GAA, as there can be no assurance that the Phase 3 PROPEL study results will meet regulatory standards for approval in every geography.

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, including AT-GAA, 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 including ongoing clinical trials of AT-GAA in additional study populations 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 product 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. AT-GAA has also received this designation from the FDA, EMA, 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 AT-GAA or our other product candidates obtains orphan drug exclusivity for and approval of a product with the same indications as our product candidates as 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 AT-GAA 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.

In December 2022, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending marketing authorization of cipaglucosidase alfa used in combination with miglustat for adults with late-onset Pompe disease (LOPD). A CHMP decision on miglustat is expected to follow. We do not know if both components of AT-GAA will be approved or, if approved, whether cipaglucosidase alfa and miglustat will receive favorable pricing. If we are unable to secure full marketing approval for both components of AT-GAA, EU or other geographies, our business and results of operations may be materially harmed.

***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.

***If we are unable to obtain marketing approval for AT-GAA, or if it is approved and the label does not support reimbursement and we are unable to successfully commercialize AT-GAA, our business could be materially harmed.***

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. In September 2021, the FDA accepted our AT-GAA BLA and NDA for review. Regulatory authorities, including FDA, may determine that AT-GAA is not effective or only moderately effective, have effect in only a limited population, 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. In October 2022, FDA informed us that it has deferred action on the AT-GAA BLA, pending inspection of the proposed manufacturing site in China. The inspection has been delayed due to restrictions related to the COVID-19 pandemic and is now scheduled. This timing is subject to change and is dependent on a number of factors, including the evolving situation on the ground in China and the outcome of an inspection. There can be no assurance that an inspection will take place when scheduled or that an inspection will be successful if and when completed all of which may impact timing or probability of any approvals. If AT-GAA fails to receive marketing approval, is significantly delayed in receiving marketing approval or if the approved labeling is not as expected, AT-GAA may fail to receive market acceptance, receive reimbursement or be able to generate material revenue, any of which could substantially harm our future business and impact our ability to meet our financial guidance.

**Risks Related to our Preclinical Product Candidates**

***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 many potential gene therapies and have 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 or that we will meet any projected timelines for development.

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

***Use of third parties to manufacture Galafold® or AT-GAA may increase the risk that we will not have sufficient quantities of Galafold® 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 Galafold® or AT-GAA. 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 product and preclinical and clinical 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 candidate ATB200 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 product 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 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;
- limitations on supply availability resulting from capacity and scheduling constraints 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®, AT-GAA, 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 AT-GAA. Different geopolitical situations, responses to COVID-19, 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 product candidates. Our product candidates and any products 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.

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. 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 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 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 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. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with 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. 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 product 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 product or product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our product or product candidates.***

We currently rely on the manufacturers of our product 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 product 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 prices 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 product or, after regulatory approval has been obtained, our product candidates, the commercial launch of our product 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 product or product candidates.

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

Manufacturing of our product 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 product and proceed with our planned clinical trials and 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 product or product candidates.

We currently rely on WuXi Biologics Co., Ltd. ("Wuxi"), a company based in the People's Republic of China (the "PRC"), as the sole supplier of our biologic product, ATB200. 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. or any of the other countries in which our products are marketed. In addition, the out-breaks of SARS, COVID-19 or other similar illnesses in the PRC could impact operations at Wuxi. Although currently there has been no impact on our ability to obtain supply of ATB200, and we and Wuxi have robust mitigation plans in place, 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 our pipeline product AT-GAA as well as our 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, 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 never be profitable on a non-GAAP or GAAP basis. For the year ended December 31, 2022, we have a net loss of $236.6 million, and we have an accumulated deficit of $2.5 billion at December 31, 2022.

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

- continue our development and commercialization of, and seek regulatory approvals for, product candidates, including Galafold® and AT-GAA 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® 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 our other product candidates in Europe, Japan and the U.S. or other territories in which we have received or may receive regulatory approval;
- prepare for launch of AT-GAA in the U.S., E.U., U.K. and other jurisdictions if approved by regulators;
- continue our gene transfer discovery and next generation product research;
- continue our preclinical studies of and potentially conduct clinical studies of ERT and gene therapy for CDD; 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 expected 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. Our ability to generate material revenue and become profitable depends upon our ability to successfully commercialize our existing product 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, including AT-GAA, 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 product 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®;
- complete and submit regulatory submissions to the FDA, EMA, MHRA, PDMA and others and obtain regulatory approval for AT-GAA;
- develop and maintain a commercial organization capable of sales, marketing, and distribution for Galafold® and any product candidates we intend to market, including AT-GAA if approved, in the countries where we have chosen to commercialize the product candidates ourselves including the U.S. 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® 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; and
- continue to navigate any adverse impacts of the COVID-19 outbreak, including due to actions by us, governments, our customers, our suppliers or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics.

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, then 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 product 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 product and product candidates for which we may receive regulatory approval, including continuing to build 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 the COVID-19 pandemic, future business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements. However, we may require substantial additional capital for the development and commercialization of our product and further development and commercialization of our product candidates.

We cannot be certain that additional 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 product or product candidates or one or more of our other research and development initiatives;
- seek collaborators for Galafold®, AT-GAA 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, product 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 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 any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own, including AT-GAA;
- 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 AT-GAA 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 product and product candidates including AT-GAA;
- 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;
- the cost of complying with new laws, rules or regulations in the geographies in which we 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® 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 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 2026 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®, AT-GAA or our other 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 July 2020, we entered into the Senior Secured Term Loan due 2026 for a $400 million credit facility with Hayfin Capital Management, with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum that requires interest-only payments until mid-2024 and matures in six years in 2026. We received net proceeds of $385.9 million in July 2020, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. The Senior Secured Term Loan due 2026 contains a minimum liquidity covenant of $75 million, tested monthly and in effect at all times, and an incremental minimum consolidated revenue covenant, measured as of the previous four consecutive fiscal quarters. The minimum consolidated revenue covenant ranges from $140 million, beginning March 31, 2021, and peaks at $225 million by June 30, 2023, continuing at that level until the loan is repaid.

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 obtain financing 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. In addition, our outlooks do not assume fluctuations in currency exchange rates. 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, 2022, we had federal and state net operating loss carry forwards ("NOLs") of approximately $1,183 million and $992 million, 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 Cuts and Jobs Act. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2022 will expire in 2029 through 2040. 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 our NOLs for the tax year 2022 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 49% of our common stock as of December 31, 2022. 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, product 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 AT-GAA, 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 AT-GAA, 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 AT-GAA. We also have several pending applications covering Galafold®, AT-GAA 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 product. 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 a product that is identical to our product 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 a competitive identical product for indications other than the one for which the product has 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 AT-GAA, 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 product 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.***

We are a party to license agreements with Nationwide Children's Hospital ("Nationwide Children's") and University of Pennsylvania ("Penn") pursuant to which we license key intellectual property relating to our gene therapy product candidates. We expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will 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 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.

***Our rights to develop and commercialize our gene therapy product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.***

The biotechnology and pharmaceutical industries, especially in the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions. We are aware of companies focused on developing gene therapies in various indications as well as several companies addressing other methods for delivering or modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

In addition to our own patents, we have acquired licenses to certain patent rights and proprietary technology from third parties, including our current partners at Nationwide Children's and Penn, that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product and product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

**Risks Related to the COVID-19 Pandemic**

***The novel coronavirus ("COVID-19") pandemic and efforts to reduce its spread may negatively impact our business and operations.***

The COVID-19 pandemic has substantially burdened healthcare systems worldwide which may impact progression of our clinical trials, development and manufacturing of our product and product candidates and continued commercialization of Galafold®. Required inspections and reviews by regulatory agencies may also be delayed due to the focus of resources on COVID-19 as well as travel and other restrictions. In October 2022, FDA informed us that it has deferred action on the AT-GAA BLA, pending inspection of the proposed manufacturing site in China. The inspection has been delayed due to restrictions related to the COVID-19 pandemic and although now scheduled, we do not know whether the FDA will inspect when scheduled, whether the situation on the ground in China will change, nor the outcome of those inspections. Significant delays in the timing of our clinical trials and in regulatory reviews could adversely affect our ability to commercialize some assets in our product pipeline. Lack of normal access by patients to the healthcare system, along with concern about the continued supply of medications, may result in changes in buying patterns throughout the supply chain, including by patients, which could increase or decrease demand for our products. COVID-19 could also have an adverse impact on our supply chain and distribution systems, which could impact our ability to distribute our products and the ability of third parties on which we rely to fulfill their obligations to us, increase our expenses and have a material adverse effect on our ability to generate revenue. In addition, the conditions created by the pandemic may intensify other risks inherent in our business, including, among other things, risks related to drug pricing and access, intellectual property protection, product safety and efficacy concerns, product liability and other litigation, and the impact of adverse global and local economic conditions.

**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, Daphne Quimi, our Chief Financial Officer, and John F. Crowley, our Executive Chairman, each of whom has significant pharmaceutical industry experience. The loss of the services of any 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, including for our Global Headquarters in Philadelphia. 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 nor 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, 2022, we had 484 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 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 biologics and gene therapy manufacturing expertise; 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 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 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; or
- laws that require the reporting of financial information or data accurately.

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, 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 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 and mitigation strategies and which is reported 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 and reports 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.

***Our business and reputation may be adversely affected by environmental, social and governance matters.***

Companies are being increasingly judged by not just their financial performance, but also by their performance on a variety of environmental, social and governance (“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, 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. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation with 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.

**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 in our operations, it could result in a material disruption of our commercialization of our product 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.

***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, such as our acquisition of Celenex in 2018 and license agreement with Penn in 2022. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, 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 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. 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 (including the COVID-19 pandemic) 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, 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. For example, 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 the Company's operations and supply chain.

Further, military conflicts or wars (such as the ongoing conflict between Russia and Ukraine) 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 product 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;
- 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 a Form S-8 registration statement 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 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 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. Finally, 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.

***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 product 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 2. PROPERTIES

The following table contains information about our current significant leased properties as of December 31, 2022.

| Location | Approximate Square Feet | Use | Lease expiry date [1] |
|---|---|---|---|
| Philadelphia, Pennsylvania, U.S. | 50,816 | Office and laboratory | September 2044 |
| 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, 2023 was $12.64 per share. As of February 13, 2023, there were 19 holders of record of our common stock.

**Dividends**

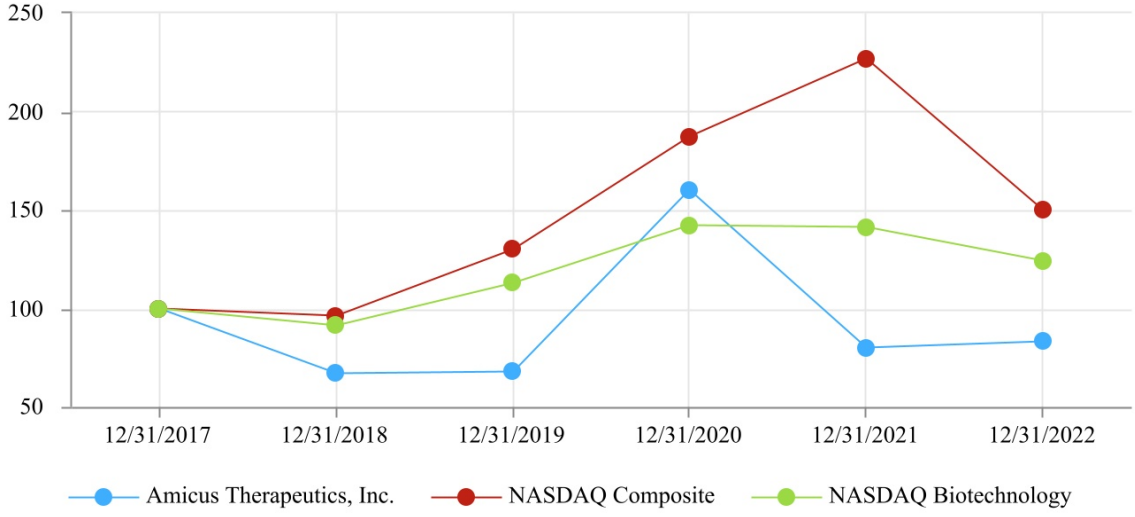
We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance the development and growth of our business. We do not intend to declare or pay cash dividends to our stockholders in the foreseeable future.

**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.




| | 12/31/2017 | 12/31/2018 | 12/31/2019 | 12/31/2020 | 12/31/2021 | 12/31/2022 |
|---|---|---|---|---|---|---|
| **Amicus Therapeutics, Inc.** | $100 | $67 | $68 | $160 | $80 | $83 |
| **NASDAQ Composite** | $100 | $96 | $130 | $187 | $227 | $150 |
| **NASDAQ Biotechnology** | $100 | $91 | $113 | $142 | $141 | $124 |

*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, 2022:

| 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, 2022 through October 31, 2022 | 21,092 | $ 10.56 | — | |
| November 1, 2022 through November 30, 2022 | 11,920 | $ 11.45 | — | |
| December 1, 2022 through December 31, 2022 | 3,090 | $ 12.13 | — | |
| Total | 36,102 | $ 10.99 | — | |

[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 have a portfolio including the first, oral monotherapy for Fabry disease that has achieved widespread global approval and a differentiated biologic for Pompe disease that is under review with the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA"), and the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA"). We are committed to discovering and developing next generation therapies in Fabry and Pompe diseases.

The cornerstone of our portfolio is Galafold® (also referred to as "migalastat"), the first and only approved oral precision medicine for people living with Fabry disease who have amenable genetic variants. Migalastat is currently approved under the trade name Galafold® in the United States ("U.S."), European Union ("E.U."), U.K., and Japan, with multiple additional approvals granted and applications pending in several geographies around the world.

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, two-component, potential best-in-class treatment for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. In September 2021, the FDA set the Prescription Drug User Fee Act ("PDUFA") target action date of May 29, 2022 for the New Drug Application ("NDA") for miglustat and July 29, 2022 for the Biologics License Application ("BLA") for cipaglucosidase alfa. The EMA validated the Marketing Authorization Application (“MAA”) in the fourth quarter of 2021. In May 2022, the FDA extended the review period for the NDA for miglustat and the BLA for cipaglucosidase alfa resulting in revised PDUFA action dates of August 29, 2022 and October 29, 2022, respectively. In October 2022, the FDA deferred action on the BLA for cipaglucosidase alfa, citing the inability to complete the manufacturing facility inspection prior to the PDUFA action date. We are actively engaged with the FDA and an inspection has been scheduled. In December 2022, the Committee for Medicinal Products for Human Use ("CHMP") of the EMA adopted a positive opinion recommending market authorization of cipaglucosidase alfa, or Pombiliti™. The regulatory submission process for AT-GAA in the U.K. was initiated in December 2022.

We continue to monitor the novel coronavirus ("COVID-19") pandemic. Our commercial operations have not been significantly impacted by the COVID-19 pandemic and we gradually continue to see an improvement in patient identification and Galafold® initiation. We have maintained operations in all geographies, secured our global supply chain for our commercial and clinical products, as well as maintained the operational integrity of our clinical trials, with minimum disruptions. We have been able to continue to meet required commercial demand for Galafold® as well as supply our ongoing Pompe disease clinical studies and access programs including the Early Access to Medicines Scheme ("EAMS") without interruption. In regard to our regulatory operations, the FDA deferred action on the pending BLA for cipaglucosidase alfa, as a facility inspection was necessary, however, could not be completed by the PDUFA action date due to COVID-19 related travel restrictions. The facility inspection has subsequently been scheduled. Per FDA guidance relating to pre-approval inspections during the COVID-19 pandemic, receipt of a deferral action indicates no deficiencies have been identified and the application otherwise satisfies the requirements for approval.

**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 2022 and 2021 items and year-to-year comparisons between 2022 and 2021. Discussions of 2020 items and year-to-year comparisons between 2021 and 2020 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, 2021, which comparisons are hereby incorporated by reference.

***Year Ended December 31, 2022 Compared to Year Ended December 31, 2021***

The following table provides selected financial information for the Company:

| | Years Ended December 31, | | |
|---|---|---|---|
| **(in thousands)** | **2022** | **2021** | **Change** |
| Net product sales | $ 329,233 | $ 305,514 | $ 23,719 |
| Cost of goods sold | 38,599 | 34,466 | 4,133 |
| Cost of goods sold as a percentage of net product sales | 11.7 % | 11.3 % | 0.4 % |
| Operating expenses: | | | |
| Research and development | 276,677 | 272,049 | 4,628 |
| Selling, general, and administrative | 213,041 | 192,710 | 20,331 |
| Changes in fair value of contingent consideration payable | 1,078 | 6,514 | (5,436) |
| Loss on impairment of assets | 6,616 | — | 6,616 |
| Depreciation and amortization | 5,342 | 6,209 | (867) |
| Other income (expense): | | | |
| Interest income | 3,024 | 509 | 2,515 |
| Interest expense | (37,119) | (32,471) | (4,648) |
| Loss on extinguishment of debt | — | (257) | 257 |
| Other income (expense) | 4,176 | (2,901) | 7,077 |
| Income tax benefit (expense) | 5,471 | (8,906) | 14,377 |
| Net loss attributable to common stockholders | $ (236,568) | $ (250,460) | $ 13,892 |

*Net Product Sales.* Net product sales increased $23.7 million during the year ended December 31, 2022 compared to the prior year. The increase was primarily due to continued growth in the U.S., Europe, and Japan markets, partially offset by the $26.1 million unfavorable impact of foreign currency exchange.

*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*** | **2022** | **2021** |
| Third-party direct project expenses | | |
| Galafold® (Fabry Disease) | $ 15,012 | $ 10,694 |
| AT-GAA (Pompe Disease) | 99,584 | 108,969 |
| Gene therapy programs | 48,948 | 47,817 |
| Pre-clinical and other programs | 124 | 872 |
| Total third-party direct project expenses | 163,668 | 168,352 |
| Other project costs | | |
| Personnel costs | 82,386 | 73,082 |
| Other costs | 30,623 | 30,615 |
| Total other project costs | 113,009 | 103,697 |
| Total research and development costs | $ 276,677 | $ 272,049 |

The $4.6 million increase in research and development expense was primarily due to an increase in personnel share-based compensation and Fabry disease clinical research. These costs were partially offset by a decrease in Pompe disease clinical research due to active studies nearing completion and the timing of manufacturing costs.

*Selling, General, and Administrative Expense.* Selling, general, and administrative expense increased $20.3 million, primarily driven by the strategic prioritization of our gene therapy portfolio that resulted in the write-off of cloud computing costs and software licensing fees, as well as increases in share-based compensation, marketing, and travel to support our organizational growth. These costs were partially offset by a reduction in third-party professional fees.

*Changes in Fair Value of Contingent Consideration Payable.* Changes in fair value of contingent consideration payable decreased $5.4 million, primarily due to achievement of two regulatory milestones during the year ended December 31, 2021, as well as changes to certain valuation inputs resulting from the strategic prioritization of our gene therapy portfolio during the year ended December 31, 2022.

*Loss on Impairment of Assets.* In connection with the strategic prioritization of our gene therapy portfolio, the Company performed an assessment of its assets and recognized a $6.6 million loss on impairment of assets.

*Interest Expense.* Interest expense increased $4.6 million during the year ended December 31, 2022. The increase was due to a higher LIBOR year over year.

*Other Income (Expense).* The $7.1 million variance was primarily related to foreign exchange gains caused by local currency remeasurement of U.S. dollar balances.

*Income Tax Benefit.* The income tax benefit for the year ended December 31, 2022 was $5.5 million. We are subject to income taxes in various jurisdictions but due to the offset of taxable income with net operating losses and full valuation allowance, there is nominal tax expense in 2022 for taxes in U.S. federal and state jurisdictions.

**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 primarily consist of sales of Galafold® for the treatment of Fabry disease. We have recorded revenue on sales where Galafold® is available either on a commercial basis or through a reimbursed early access program. Orders for Galafold® are generally received from distributors and pharmacies with the ultimate payor often a government authority.

We recognize revenue when our performance obligation with our customers have been satisfied, which occurs at a point in time when the pharmacies or distributors obtain control of Galafold®. The transaction price is determined based on fixed consideration in our customer contracts and is recorded net of estimates for variable consideration, which are primarily third-party discounts and rebates. The identified variable consideration is recorded as a reduction of revenue at the time revenue from the sale of Galafold® is recognized. 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.

***Research and Development Expenses***

As part of the process of preparing our Consolidated Financial Statements, we are required to estimate and accrue our research and development expenses, including those related to clinical studies and drug manufacturing. This process involves reviewing contracts and purchase orders, identifying services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs.

Costs for preclinical studies, clinical studies and manufacturing activities are recognized based on an evaluation of our vendors' progress towards completion of specific tasks, using data such as clinical site activations, clinical site maintenance, clinical site close out, patient out of pocket cost reimbursements, or information provided to us by our vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services were performed. We determine accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or state of completion of studies, or the services completed. Our estimates of accrued expenses as of each balance sheet date are based on the facts and circumstances known at the time. Costs that are paid in advance of performance are deferred as a prepaid expense and amortized over the service period as the services are provided.

***Share-based Compensation***

*Stock Option Grants*

In accordance with the applicable accounting guidance, we estimate the fair value of each equity award on the day of grant. We 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.

We use 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 our historical volatility since our initial public offering in May 2007. We determine the average expected life using our 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 historical analysis of actual option forfeitures.

*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 on such date. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. We expense 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. In addition, certain of our share-based awards are market- and performance-based and dependent upon achieving certain goals. The related share-based compensation expense is determined based on the estimated fair value of the underlying shares on the date of grant and is recognized on a straight-line basis over the vesting term. With respect to performance-based awards, we estimate the probability that the performance conditions will be achieved.

***Intangible Assets and Goodwill***

We record goodwill in a business combination when the total consideration exceeds the fair value of the net tangible and identifiable intangible assets acquired. Purchased in-process research and development ("IPR&D") is accounted for as an indefinite lived intangible asset until the underlying project is completed, at which point the intangible asset will be accounted for as a definite lived intangible asset, or abandoned, at which point the intangible asset will be written off or partially impaired. Goodwill and indefinite lived intangible assets are assessed annually for impairment on October 1 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. A goodwill impairment loss, if any, is measured as the amount by which our single reporting unit's carrying value, including goodwill, exceeds its fair value. An IPR&D impairment loss, if any, is measured as the amount by which the carrying amount of the asset exceeds its fair value.

***Valuation of Contingent Consideration Payable***

Consideration for the Company’s acquisitions may include future payments that are contingent upon the occurrence of a particular event. For example, milestone payments might be based on the achievement of various regulatory approvals or future sales milestones. Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved, and the consideration is paid or becomes payable. Contingent consideration obligations in business acquisitions are recorded at fair value on the acquisition date.

The Company estimates the fair value of contingent consideration obligations through a probability weighted discounted cash flow valuation approach based on various assumptions and incorporating estimated success rates. Estimated payments are discounted using present value techniques to arrive at an estimated fair value at the balance sheet date. Each period we reassess the fair value of the contingent consideration payable and recognize changes within the Consolidated Statements of Operations. Changes in the fair value of the contingent consideration payable can result from changes in estimated probability adjustments with respect to regulatory approval, changes in the assumed timing of when milestones are likely to be achieved and changes in assumed discount periods and rates. Significant judgment is employed in determining the appropriateness of these assumptions each period. Accordingly, future business and economic conditions, as well as changes in any of the assumptions described in the accounting for business combinations above can materially impact the amount of contingent consideration expense that we record and, therefore, our results of operations in any given period.

**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®, 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, Galafold® 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 ("ATM") equity program, pursuant to which we may offer to sell shares of our common stock having an aggregate offering gross proceeds of up to $250.0 million. At December 31, 2022, no shares have been issued under the ATM equity program.

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, 2022, we had cash, cash equivalents, and marketable securities of $293.6 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, 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. 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 used in operations for the year ended December 31, 2021 was $202.5 million. The components of net cash used in operations included the net loss for the year ended December 31, 2021 of $250.5 million, and the net change in operating assets and liabilities of $28.9 million. The change in operating assets was primarily due to increases in accounts receivable of $8.2 million due to increased commercial sales of Galafold®, an increase in inventory of $7.8 million, and increase in prepaid and other current assets of $5.9 million to support commercial activities for Galafold®. The net cash used in operations was also impacted by an increase in accounts payable and accrued expenses of $7.4 million, mainly related to program expenses and support for the commercial activities of Galafold®, and a decrease due to payment of contingent consideration of $10.4 million associated with meeting certain regulatory milestones during the year.

***Net Cash Provided by Investing Activities***

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 investing activities for the year ended December 31, 2021 was $78.8 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash provided by investing activities reflects $424.0 million for the sale and redemption of marketable securities, partially offset by $341.4 million for the purchase of marketable securities and $3.9 million for capital expenditures.

***Net Cash (Used in) Provided by Financing Activities***

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.

Net cash provided by financing activities for the year ended December 31, 2021 was $212.1 million. Net cash provided by financing activities primarily reflects $199.8 million in net proceeds from the September 2021 private placement of securities, $19.2 million from the exercise of warrants and $10.2 million from the exercise of stock options, partially offset by $15.0 million from payments of employee withholding taxes related to restricted stock unit vesting.

**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 Pompe Enzyme Replacement Therapy ("ERT" or "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 these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates, including AT-GAA;
- the number and development requirements of other product candidates that we pursue;
- 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 product and product candidates, including AT-GAA;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl") and, if our regulatory applications are approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and AT-GAA;
- our ability to obtain reimbursement for Galafold® and, if our regulatory applications are approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®, and, if approved and applicable, AT-GAA;
- our ability to obtain market acceptance of Galafold® and, if our regulatory applications are approved, AT-GAA;

- 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 our 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 payments from any such collaborators;
- the extent to which our business could be adversely impacted by the effects of the novel coronavirus ("COVID-19") outbreak, including actions by us, governments, our customers, our suppliers, or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards;
- 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 the COVID-19 pandemic, business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

**Contractual Obligations and Commitments**

As of December 31, 2022, remaining maturities, including interest, on our Senior Secured Term Loan due 2026 was $517.7 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, 2022, our undiscounted cash liabilities for operating leases were $168.8 million, with maturities ranging up through fiscal 2044. Refer to “— Note 12. Leases,” 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, 2022, these purchase and manufacturing obligations totaled $62.4 million. 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, 2022 Consolidated Balance Sheets.

We have no off-balance sheet arrangements as of December 31, 2022 and 2021.

**Milestone Payments / Royalties**

*Callidus* - In connection with our acquisition of Callidus Biopharma, Inc. ("Callidus"), we may be obligated to make additional payments to the former stockholders of Callidus upon the achievement of certain clinical milestones of up to $35 million and regulatory milestones of up to $80 million set forth in the merger agreement, provided that the aggregate merger consideration shall not exceed $130 million. As of December 31, 2022, $20 million and $68 million remain outstanding, respectively. Refer to “— Note 10. Assets and Liabilities Measured at Fair Value,” to the Consolidated Financial Statements.

*Celenex* - In connection with our acquisition of Celenex, Inc. ("Celenex"), we may be obligated to pay up to an additional $10 million in connection with the achievement of certain development milestones, $220 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to $75 million in tiered sales milestone payments. Celenex has an exclusive license agreement with Nationwide Children's Hospital ("Nationwide Children's"). Under this license agreement, Nationwide Children's is eligible to receive development and sales-based milestones of up to $7.8 million for each product.

*University of Pennsylvania* - In connection with our license agreement with the University of Pennsylvania ("Penn"), Penn is eligible to receive up to an aggregate of $86.5 million for the achievement of certain milestones and royalty payments with respect to licensed products for each 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 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.

**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, corporate debt securities, 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 $0.5 million as of December 31, 2022. 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, 2022, we had a $400 million Senior Secured Term Loan due 2026 that bears interest at a rate equal to the 3-month LIBOR, subject to a 1% floor, plus 6.5% per year. We do not currently hedge our variable interest rate debt. The annual average variable interest rate for our variable rate debt as of December 31, 2022 was 8.5%. A hypothetical 100 basis point increase or decrease in the average interest rate on our variable rate debt would result in $4.1 million change in the interest expense as of December 31, 2022.

The Financial Conduct Authority has announced the intent to phase out the use of LIBOR by mid-2023. If LIBOR is discontinued, we may need to renegotiate the terms of the Senior Secured Term Loan due 2026 in order to replace LIBOR with an alternative standard. As a result, we may incur incremental costs in transitioning to a new standard, and interest rates on our current or future indebtedness may be adversely affected by the new standard. The potential effect of any such event on our cost of capital cannot yet be determined, but we do not expect it to have a material impact on our consolidated financial condition, results of operations, or cash flows.

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, 2022. 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, 2022, 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, 2022 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.

| | /s/ BRADLEY L. CAMPBELL | /s/ DAPHNE QUIMI |
|---|---|---|
| Dated March 1, 2023 | 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, 2022, 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, 2022, 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, 2022 and 2021, 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, 2022, and the related notes and our report dated March 1, 2023 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
March 1, 2023

## 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, 2022 and 2021, 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, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, 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, 2022, 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 March 1, 2023 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.

**Fair Value Measurement of the Contingent Consideration**

*Description of the Matter*

As described in Note 10 to the consolidated financial statements, the Company has a $21.4 million contingent consideration liability recorded as of December 31, 2022 representing the fair value of additional amounts that management believes are likely to be paid to the former stockholders of Callidus Biopharma, Inc. The determination of the recorded amount of the contingent consideration liabilities requires the Company to make significant estimates and assumptions.

We identified the measurement of the contingent consideration liability as a critical audit matter because auditing the Company's valuation of the contingent consideration liability involved complex and challenging auditor judgment as the inputs to such valuation, such as the estimated probability of achieving milestones, the assumed timing of milestones and the discount rates, are largely unobservable.

*How We Addressed the Matter in Our Audit*

To test the estimated fair value of the contingent consideration liability, we performed audit procedures that included testing the operating effectiveness of internal controls relating to management's fair value measurement of the contingent consideration liability including controls over the Company's model, significant assumptions, and data.

Our procedures also included, among others, assessing the terms of the arrangement, evaluating the methodology used, testing the significant assumptions discussed above and the completeness, accuracy and relevance of the underlying data used by management in its analysis. We also performed analyses of certain assumptions to assess the impact of changes in certain assumptions on the Company's determination of the fair value of the contingent consideration liability. Evaluating the assumptions also involved evaluating whether the assumptions used by management were consistent with external market data and evidence obtained in other areas of the audit.

/s/ Ernst & Young LLP

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

Iselin, New Jersey
March 1, 2023

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

| | December 31, | |
|---|---|---|
| | **2022** | **2021** |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 148,813 | $ 245,197 |
| Investments in marketable securities | 144,782 | 237,299 |
| Accounts receivable | 66,196 | 52,672 |
| Inventories | 23,816 | 26,818 |
| Prepaid expenses and other current assets | 40,209 | 34,848 |
| Total current assets | 423,816 | 596,834 |
| Operating lease right-of-use assets, net | 29,534 | 20,586 |
| Property and equipment, less accumulated depreciation of $22,281 and $19,882 at December 31, 2022 and 2021, respectively | 30,778 | 42,496 |
| In-process research & development | 23,000 | 23,000 |
| Goodwill | 197,797 | 197,797 |
| Other non-current assets | 19,242 | 24,427 |
| **Total Assets** | $ 724,167 | $ 905,140 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 15,413 | $ 21,513 |
| Accrued expenses and other current liabilities | 93,636 | 98,153 |
| Contingent consideration payable | 21,417 | 18,900 |
| Operating lease liabilities | 8,552 | 7,409 |
| Total current liabilities | 139,018 | 145,975 |
| Long-term debt | 391,990 | 389,357 |
| Operating lease liabilities | 51,578 | 43,363 |
| Deferred income taxes | 4,939 | 4,930 |
| Deferred reimbursements | 4,656 | 5,906 |
| Other non-current liabilities | 8,939 | 8,240 |
| Total liabilities | 601,120 | 597,771 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Common stock, $0.01 par value, 500,000,000 shares authorized, 281,108,273 and 278,912,800 shares issued and outstanding at December 31, 2022 and 2021, respectively | 2,815 | 2,808 |
| Additional paid-in capital | 2,664,744 | 2,595,419 |
| Accumulated other comprehensive (loss) gain: | | |
| Foreign currency translation adjustment | (11,989) | 5,251 |
| Unrealized loss on available-for-sale securities | (116) | (270) |
| Warrants | 83 | 83 |
| Accumulated deficit | (2,532,490) | (2,295,922) |
| Total stockholders' equity | 123,047 | 307,369 |
| **Total Liabilities and Stockholders' Equity** | $ 724,167 | $ 905,140 |

*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, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| Net product sales | $ 329,233 | $ 305,514 | $ 260,886 |
| Cost of goods sold | 38,599 | 34,466 | 31,044 |
| Gross profit | 290,634 | 271,048 | 229,842 |
| Operating expenses: | | | |
| Research and development | 276,677 | 272,049 | 308,443 |
| Selling, general, and administrative | 213,041 | 192,710 | 156,407 |
| Changes in fair value of contingent consideration payable | 1,078 | 6,514 | 3,144 |
| Loss on impairment of assets | 6,616 | — | — |
| Depreciation and amortization | 5,342 | 6,209 | 8,846 |
| Total operating expenses | 502,754 | 477,482 | 476,840 |
| Loss from operations | (212,120) | (206,434) | (246,998) |
| Other income (expense): | | | |
| Interest income | 3,024 | 509 | 3,226 |
| Interest expense | (37,119) | (32,471) | (22,425) |
| Loss on extinguishment of debt | — | (257) | (7,276) |
| Other income (expense) | 4,176 | (2,901) | (781) |
| Loss before income tax | (242,039) | (241,554) | (274,254) |
| Income tax benefit (expense) | 5,471 | (8,906) | (2,598) |
| **Net loss attributable to common stockholders** | $ (236,568) | $ (250,460) | $ (276,852) |
| Net loss attributable to common stockholders per common share — basic and diluted | $ (0.82) | $ (0.92) | $ (1.07) |
| Weighted-average common shares outstanding — basic and diluted | 289,057,198 | 271,421,986 | 258,867,380 |

*See accompanying Notes to Consolidated Financial Statements*

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

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Net loss | $ (236,568) | $ (250,460) | $ (276,852) |
| Other comprehensive (loss) gain: | | | |
| Foreign currency translation adjustment (loss) gain | (17,240) | (3,161) | 5,627 |
| Unrealized gain (loss) on available-for-sale securities | 154 | (85) | (225) |
| Other comprehensive (loss) gain | (17,086) | (3,246) | 5,402 |
| Comprehensive loss | $ (253,654) | $ (253,706) | $ (271,450) |

*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, 2019 | 255,417,869 | $ 2,598 | $ 2,227,225 | $ 12,387 | $ 2,825 | $ (1,768,610) | $ 476,425 |
| Stock options exercised, net | 5,233,672 | 52 | 42,230 | — | — | — | 42,282 |
| Vesting of restricted stock units, net of taxes | 1,411,920 | — | (10,028) | — | — | — | (10,028) |
| Share-based compensation | — | — | 49,151 | — | — | — | 49,151 |
| Unrealized loss on available-for-sale securities | — | — | — | — | (225) | — | (225) |
| Foreign currency translation adjustment | — | — | — | — | 5,627 | — | 5,627 |
| Net loss | — | — | — | — | — | (276,852) | (276,852) |
| 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 | 11,296,660 | 112 | 199,552 | 83 | — | — | 199,747 |
| Vesting of restricted stock units, net of taxes | 1,064,135 | — | (15,009) | — | — | — | (15,009) |
| Share-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) |
| Share-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 |

*See accompanying Notes to Consolidated Financial Statements*

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

| | Years Ended December 31, | | |
|---|---|---|---|
| | **2022** | **2021** | **2020** |
| **Operating activities** | | | |
| Net loss | $ (236,568) | $ (250,460) | $ (276,852) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Amortization of debt discount and deferred financing | 2,634 | 2,490 | 1,794 |
| Depreciation and amortization | 5,342 | 6,209 | 8,846 |
| Share-based compensation | 76,512 | 57,838 | 49,151 |
| Loss on extinguishment of debt | — | 257 | 7,276 |
| Non-cash changes in the fair value of contingent consideration payable | 1,078 | 6,514 | 3,144 |
| Foreign currency remeasurement loss | 6,121 | 3,565 | 5,471 |
| Non-cash deferred taxes | 9 | 34 | (155) |
| Asset impairment charges and other asset write-offs | 18,177 | — | 99 |
| Changes in operating assets and liabilities: | | | |
| Accounts receivable | (17,330) | (8,189) | (11,219) |
| Inventories | (5,343) | (7,790) | (4,639) |
| Prepaid expenses and other current assets | (6,194) | (5,919) | (8,766) |
| Accounts payable, accrued expenses, and other current liabilities | (6,377) | 7,430 | (10,610) |
| Other non-current assets and liabilities | (4,636) | (4,117) | 3,170 |
| Payment of contingent consideration | — | (10,353) | — |
| Net cash used in operating activities | $ (166,575) | $ (202,491) | $ (233,290) |
| **Investing activities** | | | |
| Sale and redemption of marketable securities | 335,926 | 424,043 | 354,826 |
| Purchases of marketable securities | (243,255) | (341,398) | (365,178) |
| Capital expenditures | (3,766) | (3,884) | (3,227) |
| Proceeds from sale of assets | 3,411 | — | — |
| Net cash provided by (used in) investing activities | $ 92,316 | $ 78,761 | $ (13,579) |
| **Financing activities** | | | |
| Proceeds from issuance of common stock from equity financing and pre-funded warrants, net of issuance costs | — | 199,750 | — |
| Payment of long-term debt | — | — | (155,249) |
| Proceeds from long-term debt, net of issuance costs | — | — | 385,929 |
| Payment of finance leases | (283) | (479) | (76) |
| Purchase of vested restricted stock units, net of taxes | (11,490) | (15,009) | (10,028) |
| Proceeds from stock options exercised, net | 4,310 | 10,228 | 42,282 |
| Proceeds from warrants exercised, net | — | 19,230 | — |
| Payment of contingent consideration | — | (1,647) | — |
| Net cash (used in) provided by financing activities | $ (7,463) | $ 212,073 | $ 262,858 |
| Effect of exchange rate changes on cash, cash equivalents, and restricted cash | $ (14,619) | $ (5,049) | $ 3,830 |
| **Net increase in cash, cash equivalents, and restricted cash** | (96,341) | 83,294 | 19,819 |
| Cash, cash equivalents, and restricted cash at the beginning of the year | 249,456 | 166,162 | 146,343 |
| **Cash, cash equivalents, and restricted cash at the end of the year** | $ 153,115 | $ 249,456 | $ 166,162 |

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| **Supplemental disclosures of cash flow information** | | | |
| Tenant improvements paid through lease incentive | $ — | $ 300 | $ 470 |
| Cash paid during the period for interest | $ 34,358 | $ 30,468 | $ 24,683 |
| Capital expenditures unpaid at the end of period | $ 1,141 | $ 1,448 | $ 985 |
| Cash paid for income taxes | $ 1,609 | $ 20,032 | $ 10,371 |

*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 has a portfolio including the first, oral monotherapy for Fabry disease that has achieved widespread global approval and a differentiated biologic for Pompe disease, that is under review with the U.S. Food and Drug Administration ("FDA"), European Medicines Agency ("EMA"), and the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA"). The Company is committed to discovering and developing next generation therapies in Fabry and Pompe diseases.

The cornerstone of the Company's portfolio is Galafold® (also referred to as "migalastat"), the first and only approved oral precision medicine for people living with Fabry disease who have amenable genetic variants. Migalastat is currently approved under the trade name Galafold® in the United States ("U.S."), European Union ("E.U."), U.K., and Japan, with multiple additional approvals granted and applications pending in several geographies around the world.

The lead biologics program of the Company's pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, two-component, potential best-in-class treatment for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. In September 2021, the FDA set the Prescription Drug User Fee Act ("PDUFA") target action date of May 29, 2022 for the New Drug Application ("NDA") for miglustat and July 29, 2022 for the Biologics License Application ("BLA") for cipaglucosidase alfa. The EMA validated the Marketing Authorization Application (“MAA”) in the fourth quarter of 2021. In May 2022, the FDA extended the review period for the NDA for miglustat and the BLA for cipaglucosidase alfa resulting in revised PDUFA action dates of August 29, 2022 and October 29, 2022, respectively. In October 2022, the FDA deferred action on the BLA for cipaglucosidase alfa, citing the inability to complete the manufacturing facility inspection prior to the PDUFA action date. The Company is actively engaged with the FDA and an inspection has been scheduled. In December 2022, the Committee for Medicinal Products for Human Use ("CHMP") of the EMA adopted a positive opinion recommending market authorization of cipaglucosidase alfa, or Pombiliti™. The regulatory submission process for AT-GAA in the U.K. was initiated in December 2022.

The Company continues to monitor the novel coronavirus (“COVID-19”) pandemic. The Company's commercial operations have not been significantly impacted by the COVID-19 pandemic and the Company gradually continues to see an improvement in patient identification and Galafold® initiation. The Company has maintained operations in all geographies, secured its global supply chain for its commercial and clinical products, as well as maintained the operational integrity of its clinical trials, with minimum disruptions. The Company has been able to continue to meet required commercial demand for Galafold® as well as supply its ongoing Pompe disease clinical studies and access programs including the Early Access to Medicines Scheme ("EAMS") without interruption. In regard to the Company’s regulatory operations, the FDA deferred action on the pending BLA for cipaglucosidase alfa, as a facility inspection was necessary, however, could not be completed by the PDUFA action date due to COVID-19 related travel restrictions. The facility inspection has subsequently been scheduled. Per FDA guidance relating to pre-approval inspections during the COVID-19 pandemic, receipt of a deferral action indicates no deficiencies have been identified and the application otherwise satisfies the requirements for approval.

The Company had an accumulated deficit of $2.5 billion as of December 31, 2022 and anticipates incurring losses through the fiscal year ending December 31, 2023. The Company has historically funded its operations through stock offerings, Galafold® revenues, debt issuances, collaborations, and other financing arrangements.

Based on its current operating model, the Company believes that 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 impacts of the COVID-19 pandemic, business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact the Company's future 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.

***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 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.

***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.

Additionally, the Company assessed the impact the COVID-19 pandemic had on its operations and financial results as of December 31, 2022 and through the issuance of these financial statements. The Company’s analysis was informed by the facts and circumstances as they were known to the Company. This assessment considered the impact COVID-19 may have on financial estimates and assumptions that affect the reported amounts of assets and liabilities and revenue and expenses.

***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 (loss) gain 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 in other current assets and 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 related to its product sales of Galafold®. The Company's accounts receivable at December 31, 2022 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, 2022, 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 charged to income in the period in which the costs are 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’s net product sales consist primarily of sales of Galafold® for the treatment of Fabry disease. Galafold® sales for the years ended December 31, 2022, 2021 and 2020 were $329.0 million, $305.5 million and $260.9 million, respectively. The Company has recorded revenue on sales where Galafold® is available either on a commercial basis or through a reimbursed early access program. Orders for Galafold® are generally received from distributors and pharmacies, with the ultimate payor often a government authority. In 2022, one customer accounted for 27% of net product sales and 14% of accounts receivable from product sales. In 2021, one customer accounted for 24% 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 Galafold®. 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 are third party discounts and rebates. The identified variable consideration is recorded as a reduction of revenue at the time revenue from the sale of Galafold® 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 geographic area:

| (in thousands) | For the Year 2022 | 2021 | 2020 |
|---|---|---|---|
| U.S. | $ 115,946 | $ 95,387 | $ 80,046 |
| Ex-U.S. | 213,287 | 210,127 | 180,840 |
| Total net product sales | $ 329,233 | $ 305,514 | $ 260,886 |

***Inventories and Cost of Goods Sold***

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 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.

***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 (Loss) Gain***

Components of other comprehensive (loss) gain include unrealized gains and losses on available-for-sale securities and (loss) gain 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 to the Company 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 Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments.

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, 2022, 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, unvested restricted stock units, and certain warrants would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same. See "— Note 15. Basic and Diluted Net Loss per Common Share" for further discussion on net loss per share.

***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 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 payment, 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. The short term and long term portions of the contingent consideration payable is shown on the Company's Consolidated Balance Sheets. The fair value of the contingent consideration payable will be determined each period end and the resulting change will be recorded on the Consolidated Statements of Operations.

***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. Purchased IPR&D is accounted for as an indefinite lived intangible asset until the underlying project is completed, at which point the intangible asset will be accounted for as a definite lived intangible asset, or abandoned, at which point the intangible asset will be written off or partially impaired. Goodwill and indefinite lived intangible assets are 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 or IPR&D impairment test is conducted. If it is determined the full carrying amount of IPR&D is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. 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. No indicators of impairment were noted during the years ended December 31, 2022 and 2021.

***Recent Accounting Developments***

The Company has evaluated recent accounting pronouncements and believes that none of them will have a material effect on the Company's Consolidated Financial Statements or related disclosures.

**3. Goodwill and Intangible Assets**

As of December 31, 2022, in connection with the acquisitions, the Company had goodwill of $197.8 million and IPR&D of $23.0 million, which are reported at fair value on the Company's Consolidated Balance Sheets. Intangible assets related to IPR&D assets are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. During the period the assets are considered indefinite-lived, they will not be amortized but will be tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D assets below their respective carrying amounts.

Goodwill and intangible assets are assessed annually for impairment on October 1 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. A goodwill impairment loss, if any, is measured as the amount by which the Company's single reporting unit's carrying value, including goodwill, exceeds its fair value. An IPR&D impairment loss, if any, is measured as the amount by which the carrying amount of the asset exceeds its fair value.

The following table represents the changes in IPR&D for the years ended December 31, 2022 and 2021, respectively:

| | (in millions) |
|---|---|
| Balance at December 31, 2020 | $ 23.0 |
| Change in IPR&D | — |
| Balance at December 31, 2021 | $ 23.0 |
| Change in IPR&D | — |
| Balance at December 31, 2022 | $ 23.0 |

The following table represents the changes in Goodwill for the years ended December 31, 2022 and 2021, respectively:

| | (in millions) |
|---|---|
| Balance at December 31, 2020 | $ 197.8 |
| Change in goodwill | — |
| Balance at December 31, 2021 | $ 197.8 |
| Change in goodwill | — |
| Balance at December 31, 2022 | $ 197.8 |

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

As of December 31, 2022, the Company held $148.8 million in cash and cash equivalents and $144.8 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 (loss) gain 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 earnings 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 earnings.

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 many of these securities are either government backed or of the highest 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, 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 |
| Certificate 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 |

| | As of December 31, 2021 | | | |
|---|---|---|---|---|
| (in thousands) | Cost | Gross Unrealized Gain | Gross Unrealized Loss | Fair Value |
| Cash and cash equivalents | $ 245,197 | $ — | $ — | $ 245,197 |
| Commercial paper | 174,578 | 7 | (54) | 174,531 |
| Corporate debt securities | 32,322 | — | (11) | 32,311 |
| Asset-backed securities | 30,070 | — | (14) | 30,056 |
| Money market | 350 | — | — | 350 |
| Certificate of deposit | 51 | — | — | 51 |
| | $ 482,568 | $ 7 | $ (79) | $ 482,496 |
| Included in cash and cash equivalents | $ 245,197 | $ — | $ — | $ 245,197 |
| Included in marketable securities | 237,371 | 7 | (79) | 237,299 |
| Total cash, cash equivalents, and marketable securities | $ 482,568 | $ 7 | $ (79) | $ 482,496 |

For both the years ended December 31, 2022 and 2021, there were no realized gains or losses. The cost of securities sold is based on the specific identification method.

The Company had no marketable securities in an unrealized loss position as of December 31, 2022. Unrealized loss positions in the marketable securities as of December 31, 2021 reflect temporary impairments and were not a result of credit loss. Additionally, as these positions were in a loss position for less than twelve months and the Company did not intend to sell these securities before recovery, the losses were recognized in other comprehensive (loss) gain. The fair value of these marketable securities in unrealized loss positions was $173.4 million as of December 31, 2021.

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, 2022 | December 31, 2021 | December 31, 2020 |
|---|---|---|---|
| Cash and cash equivalents | $ 148,813 | $ 245,197 | $ 163,240 |
| Restricted cash | 4,302 | 4,259 | 2,922 |
| Cash, cash equivalents, and restricted cash shown in the Consolidated Statements of Cash Flows | $ 153,115 | $ 249,456 | $ 166,162 |

## 5. Inventories

Inventories consist of raw materials, work in process, and finished goods related to the manufacture of Galafold®. The following table summarizes the components of inventories:

| (in thousands) | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Raw materials | $ 10,054 | $ 12,289 |
| Work-in-process | 9,615 | 10,699 |
| Finished goods | 4,147 | 3,830 |
| Total inventories | $ 23,816 | $ 26,818 |

The Company's reserve for inventory was $0.4 million and $1.1 million as of December 31, 2022 and 2021, respectively.

## 6. Property and Equipment

Property and equipment consist of the following:

| (in thousands) | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Leasehold improvements | $ 24,162 | $ 24,168 |
| Research equipment | 16,345 | 16,663 |
| Computer equipment | 4,486 | 5,720 |
| Construction in progress | 4,160 | 8,229 |
| Furniture and fixtures | 2,734 | 3,163 |
| Computer software | 1,106 | 1,174 |
| Vehicles | 66 | 71 |
| Land | — | 3,190 |
| Gross property and equipment | 53,059 | 62,378 |
| Less accumulated depreciation | (22,281) | (19,882) |
| Net property and equipment | $ 30,778 | $ 42,496 |

Depreciation expense was $4.8 million and $5.7 million for the years ended December 31, 2022 and 2021, respectively. Additionally, during the year ended December 31, 2022, in connection with the strategic prioritization 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, 2022 | December 31, 2021 |
|---|---|---|
| Accrued compensation and benefits | $ 25,701 | $ 24,258 |
| Accrued sales rebates and discounts | 21,886 | 15,989 |
| Accrued program fees | 10,515 | 13,294 |
| Accrued contract manufacturing & contract research costs | 8,230 | 20,361 |
| Accrued royalties | 6,908 | 4,522 |
| Accrued professional fees | 6,868 | 9,377 |
| Accrued taxes | 5,938 | 6,154 |
| Other | 7,590 | 4,198 |
| | $ 93,636 | $ 98,153 |

## 8. Stockholders' Equity

***Common Stock and Warrants***

As of December 31, 2022, 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 ("ATM") equity 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. At December 31, 2022, no shares have been issued under the ATM equity program.

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.

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.

During the first and third quarters of 2021, the Company entered into separate, privately negotiated exchange agreements with the holders of the Convertible Notes (the "Holders"). Under the terms of the exchange agreements, the Holders agreed to exchange the remaining aggregate principal amount of $2.8 million of Convertible Notes held by them in exchange for an aggregate of approximately 472,356 shares of Company common stock, par value $0.01 per share. This transaction resulted in an increase of $2.7 million and five thousand dollars to additional paid-in-capital and common stock, respectively.

***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 $5.5 million and $4.8 million as of December 31, 2022 and 2021, 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, 2022, the Company has reserved up to 15,472,672 shares for issuance under the Plan.

**9. Share 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 Company's historical volatility. 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 voluntary termination behavior, as well as a historical analysis of actual option forfeitures.

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

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Expected stock price volatility | 62.1 % | 65.4 % | 75.1 % |
| Risk free interest rate | 1.7 % | 0.6 % | 1.6 % |
| Expected life of options (years) | 5.34 | 5.40 | 5.67 |
| Expected annual dividend per share | $ — | $ — | $ — |

The weighted average grant-date fair value per share of options granted during 2022, 2021, and 2020 were $6.11, $9.08, and $6.40, respectively.

A summary of the Company's stock options for the year ended December 31, 2022 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, 2019 | 16,724 | $ 9.15 | | |
| Granted | 4,362 | $ 9.98 | | |
| Exercised | (5,243) | $ 8.11 | | |
| Forfeited | (1,376) | $ 10.42 | | |
| Expired | (435) | $ 13.33 | | |
| 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 | 6.6 | $ 36.7 |
| Vested and unvested expected to vest, December 31, 2022 | 17,492 | $ 11.22 | 6.4 | $ 35.1 |
| Exercisable at December 31, 2022 | 10,938 | $ 10.59 | 5.0 | $ 29.0 |

The aggregate intrinsic value of options exercised during the years ended December 31, 2022, 2021 and 2020 was $2.5 million, $8.5 million, and $40.9 million, respectively. Cash proceeds from stock options exercised during the years ended December 31, 2022, 2021, and 2020 were $4.3 million, $10.2 million, and $42.3 million, respectively. As of December 31, 2022, the total unrecognized compensation cost related to non-vested stock options granted was $31.1 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, 2022 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, 2019 | 5,792 | $ 11.18 | | |
| Granted | 4,692 | $ 11.29 | | |
| Vested | (2,164) | $ 10.70 | | |
| Forfeited | (1,240) | $ 11.14 | | |
| 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 | 2.1 | $ 118.6 |

As of December 31, 2022, there was $50.4 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 Consolidated Statements of Operations related to the equity awards:

| | Years Ended December 31, | | |
|---|---|---|---|
| (in thousands) | 2022 | 2021 | 2020 |
| Research and development expense | $ 25,089 | $ 17,340 | $ 20,817 |
| Selling, general, and administrative expense | 51,423 | 40,498 | 28,334 |
| Total equity compensation expense | $ 76,512 | $ 57,838 | $ 49,151 |

**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, 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 |

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, 2021 are identified in the following tables:

| (in thousands) | Level 2 | Total |
|---|---|---|
| ***Assets:*** | | |
| Commercial paper | $ 174,531 | $ 174,531 |
| Corporate debt securities | 32,311 | 32,311 |
| Asset-backed securities | 30,056 | 30,056 |
| Money market | 5,150 | 5,150 |
| | $ 242,048 | $ 242,048 |

| (in thousands) | Level 2 | Level 3 | Total |
|---|---|---|---|
| ***Liabilities:*** | | | |
| Contingent consideration payable | $ — | $ 20,339 | $ 20,339 |
| Deferred compensation plan liability | 4,800 | — | 4,800 |
| | $ 4,800 | $ 20,339 | $ 25,139 |

The Company's Senior Secured Term Loan due 2026 falls into the Level 2 category within the fair value level hierarchy and the fair value was determined using quoted prices for similar liabilities in active markets, as well as inputs that are observable for the liability (other than quoted prices), such as interest rates that are observable at commonly quoted intervals. The carrying value of the Senior Secured Term Loan due 2026 approximates the fair value.

The Company did not have any Level 3 assets as of December 31, 2022 or 2021.

***Cash, Money Market Funds and Marketable Securities***

The Company classifies its cash 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 and the money market funds 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, 2022. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2022.

***Contingent Consideration Payable***

The contingent consideration payable resulted from the acquisition of Callidus Biopharma, Inc. ("Callidus") in November 2013. The most recent valuation was determined using a probability weighted discounted cash flow valuation approach. Gains and losses are included in the Consolidated Statements of Operations.

The contingent consideration payable for Callidus has been classified as a Level 3 recurring liability as its valuation requires substantial judgment and estimation of factors that are not currently observable in the market. If different assumptions were used for the various inputs to the valuation approach, the estimated fair value could be significantly higher or lower than the fair value the Company determined.

The following significant unobservable inputs were used in the valuation of the contingent consideration payable of Callidus for the ATB200 Pompe disease program:

| Contingent Consideration Liability | Fair Value as of December 31, 2022 (in thousands) | Valuation Technique | Unobservable Input | Range |
|---|---|---|---|---|
| | | | Discount rate | 10.2% |
| Clinical and regulatory milestones | $ 21,417 | Probability weighted discounted cash flow | Probability of achievement of milestones | 88%-98% |
| | | | Projected year of payments | 2023 |

Contingent consideration liabilities are remeasured to fair value each reporting period using discount rates, probabilities of payment, and projected payment dates. Projected contingent payment amounts related to clinical and regulatory based milestones are discounted back to the current period using a discounted cash flow model. Increases in discount rates and the time to payment may result in lower fair value measurements. Increases or decreases in any of those inputs together, or in isolation, may result in a significantly lower or higher fair value measurement. There is no assurance that any of the conditions for the milestone payments will be met.

The Company reached a regulatory milestone in September 2021 associated with FDA approval of the first BLA and in November 2021 associated with EMA validation of the MAA, both related to the contingent consideration of Callidus for the ATB200 Pompe disease program. The satisfaction of these milestones resulted in the collective milestone payment of $12.0 million.

The following table shows the change in the balance of contingent consideration payable for the year ended December 31, 2022 and 2021, respectively:

| | Years ended December 31, | |
|---|---|---|
| **(in thousands)** | **2022** | **2021** |
| Balance, beginning of the period | $ 20,339 | $ 25,825 |
| Changes in fair value during the period, included in the Consolidated Statements of Operations | 1,078 | 6,514 |
| Payment of contingent consideration in cash | — | (12,000) |
| Balance, end of the period[1] | $ 21,417 | $ 20,339 |

[1] As certain milestones are expected to be reached within the next twelve months, the December 31, 2022 balance was recorded as a current liability in the Consolidated Balance Sheets.

## 11. Debt

The Company's debt consists of the following:

| **(in thousands)** | **December 31, 2022** | **December 31, 2021** |
|---|---|---|
| **Senior Secured Term Loan due 2026:** | | |
| Principal | $ 400,000 | $ 400,00 |
| Less: debt discount [1] | (4,571) | (6,07 |
| Less: deferred financing [1] | (3,439) | (4,56 |
| Net carrying value of Long-term debt | $ 391,990 | $ 389,35 |

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

***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 will 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. This transaction resulted in net proceeds of $385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. The Company used the proceeds to voluntarily settle the Senior Secured Term Loan with BioPharma Credit PLC, which included the $150 million principal, $1.1 million accrued interest, and $5.2 million in early settlement premiums. As a result of this early extinguishment, the Company recognized a loss on extinguishment of debt of $7.3 million in the Consolidated Statements of Operations.

The Senior Secured Term Loan due 2026 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 2026. The Company may prepay the Senior Secured Term Loan due 2026 in whole, at its option at any time. Any prepayment of the Senior Secured Term Loan due 2026 is subject to certain make-whole premiums and prepayment premiums, the latter of which decrease until the fourth anniversary of the transaction date at which point no prepayment penalty shall exist. The obligations under the Senior Secured Term Loan due 2026 are secured by a first lien security interest in certain assets of the Company. The Senior Secured Term Loan due 2026 contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to the Company. The Senior Secured Term Loan due 2026 also contains a minimum liquidity covenant of $75 million, and an incremental minimum consolidated revenue covenant, measured as of the previous four consecutive fiscal quarters. The minimum consolidated revenue covenant ranges from $140 million, beginning March 31, 2021, and peaks at $225 million by June 30, 2023, continuing at that level until the Senior Secured Term Loan due 2026 is repaid. If an event of default occurs and is continuing, Hayfin Capital Management may declare all amounts outstanding under the Senior Secured Term Loan due 2026 to be immediately due and payable.

***Interest Expense***

The following table sets forth interest expense recognized related to the Company's debt for the years ended December 31, 2022 and 2021, respectively:

| (in thousands, except interest rate amounts) | December 31, 2022 | December 31, 2021 |
|---|---|---|
| Contractual interest expense | $ 34,446 | $ 30,473 |
| Amortization of debt discount | $ 1,503 | $ 1,462 |
| Amortization of deferred financing | $ 1,131 | $ 1,028 |
| Effective interest rate of the liability component, Senior Secured Term Loan due 2026 | 12.1 % | 8.4 % |

**12. Leases**

The Company currently has operating leases for office and research laboratory space, equipment, and vehicles under agreements expiring at various dates through 2044, which include renewal options on leases which the Company is reasonably certain to exercise.

For the years ended December 31, 2022, and 2021, operating lease expense was $9.8 million and $10.0 million and variable lease expense was $1.7 million and $2.1 million, respectively. For the years ended December 31, 2022, and 2021, the Company paid $8.3 million and $8.4 million, respectively, for amounts included in the measurement of operating lease liabilities and recorded $8.9 million and $0.3 million, respectively, of right-of-use assets. For the year ended December 31, 2022, there were no tenant improvements paid through lease incentives in exchange for new operating lease liabilities. For the year ended December 31, 2021, there were $0.3 million of tenant improvements paid through lease incentives in exchange for new operating lease liabilities.

Commitments under finance leases are not significant for the year ended December 31, 2022.

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

| (in thousands, except year and discount rate amounts) | December 31, 2022 | December 31, 2 |
|---|---|---|
| Operating lease ROU assets, net | $ 29,534 | $ 20,586 |
| Current portion of the operating lease liabilities | $ 8,552 | $ 7,409 |
| Non-current portion of the operating lease liabilities | 51,578 | 43,363 |
| Total operating lease liability | $ 60,130 | $ 50,772 |
| Weighted-average remaining lease terms (years) | 17.0 | 1 |
| Weighted-average discount rate | 12.2 % | 13.1 |

At December 31, 2022, the future minimum operating lease payments were as follows:

| (in thousands) | Operating Lease |
|---|---|
| 2023 | $ 9,466 |
| 2024 | 8,624 |
| 2025 | 8,419 |
| 2026 | 8,571 |
| 2027 | 8,754 |
| Thereafter | 124,979 |
| Total lease payments | 168,813 |
| Less lease incentives | (22,299) |
| Less imputed interest | (86,384) |
| Total operating lease liability | $ 60,130 |

**13. Income Taxes**

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

| (in thousands) | Years Ended December 31, 2022 | 2021 | 2020 |
|---|---|---|---|
| United States | $ (343,424) | $ (333,571) | $ (365,332) |
| Foreign | 101,385 | 92,017 | 91,078 |
| Total | $ (242,039) | $ (241,554) | $ (274,254) |

Following were the components of income tax expense (benefit) for the years ended December 31, 2022, 2021, and 2020:

| (in thousands) | Years Ended December 31, 2022 | 2021 | 2020 |
|---|---|---|---|
| Current | | | |
| Federal | $ — | $ — | $ — |
| State | 6 | 15 | 11 |
| Foreign | (5,760) | 8,857 | 4,163 |
| Deferred | | | |
| Federal | 274 | — | (1,421) |
| State | 9 | 34 | (155) |
| Foreign | — | — | — |
| Total | $ (5,471) | $ 8,906 | $ 2,598 |

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2022, 2021, and 2020 are as follows:

| | Years Ended December 31, 2022 | 2021 | 2020 |
|---|---|---|---|
| Statutory rate | (21)% | (21)% | (21)% |
| Tax credits | (11) | (9) | (7) |
| Impact of foreign operations | 18 | 3 | 4 |
| Other | 3 | 3 | 2 |
| Valuation allowance | 9 | 28 | 23 |
| Net | (2)% | 4 % | 1 % |

On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act ("Tax Act"). The Tax Act significantly revises 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)** | **2022** | **2021** |
| Deferred tax assets | | |
| Intellectual property | $ 68,567 | $ 105,453 |
| Research tax credit | 223,366 | 205,095 |
| Capitalized research and development costs | 29,317 | — |
| Net operating loss carry forwards | 315,444 | 334,762 |
| Share-based compensation | 16,417 | 11,779 |
| Interest carry forward limitation | 12,558 | 8,285 |
| Lease liability | 11,428 | 9,105 |
| Inventory | 10,400 | — |
| Other | 20,109 | 17,748 |
| Gross deferred tax assets | 707,606 | 692,227 |
| Deferred tax liabilities | | |
| Business acquisition | (4,939) | (4,930) |
| Royalty payable | (68,567) | (105,453) |
| Other | (6,806) | (4,932) |
| Total net deferred tax assets | 627,294 | 576,912 |
| Less: valuation allowance | (632,233) | (581,842) |
| Net deferred tax liability | $ (4,939) | $ (4,930) |

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, 2022 and 2021, the Company recorded valuation allowances of $632.2 million and $581.8 million, respectively, representing an increase in the valuation allowance of $50.4 million in 2022, 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 IPR&D acquired by the Company. The Company's policy is to record a deferred tax liability related to acquired IPR&D 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, 2022, the Company had federal and state net operating loss carry forwards ("NOLs") of approximately $1,183 million and $992 million, 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. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2022 will expire in 2029 through 2040. 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 2022 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 research and experimentation and orphan drug credit carryforwards of approximately $36.4 million and $187.0 million, respectively, which will expire in the years 2030 through 2040. Deferred tax assets for these carryforwards are subject to a full valuation allowance.

**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.

The contingent milestone payments due to GSK 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, 2022, under the GSK collaboration agreements, the Company incurred approximately $25.1 million of royalty expenses. As of December 31, 2022, $7.4 million was recorded as deferred reimbursements and the Company recognized a liability of $6.9 million related to royalties payable to GSK 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 and will 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:

| (in thousands, except per share amounts) | Years Ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Numerator: | | | |
| Net loss attributable to common stockholders | $ (236,568) | $ (250,460) | $ (276,852) |
| Denominator: | | | |
| Weighted average common shares outstanding — basic and diluted | 289,057,198 | 271,421,986 | 258,867,380 |

Dilutive common stock equivalents would include the dilutive effect of outstanding common stock options, unvested RSUs, outstanding warrants for common stock equivalents, and convertible debt units. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect.

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:

| (in thousands) | Years ended December 31, | | |
|---|---|---|---|
| | 2022 | 2021 | 2020 |
| Options to purchase common stock | 19,064 | 14,731 | 14,032 |
| Unvested restricted stock units | 9,717 | 7,341 | 7,080 |
| Outstanding warrants, convertible to common stock | — | — | 2,555 |
| Convertible notes | — | — | 462 |
| Total number of potentially issuable shares | 28,781 | 22,072 | 24,129 |

**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, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of 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, 2022, 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, 2022 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.***

None.

**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 2023 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:

Management's Report on Consolidated Financial Statements and Internal Control over Financial Reporting
Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)
Consolidated Balance Sheets as of December 31, 2022 and 2021
Consolidated Statements of Operations for the years ended December 31, 2022, 2021, and 2020
Consolidated Statements of Comprehensive Loss for the years ended December 31, 2022, 2021, and 2020
Consolidated Statements of Changes in Stockholders' Equity for the years ended December 31, 2022, 2021, and 2020
Consolidated Statements of Cash Flows for the years ended December 31, 2022, 2021, and 2020
Notes To Consolidated Financial Statements

*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*

| Exhibit No. | Filed Exhibit Description | Incorporated by Reference to SEC Filing | | | Filed with this Form 10-K |
|---|---|---|---|---|---|
| | | Form | Date | Exhibit No. | |
| 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 | Amendment to Agreement and Plan of Merger, dated September 30, 2015, by and among the Registrant, Titan Merger Sub Corp. and Scioderm, Inc. | Form 8-K | 9/30/2015 | 2.2 | |
| +2.3 | 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 | |
| +2.4 | 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 | Restated By-laws of the Registrant. | S-1/A (333-141700) | 4/27/2007 | 3.4 | |
| 3.3 | Certificate of Amendment to the Registrant's Restated Certificate of Incorporation, as amended. | 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 | |

| 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 (333-141700) | 3/30/2007 | 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 | |
| 4.6 | Securities Purchase Agreement, dated September 29, 2021, by and between the Company and Perceptive Life Sciences Master Fund, Ltd. | Form 8-K | 9/29/2021 | 10.4 | |
| 4.7 | Securities Purchase Agreement, dated September 29, 2021, by and among the Company and the Purchasers identified on the signature pages thereto | Form 8-K | 9/29/2021 | 10.5 | |
| *10.1 | 2002 Equity Incentive Plan, as amended, and forms of option agreements thereunder | S-1/A (333-141700) | 4/27/2007 | 10.1 | |
| 10.2 | Form of Director and Officer Indemnification Agreement | 8-K | 12/28/2022 | 10.1 | |
| *10.3 | Amended and Restated 2007 Director Option Plan and form of option agreement | Form 8-K | 6/18/2010 | 10.2 | |
| 10.4 | 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 | |
| +10.5 | Second Restated Agreement, dated November 19, 2013 by and between the Registrant and Glaxo Group Limited | Form 10-K | 3/3/2014 | 10.46 | |
| *10.6 | Amicus Amicus Therapeutics, Inc. Amended and Restated Restricted Stock Unit Deferral Plan | Form 8-K | 12/28/2017 | 10.1 | |
| *10.7 | Amended and Restated 2007 Equity Incentive Plan | DEF 14A | 4/27/2021 | A | |
| *10.8 | Amicus Therapeutics, Inc. Cash Deferral Plan | Form 8-K | 10/28/2016 | 10.1 | |
| 10.9 | 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 | |
| 10.10 | Amendment #1 to the Amicus Therapeutics, Inc. Cash Deferral Plan. | Form 8-K | 10/26/2014 | 10.1 | |
| 10.11 | Amendment #2 to the Amicus Therapeutics, Inc. Cash Deferral Plan. | Form 8-K | 12/19/2019 | 10.1 | |
| *10.12 | Employment Agreement, dated August 1, 2022, by and between the Registrant and Bradley L. Campbell. | Form 8-K | 8/1/2022 | 10.1 | |
| *10.13 | Employment Agreement, dated February 23, 2022, by and between the Registrant and John F. Crowley. | Form 8-K | 2/24/2022 | 10.2 | |
| *10.14 | Employment Agreement dated February 18, 2020 between the Registrant and Ellen S. Rosenberg | Form 10-K | 3/2/2020 | 10.45 | |
| *10.15 | Employment Agreement dated February 18, 2020, between the Registrant and Daphne Quimi | Form 10-K | 3/2/2020 | 10.48 | |
| *10.16 | Employment Agreement dated February 18, 2020 between the Registrant and Hung Do | Form 10-K | 3/2/2020 | 10.49 | |

| Exhibit No. | Filed Exhibit Description | Incorporated by Reference to SEC Filing | | | Filed with this Form 10-K |
|---|---|---|---|---|---|
| | | Form | Date | Exhibit No. | |
| *10.17 | Amendment to Employment and Confidentiality Agreements dated September 28, 2021 by and between the Registrant and Hung Do. | Form 8-K | 9/29/2021 | 10.8 | |
| *10.18 | Employment Agreement dated February 18, 2020 between the Registrant and David Clark | | | | X |
| *10.19 | Employment Agreement dated February 18, 2020 between the Registrant and Jeffrey Castelli | | | | X |
| 10.20 | Loan Agreement, dated as of July 17, 2020, by and among Amicus Therapeutics International Holding Ltd, as Borrower, Amicus Therapeutics, Inc. as Parent and a Guarantor, certain subsidiaries of Parent as additional Guarantors, and Hayfin Services LLP as Agent for certain lenders | Form 10-Q | 8/10/2020 | 10.2 | |
| *10.21 | 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 | |
| *10.22 | Form of Board Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan | Form 10-K | 3/1/2021 | 10.41 | |
| *10.23 | Form of Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan | Form 10-K | 3/1/2021 | 10.42 | |
| *10.24 | Form of Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan | Form 10-K | 2/24/2022 | 10.25 | |
| ++10.25 | License Agreement dated December 22, 2022, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania | | | | X |
| ++10.26 | Mutual Termination Agreement dated December 22, 2022, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania. | | | | X |
| 21 | 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 |

| 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, 2021, 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, 2021 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.

++ Subject to confidential treatment request.

* Indicates management contract or compensatory plan.

** Certain confidential portions of this exhibit were omitted in accordance with Item 601(b)(10) of Regulation S-K.

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 March 1, 2023.

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<br>(Bradley L. Campbell) | President and Chief Executive Officer<br>(Principal Executive Officer) | March 1, 2023 |
| /s/ Daphne Quimi<br>(Daphne Quimi) | Chief Financial Officer<br>(Principal Financial Officer and Principle Accounting Officer) | March 1, 2023 |
| /s/ John F. Crowley<br>(John F. Crowley) | Executive Chairman | March 1, 2023 |
| /s/ Margaret G. McGlynn<br>(Margaret G. McGlynn) | Director | March 1, 2023 |
| /s/ Michael G. Raab<br>(Michael G. Raab) | Director | March 1, 2023 |
| /s/ Glenn Sblendorio<br>(Glenn Sblendorio) | Director | March 1, 2023 |
| /s/ Craig Wheeler<br>(Craig Wheeler) | Director | March 1, 2023 |
| /s/ Lynn Bleil<br>(Lynn Bleil) | Director | March 1, 2023 |

| Signature | Title | Date |
|---|---|---|
| /s/ Burke Whitman<br>(Burke Whitman) | Director | March 1, 2023 |
| /s/ Michael A. Kelly<br>(Michael A. Kelly) | Director | March 1, 2023 |
| /s/ Eiry W. Roberts, M.D.<br>(Eiry W. Roberts, M.D.) | Director | March 1, 2023 |

**EMPLOYMENT AGREEMENT**

**THIS EMPLOYMENT AGREEMENT** (this "Agreement"), dated as of February 18, 2020 (the "Effective Date"), between AMICUS THERAPEUTICS, INC., a Delaware corporation having an office at 6400 Sanger Road, Orlando FL 32827 (the "Company"), and David Clark, an individual residing at […], ("Employee") (together, the "parties").

**WHEREAS,** the Company wishes to **continue to** employ Employee, and Employee wishes to **continue to** be employed by Company, on the terms and conditions set forth herein;

**NOW, THEREFORE,** in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the sufficiency and receipt whereof is hereby acknowledged, the parties agree as follows:

Section 1. Definitions. Unless otherwise defined herein, the following terms shall have the following respective meanings:

"Accrued Amounts" means, as of the termination of Employee's employment:
(a) the total of any expenses properly incurred by Employee under Section 3.4(b) that have not previously been reimbursed as of the effective date of the termination; (b) the sum of
Employee's accrued, but unused, vacation time, if any, as of the effective date of the termination; and (c) any accrued and unpaid Base Salary through and including the effective date of
Employee's termination.

"Affiliate" shall mean any other company, directly or indirectly, controlling, controlled by or under common control with the Company.

"Cause" means Employee's: (i) willful or deliberate misconduct that has or could reasonably be expected to have a materially adverse impact on the reputation or business of the Company (or an Affiliate), or that results in gain or personal enrichment of Employee to the detriment of the Company (or an Affiliate); (ii) violation of Company policy including, but not limited to, policies prohibiting harassment and other workplace misconduct, and policies governing corporate compliance; (iii) misappropriation of the funds or assets of the Company (or an Affiliate); (iv) conviction, plea of guilty, admission to facts sufficient for a finding of guilt, or plea of no contest (or nolo contendere) to: (a) any felony, or (b) any misdemeanor involving fraud, theft, dishonesty, wrongful taking of property, embezzlement, bribery, forgery or extortion; (v) material breach of this Agreement; (vi) material breach of the Confidentiality, Non- Disclosure and Non-Competition Agreement attached as Exhibit A; (vii) breach of Employee's duty of loyalty to the Company; (viii) disqualification, bar or suspension by any governmental authority from performing any of the duties contemplated by this Agreement; (ix) material failure to perform Employee's duties or obligations hereunder (other than as a result of being Unable to Work); or (x) willful failure to adhere to or carry out lawful duties or directives of the Company's Chief Executive Officer ("CEO") or Board of Directors ("Board"). Notwithstanding anything to the contrary herein, the Company shall not be deemed to have terminated Employee for Cause for the events described above in subsections (ix) or (x) unless the CEO or Board, as

applicable, has determined that such events are amenable to cure and given Employee written notice of the occurrence of the claimed event(s) constituting Cause and Employee has failed to cure such event(s) within fourteen (14) calendar days after Employee's receipt of such notice (or such other period as may be deemed reasonable by the CEO or Board under the circumstances and communicated to Employee). The other events described above are not subject to an opportunity to cure but the Company may, in its sole discretion, conduct an investigation into those events and provide the employee a full opportunity to participate.

"Change in Control Event" means any of the following: (i) when any person or entity who is not currently a stockholder of the Company (as of the date of this Agreement) becomes the beneficial owner of greater than 50% of the then-outstanding voting power of the Company; (ii) when a merger or consolidation with another entity occurs that causes the voting securities of the Company outstanding immediately before the transaction to constitute less than a majority of the voting power of the voting securities of the Company or the surviving entity outstanding immediately after the transaction; or (iii) when a sale or disposition of all or substantially all of the Company's assets occurs. Notwithstanding the foregoing, no event shall be deemed to be a Change in Control Event unless such event would also be a Change in Control under Section 409A and the rules and regulations promulgated thereunder (collectively, "Section 409") of the Internal Revenue Code of 1986, as amended (the "Code") or would otherwise be a permitted distribution event under Section 409A.

"Change in Control Severance Benefits" means: (i) payment of an amount equal to one and one-half (1.5) times Employee's then current Base Salary, payable in installments over eighteen (18) months, commencing within sixty (60) calendar days after the resignation or termination (collectively, "termination') of Employee's employment with the Company, in accordance with the Company's customary payroll practices for its senior management personnel; (ii) payment of an amount equal to 100% of the target Bonus for the calendar year in which such termination occurs (such amount being payable in a lump sum), payable within seventy five (75) calendar days following such termination ; (iii) the accelerated vesting of stock options held by Employee immediately prior to such termination ("Options"), such that all Options will become vested as of the date of Employee's termination; (iv) the accelerated vesting of restricted stock grants held by Employee immediately prior to such termination ("Grants"), such that all Grants will become vested as of the date of Employee's termination; (v) the accelerated vesting of performance restricted stock units held by Employee immediately prior to such termination at the applicable performance targets or such greater amounts as determined by the Board of Directors in their sole discretion; and (vi) in the event that Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall remain eligible to continue their participation in such plans for a period of eighteen (18) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 18 month period. Notwithstanding any other provision of this Agreement, Employee's receipt of Change in Control Severance Benefits is conditioned on Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company.

Employee's Initials /s/DC

"Good Reason" means the occurrence of one or both of the following events without Employee's consent: (i) the Company's material diminution of Employee's authority, duties, or responsibilities as set forth in this Agreement; or (ii) the Company's change in the principal geographic location at which Employee provides services to the Company to a location more than thirty (30) miles from Employee's assigned primary office location, unless such relocation is only temporary, for a reasonable period of time, or unless such relocation merely constitutes travel reasonably required in connection with the performance of Employee's duties. Notwithstanding anything to the contrary herein, Employee shall not be deemed to have resigned for Good Reason unless: (a) Employee had provided to the Company written notice within thirty (30) calendar days of the occurrence of the claimed event(s) constituting Good Reason, specifying in detail the basis for such Good Reason; (b) the Company fails to cure the Good Reason within thirty (30) calendar days after its receipt of such notice, and (c) Employee terminates employment within sixty (60) calendar days after providing notice to Company of the claimed event(s) constituting Good Reason.

"Severance Benefits" means (i) payment of an amount equal to Employee's then current Base Salary, payable in installments over twelve (12) months, commencing within sixty (60) calendar days of the termination of Employee's employment with the Company, in accordance with the Company's customary payroll practices then in effect for its senior management personnel; (ii) payment of a bonus equal to 100% of the target Bonus for the calendar year in which such termination occurs pro-rated for the number of days actually worked in the year of termination, payable within seventy five (75) calendar days following such termination; (iii) the accelerated vesting of the Options, such that the portion of the Options that was otherwise scheduled to vest during the twelve (12) month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; (iv) the accelerated vesting of RSUs, such that the portion of RSUs that was otherwise scheduled to vest during the twelve (12) month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; (v) the accelerated vesting of PRSUs, such that the portion of PRSUs that was otherwise scheduled to vest during the twelve month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; and (vi)in the event that Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall remain eligible to continue their participation in such plans for a period of twelve (12) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 12 month period.
Notwithstanding any other provision of this Agreement, Employee's receipt of Severance Benefits is conditioned on Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company.

"Unable to Work" means the determination by the Company, following an interactive process, that Employee has become physically or mentally incapable of performing

Employee's essential job functions, with or without a reasonable accommodation, following any period during which such status would be protected under applicable law.

Section 2. Employment.

2.1. Duties and Responsibilities. Subject to the terms and conditions of this Agreement, Employee will be employed by the Company as Chief People Officer or in such other position as may be mutually agreed upon by the parties. A Job Description setting forth Employee's duties and responsibilities is attached as Exhibit C. Employee accepts such employment, and agrees to perform all of the duties and accept all of the responsibilities accompanying such position. Employee agrees to serve the Company faithfully and to the best
of Employee's abilities, and to devote all of Employee's business time, skill and attention to such service. Employee is expected to be available for meetings on a regular basis, upon request by the Company, at the Company's Cranbury, New Jersey, and Philadelphia, Pennsylvania, locations or such other Company locations as needed including, but not limited to, the Company's international offices.

2.2. Full Time and Attention. Employee shall devote Employee's full business time and best efforts to the performance of Employee's duties and to the furtherance of the Company's interests. During Employee's employment with the Company, Employee may not hold another position of employment, or be retained as a consultant, or engage in any other business activity (whether full-time or part-time, whether or not for compensation), unless the Company gives Employee prior written permission to do so. Notwithstanding anything stated in this provision to the contrary, Employee is permitted to engage in charitable activities, as long as they do not interfere with Employee's employment obligations to the Company.

2.3. Company Policies. During Employee's employment with the Company, Employee will be subject to all applicable employment and other policies of the Company, as outlined in the Amicus Employee Handbook and as otherwise published by the Company in writing.

Section 3. Compensation and Benefits.

3.1. Base Salary. During Employee's employment, the Company shall pay Employee a salary at the gross annual rate of $427,450 (less applicable withholding) or such greater amount as the Board or a committee thereof may from time to time establish pursuant to the terms hereof (the "Base Salary"). Such Base Salary shall be reviewed annually and may be increased, but not decreased, by the Board or a committee thereof in its sole discretion. The Base Salary shall be payable in accordance with the Company's customary payroll practices for its senior management personnel.

3.2. Bonus. During Employee's employment, Employee shall be eligible to participate in the Company's bonus programs as may be in effect with respect to senior management personnel. Employee shall be eligible to earn an annual target bonus of 100% of the Base Salary in cash (the "Bonus") such actual amount determined by the Company Compensation Committee in its absolute discretion and at 40% of base salary; provided,

however, that notwithstanding anything to the contrary herein or in any bonus program, Employee must be employed by the Company as of December 31 of the applicable calendar year, in order to be eligible to earn a Bonus for such calendar year. Any Bonus payment to which Employee becomes entitled hereunder shall be paid to Employee in a lump sum (less applicable withholding) on or before the 15th day of the third month following the end of the calendar year in which the Bonus was earned.

3.3. Equity. Subject to the terms and conditions of the Company's Amended and Restated 2007 Equity Incentive Plan and such other equity plans as the Company may adopt from time to time including, but not limited to, an Employee Stock Purchase Plan, during
Employee's employment with the Company, Employee will be eligible to receive stock options, Restricted Stock Units and Performance Restricted Stock Units pursuant to any Award
Agreement (as that term is defined in the Company's Equity Incentive Plan) between Employee and the Company. Unless otherwise provided in this Agreement, the terms and conditions of the applicable equity plan will govern all equity grants to Employee (including vesting of options and units), including with regard to the impact of the end of Employee's employment on such equity grants.

3.4. Benefits.

(a) Benefit Plans. During Employee's employment, Employee may participate in any benefit plans (including health and medical insurance) as may be in effect with respect to senior management personnel of the Company, including any equity plan, subject to the eligibility and contribution requirements, enrollment criteria and other terms and conditions of such plans. The Company reserves the right to modify, amend and eliminate any such plans, in its sole and absolute discretion.

(b) Reimbursement of Expenses. During Employee's employment, the Company shall pay or promptly reimburse Employee, upon submission of proper invoices or other documentation in accordance with the Company's policies and procedures, for all reasonable out-of-pocket business, entertainment and travel expenses incurred by Employee in
the performance of Employee's duties. Any taxable reimbursement of business or other expenses as specified under this Agreement shall be subject to the following conditions: (i) the expenses eligible for reimbursement in one taxable year shall not affect the expenses eligible for reimbursement in any other taxable year; (ii) the reimbursement of an eligible expense shall be made no later than the end of the calendar year after the year in which such expense was incurred; and (iii) the right to reimbursement shall not be subject to liquidation or exchange for another benefit.

(c) Vacation. During Employee's employment, Employee shall be entitled to vacation in accordance with the policies of the Company applicable to senior management personnel as may be in effect from time to time.

(d) Withholding. The Company shall withhold from all amounts payable or benefits accorded to Employee all federal, state and local income, employment and other taxes, as and in such amounts as may be required by applicable law.

Employee's Initials /s/DC

Section 4. Duration of Employment. Employee's employment with the Company shall begin on the Effective Date and continue until Employee's employment is terminated by either Employee or the Company. At all times, Employee's employment with the Company shall be "at-will," meaning that either Employee or the Company may terminate the employment at any time, for no reason or any lawful reason.

Section 5. Termination; Severance Benefits.

5.1. Notice of Termination. Any termination of Employee's employment by the Company or by Employee (other than on account of death) shall be communicated to the other party by written notice that indicates the specific termination provision in this Agreement relied upon. Except as otherwise expressly provided in this Agreement or the notice, the termination shall take effect immediately. The parties agree that the notice requirements set forth in this Agreement do not alter the "at will" nature of Employee's employment, as described in Section 4.

5.2. Generally. Upon termination of Employee's employment for any reason, Employee shall be deemed simultaneously to have resigned as a member of the Board, if applicable, and from any other position or office Employee may at the time hold with the Company or any of its Affiliates. Employee agrees to cooperate with the Company by signing any necessary documents and taking any other steps necessary to effectuate Employee's resignation from the Board, if applicable, and from any other position or office Employee may hold with the Company or any of its Affiliates. In addition, upon termination of Employee's employment for any reason, the Company shall pay Employee the Accrued Amounts. The Accrued Amounts will be paid within the time required by applicable law. The impact of the termination of Employee's employment on the Employee's participation in the Company's health plans is addressed in Section 5.3 and Section 5.4.

5.3. Termination by Employee.

(a) Resignation Independent of a Change in Control Event. If Employee resigns and a Change in Control Event has not occurred in the prior 12 months, then (irrespective of whether the resignation was with or without Good Reason): (i) Employee shall receive no further compensation or remuneration of any kind other than the Accrued Amounts; and (ii) at the end of the month in which the resignation takes effect, Employee shall cease to be covered under or permitted to participate in or receive any of the benefits described in Section 3.4, except that, if Employee is enrolled and participating in the Company's health benefit plans at the time of termination, the Company will allow Employee to continue as a member of those plans at Employee's expense in accordance with the terms of those plans and the Consolidated Omnibus Budget Reconciliation Act (COBRA) for the legally required benefit continuation period.

(b) Good Reason Resignation Within 12 Months of a Change in Control Event. If Employee resigns for Good Reason within twelve (12) months after a Change in Control Event, Employee will be entitled to receive, in addition to the Accrued Amounts, Change in Control Severance Benefits. All payments and benefits under this section, except for

the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

5.4. Termination by the Company.

(a) Without Cause Within 12 Months After a Change in Control Event. If the Company terminates Employee's employment without Cause within 12 months after a Change in Control Event, then in lieu of any other payments, rights or benefits under Section 5.4(a), Employee will be entitled to receive Change in Control Severance Benefits in addition to the Accrued Amounts. All payments and benefits under this section, except for the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

(b) Without Cause Not Within 12 Months After a Change in Control Event. If the Company terminates Employee's employment without Cause (other than within 12 months after a Change in Control Event), then Employee will be entitled to receive Severance Benefits in addition to the Accrued Amounts. All payments and benefits under this section, except for the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

(c) For Cause. If the Company terminates Employee's employment for Cause at any time, Employee shall: (i) receive no further compensation or remuneration of any kind (including any Base Salary or Bonus hereunder) other than the Accrued Amounts; and
(ii) at the end of the month in which the termination takes effect, cease to be covered under or be permitted to participate in or receive any of the benefits described in Section 3.4, except that, if Employee is enrolled and participating in the Company's health benefit plans at the time of termination, the Company will allow Employee to continue as a member of those plans at Employee's expense in accordance with the terms of those plans and the Consolidated Omnibus Budget Reconciliation Act (COBRA) for the legally required benefit continuation period.

5.5. Termination upon Death or Inability to Work.

(a) Death. Employee's employment shall terminate immediately upon Employee's death. In the event of Employee's death during the course of Employee's
employment with the Company, the Company will pay the Employee's estate the Accrued Amounts.

(b) Inability to Work. Except as otherwise provided by applicable
law, the Company may terminate Employee's employment in the event Employee is Unable to Work. In the event of Employee's death or termination by the Company due to Employee being Unable to Work, Employee shall receive: (a) the Accrued Amounts, and (b) in the event that
Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall

remain eligible to continue their participation in such plans for a period of twelve (12) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 12 month period.

5.6. General Release and Compliance Required. Employee's receipt of any right, payment or benefit under Section 5.3(b) or Section 5.4(a) or Section 5.4(b) is subject to and conditioned upon: (a) Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company; and (b) Employee's reaffirmation of and continuing compliance with Employee's contractual and legal obligations to the Company, as expressly set forth in the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A.

5.7. Section 409A.

(a) Purpose. This section is intended to help ensure that compensation paid or delivered to Employee pursuant to this Agreement either is paid in compliance with, or is exempt from, IRC Section 409A. However, the Company does not warrant to Employee that all compensation paid or delivered to Employee for Employee's services will be exempt from, or paid in compliance with, Section 409A.

(b) Amounts Payable On Account of Termination. For the purposes of determining when amounts otherwise payable on account of Employee's termination of employment under this Agreement will be paid, which amounts become due because of
Employee's termination of employment, "termination of employment" or words of similar import, as used in this Agreement, shall be construed as the date that Employee first incurs a "separation from service" for purposes of Section 409A on or following termination of
employment. Furthermore, if Employee is a "specified employee" of a public company as determined pursuant to Section 409A as of Employee's termination of employment, any amounts payable on account of Employee's termination of employment that constitute deferred compensation within the meaning of Section 409A and that are otherwise payable during the first six months following Employee's termination (or prior to Employee's death after termination) shall be paid to Employee in a cash lump-sum on the earlier of: (i) the date of Employee's death; or (ii) the first business day of the seventh calendar month immediately following the month in which Employee's termination occurs.

(c) Series of Payments. Any right to a series of installment payments shall be treated as a right to a series of separate payments.

(d) Interpretative Rules. In applying Section 409A to amounts paid pursuant to this Agreement, any right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments.

5.8. Participation in Other Severance Plans. Employee agrees and acknowledges that Employee shall not be eligible to participate in or have any right to

compensation or benefits pursuant to the Company's Change in Control Severance Plan (or any successor plan thereto) or any other Severance Plan issued by the Company.

5.9. Exclusivity. In the event Employee's employment is terminated for any reason, Employee (and Employee's eligible dependents, if any) shall not be entitled to any payments or benefits from the Company or any of its Affiliates except as specifically set forth in this Section 5.

Section 6. Federal Excise Tax.

6.1. General Rule. Employee's payments and benefits under this Agreement and all other arrangements or programs related thereto shall not, in the aggregate, exceed the maximum amount that may be paid to Employee without triggering golden parachute penalties under Section 280G of the Code, and the provisions related thereto with respect to such payments. If Employee's benefits must be cut back to avoid triggering such penalties, such reduction shall be made in the following order: (i) first, any future cash payments (if any) shall be reduced (if necessary, to zero); (ii) second, any current cash payments shall be reduced (if necessary, to zero); (iii) third, all non-cash payments (other than equity or equity derivative related payments) shall be reduced (if necessary, to zero); and (iv) fourth, all equity or equity derivative payments shall be reduced. If an amount in excess of the limit set forth in this Section is paid to Employee, Employee must repay the excess amount to the Company upon demand, with interest at the rate provided in Section 1274(b)(2)(B) of the Code. Employee and the Company agree to cooperate with each other reasonably in connection with any administrative or judicial proceedings concerning the existence or amount of golden parachute penalties on payments or benefits Employee receives.

6.2. Exception. Section 6.1 shall apply only if it increases the net amount Employee would realize from payments and benefits subject to Section 6.1 after payment of income and excise taxes by Employee on such payments and benefits.

6.3. Determinations. The determination of whether the golden parachute penalties under Section 280G of the Code and the provisions related thereto shall be made by counsel chosen by Employee and reasonably acceptable to the Company. All other determinations needed to apply this Section 6 shall be made in good faith by the Company's independent auditors.

Section 7. Company Computers, Property and Records. Employee agrees to handle all Company property in accordance with the Company's policies and procedures. Employee's authorization to access the Company's computer systems is limited and use of such systems to compete or prepare to compete with the Company constitutes unauthorized access that is strictly prohibited. All records received or created by Employee in the course of employment related to the Company's business (such as but not limited to, email, notes, files, contact lists, agendas, drawings, maps, specifications, and calendars) are the property of the Company.

Section 8. Resolution of Disputes. Employee and the Company hereby agree that, except for disputes regarding alleged or anticipated violations of the Confidentiality, Non-

Disclosure and Non-Competition Agreement attached as Exhibit A, any and all disputes between them shall be resolved solely in accordance with the Mutual Agreement to Arbitrate Disputes on an Individual Basis attached as Exhibit B and, to the greatest extent permitted by law, Employee and the Company expressly waive their respective right to a trial by jury for any and all such disputes between them.

Section 9. General.

9.1. No Conflict. Employee represents and warrants that Employee has not entered, nor will Employee enter, into any other agreements that restrict Employee's ability to fulfill Employee's obligations under this Agreement.

9.2. Governing Law. This Agreement shall be construed, interpreted and governed by the laws of the state of Employee's assigned primary office location during the last six months of Employee's employment with the Company, without regard to the conflicts of law principles.

9.3. Binding Effect. This Agreement shall extend to and be binding upon Employee, Employee's legal representatives, heirs and distributees and upon the Company, its successors and assigns regardless of any change in the business structure of the Company.

9.4. Assignment. The Company's rights and obligations under this Agreement, including the restrictions in the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A, shall automatically transfer with any sale, transfer or other disposition of all or substantially all of its assets, stock or business. Employee consents to that transfer. Employee may not assign any rights or obligations under this Agreement without the Company's prior written consent.

9.5. Entire Agreement. This Agreement contains the entire agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements, understandings, discussions, negotiations and undertakings, whether written or oral, between the parties with respect thereto**,** including all Employee's prior Agreements, except this Agreement does not supersede the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A or the Mutual Agreement to Arbitrate Disputes on an Individual Basis attached as Exhibit B. Nor does this Agreement supersede any Award Agreement (as that term is defined in the Company's Equity Incentive Plan) between Employee and the Company. No waiver, modification or change of any provision of this Agreement shall be valid unless in writing and signed by both parties.

9.6. Waiver. The waiver of any breach of any duty, term or condition of this Agreement shall not be deemed to constitute a waiver of any preceding or succeeding breach of the same or any other duty, term or condition of this Agreement.

9.7. Severability. If any provision of this Agreement shall be unenforceable in any jurisdiction in accordance with its terms, the provision shall be enforceable to the fullest extent permitted in that jurisdiction and shall continue to be enforceable in accordance with its

terms in any other jurisdiction and the validity, legality and enforceability of the remaining provisions contained herein shall not be affected thereby.

9.8. Notices. All notices pursuant to this Agreement shall be in writing and shall be sent by prepaid certified mail, return receipt requested or by recognized air courier service addressed as follows:

(i) If to the Company to:

Amicus Therapeutics, Inc. 1 Cedar Brook Drive

Cranbury, New Jersey 08512 c/o CEO or General Counsel

(ii) If to Employee to:

David Clark
at the address identified herein or in Employee's personnel records,

or to such other addresses as may hereinafter be specified by notice in writing by either of the parties, and shall be deemed given three (3) business days after the date so mailed or sent.

9.9. Compliance. If reasonably requested in writing, Employee agrees within fifteen (15) business days to provide the Company with an executed IRS Form 4669 (Statement of Payments Received) with respect to any taxable amount paid to Employee by the Company.

9.10. Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original but all of which shall together constitute one and the same agreement.

9.11. Knowing and Voluntary Nature of Agreement. Employee acknowledges and agrees that Employee is executing this Agreement knowingly and voluntarily and without any duress or undue influence by the Company or anyone else. Employee further acknowledges and agrees that Employee has carefully read this Agreement and fully understands it. Employee further agrees that Employee has been provided an opportunity to seek, and has received, the advice of an attorney of Employee's choice (at Employee's expense) before signing this Agreement.

*[Signature Page Follows]*

IN WITNESS WHEREOF, the parties have executed this Agreement on the date first above written.

/s/ David Clark

David Clark

AMICUS THERAPEUTICS, INC.

By: /s/ John Crowley

Name: John Crowley Title: Chairman & CEO

Employee's Initials /s/DC

**EXHIBIT A**

CONFIDENTIALITY, NON-DISCLOSURE AND NON-COMPETITION AGREEMENT

**EXHIBIT B**

MUTUAL AGREEMENT TO ARBITRATE DISPUTES ON AN INDIVIDUAL BASIS

**EXHIBIT C**

JOB DESCRIPTION

# EMPLOYMENT AGREEMENT

**THIS EMPLOYMENT AGREEMENT** (this "Agreement"), dated as of February 18, 2020 (the "Effective Date"), between AMICUS THERAPEUTICS, INC., a Delaware corporation having an office at 3675 Market Street, Philadelphia, PA 19104 (the "Company"), and Jeffrey Castelli, an individual residing at […], ("Employee") (together, the "parties").

**WHEREAS,** the Company wishes to **continue to** employ Employee, and Employee wishes to **continue to** be employed by Company, on the terms and conditions set forth herein;

**NOW, THEREFORE,** in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the sufficiency and receipt whereof is hereby acknowledged, the parties agree as follows:

Section 1. Definitions. Unless otherwise defined herein, the following terms shall have the following respective meanings:

"Accrued Amounts" means, as of the termination of Employee's employment:
(a) the total of any expenses properly incurred by Employee under Section 3.4(b) that have not previously been reimbursed as of the effective date of the termination; (b) the sum of Employee's accrued, but unused, vacation time, if any, as of the effective date of the termination; and (c) any accrued and unpaid Base Salary through and including the effective date of Employee's termination.

"Affiliate" shall mean any other company, directly or indirectly, controlling, controlled by or under common control with the Company.

"Cause" means Employee's: (i) willful or deliberate misconduct that has or could reasonably be expected to have a materially adverse impact on the reputation or business of the Company (or an Affiliate), or that results in gain or personal enrichment of Employee to the detriment of the Company (or an Affiliate); (ii) violation of Company policy including, but not limited to, policies prohibiting harassment and other workplace misconduct, and policies governing corporate compliance; (iii) misappropriation of the funds or assets of the Company (or an Affiliate); (iv) conviction, plea of guilty, admission to facts sufficient for a finding of guilt, or plea of no contest (or nolo contendere) to: (a) any felony, or (b) any misdemeanor involving fraud, theft, dishonesty, wrongful taking of property, embezzlement, bribery, forgery or extortion; (v) material breach of this Agreement; (vi) material breach of the Confidentiality, Non- Disclosure and Non-Competition Agreement attached as Exhibit A; (vii) breach of Employee's duty of loyalty to the Company; (viii) disqualification, bar or suspension by any governmental authority from performing any of the duties contemplated by this Agreement; (ix) material failure to perform Employee's duties or obligations hereunder (other than as a result of being Unable to Work); or (x) willful failure to adhere to or carry out lawful duties or directives of the Company's Chief Executive Officer ("CEO") or Board of Directors ("Board"). Notwithstanding anything to the contrary herein, the Company shall not be deemed to have terminated Employee for Cause for the events described above in subsections (ix) or (x) unless the CEO or Board, as

applicable, has determined that such events are amenable to cure and given Employee written notice of the occurrence of the claimed event(s) constituting Cause and Employee has failed to cure such event(s) within fourteen (14) calendar days after Employee's receipt of such notice (or such other period as may be deemed reasonable by the CEO or Board under the circumstances and communicated to Employee). The other events described above are not subject to an opportunity to cure but the Company may, in its sole discretion, conduct an investigation into those events and provide the employee a full opportunity to participate.

"Change in Control Event" means any of the following: (i) when any person or entity who is not currently a stockholder of the Company (as of the date of this Agreement) becomes the beneficial owner of greater than 50% of the then-outstanding voting power of the Company; (ii) when a merger or consolidation with another entity occurs that causes the voting securities of the Company outstanding immediately before the transaction to constitute less than a majority of the voting power of the voting securities of the Company or the surviving entity outstanding immediately after the transaction; or (iii) when a sale or disposition of all or substantially all of the Company's assets occurs. Notwithstanding the foregoing, no event shall be deemed to be a Change in Control Event unless such event would also be a Change in Control under Section 409A and the rules and regulations promulgated thereunder (collectively, "Section 409") of the Internal Revenue Code of 1986, as amended (the "Code") or would otherwise be a permitted distribution event under Section 409A.

"Change in Control Severance Benefits" means: (i) payment of an amount equal to one and one-half (1.5) times Employee's then current Base Salary, payable in installments over eighteen (18) months, commencing within sixty (60) calendar days after the resignation or termination (collectively, "termination') of Employee's employment with the Company, in accordance with the Company's customary payroll practices for its senior management personnel; (ii) payment of an amount equal to 100% of the target Bonus for the calendar year in which such termination occurs (such amount being payable in a lump sum), payable within seventy five (75) calendar days following such termination ; (iii) the accelerated vesting of stock options held by Employee immediately prior to such termination ("Options"), such that all Options will become vested as of the date of Employee's termination; (iv) the accelerated vesting of restricted stock grants held by Employee immediately prior to such termination ("Grants"), such that all Grants will become vested as of the date of Employee's termination; (v) the accelerated vesting of performance restricted stock units held by Employee immediately prior to such termination at the applicable performance targets or such greater amounts as determined by the Board of Directors in their sole discretion; and (vi) in the event that Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall remain eligible to continue their participation in such plans for a period of eighteen (18) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 18 month period. Notwithstanding any other provision of this Agreement, Employee's receipt of Change in Control Severance Benefits is conditioned on Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company.

Employee's Initials /s/JC

"Good Reason" means the occurrence of one or both of the following events without Employee's consent: (i) the Company's material diminution of Employee's authority, duties, or responsibilities as set forth in this Agreement; or (ii) the Company's change in the principal geographic location at which Employee provides services to the Company to a location more than thirty (30) miles from Employee's assigned primary office location, unless such relocation is only temporary, for a reasonable period of time, or unless such relocation merely

constitutes travel reasonably required in connection with the performance of Employee's duties. Notwithstanding anything to the contrary herein, Employee shall not be deemed to have resigned for Good Reason unless: (a) Employee had provided to the Company written notice within thirty
(30) calendar days of the occurrence of the claimed event(s) constituting Good Reason, specifying in detail the basis for such Good Reason; (b) the Company fails to cure the Good Reason within thirty (30) calendar days after its receipt of such notice, and (c) Employee terminates employment within sixty (60) calendar days after providing notice to Company of the claimed event(s) constituting Good Reason.

"Severance Benefits" means (i) payment of an amount equal to Employee's then current Base Salary, payable in installments over twelve (12) months, commencing within sixty
(60) calendar days of the termination of Employee's employment with the Company, in accordance with the Company's customary payroll practices then in effect for its senior management personnel; (ii) payment of a bonus equal to 100% of the target Bonus for the calendar year in which such termination occurs pro-rated for the number of days actually worked in the year of termination, payable within seventy five (75) calendar days following such termination; (iii) the accelerated vesting of the Options, such that the portion of the Options that was otherwise scheduled to vest during the twelve (12) month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; (iv) the accelerated vesting of RSUs, such that the portion of RSUs that was otherwise scheduled to vest during the twelve (12) month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; (v) the accelerated vesting of PRSUs, such that the portion of PRSUs that was otherwise scheduled to vest during the twelve month period immediately following such termination (had Employee remained employed with the Company for that period) will become vested as of the date of Employee's termination; and (vi)in the event that Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall remain eligible to continue their participation in such plans for a period of twelve (12) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 12 month period. Notwithstanding any other provision of this Agreement, Employee's receipt of Severance Benefits is conditioned on Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company.

"Unable to Work" means the determination by the Company, following an interactive process, that Employee has become physically or mentally incapable of performing

Employee's essential job functions, with or without a reasonable accommodation, following any period during which such status would be protected under applicable law.

Section 2. Employment.

2.1. Duties and Responsibilities. Subject to the terms and conditions of this Agreement, Employee will be employed by the Company as Chief Portfolio Officer and Head of Gene Therapy or in such other position as may be mutually agreed upon by the parties. A Job Description setting forth Employee's duties and responsibilities is attached as Exhibit C. Employee accepts such employment, and agrees to perform all of the duties and accept all of the responsibilities accompanying such position. Employee agrees to serve the Company faithfully and to the best of Employee's abilities, and to devote all of Employee's business time, skill and attention to such service. Employee is expected to be available for meetings on a regular basis, upon request by the Company, at the Company's Cranbury, New Jersey, and Philadelphia, Pennsylvania, locations or such other Company locations as needed including, but not limited to, the Company's international offices.

2.2. Full Time and Attention. Employee shall devote Employee's full business time and best efforts to the performance of Employee's duties and to the furtherance of the Company's interests. During Employee's employment with the Company, Employee may not hold another position of employment, or be retained as a consultant, or engage in any other business activity (whether full-time or part-time, whether or not for compensation), unless the Company gives Employee prior written permission to do so. Notwithstanding anything stated in this provision to the contrary, Employee is permitted to engage in charitable activities, as long as they do not interfere with Employee's employment obligations to the Company.

2.3. Company Policies. During Employee's employment with the Company, Employee will be subject to all applicable employment and other policies of the Company, as outlined in the Amicus Employee Handbook and as otherwise published by the Company in writing.

Section 3. Compensation and Benefits.

3.1. Base Salary. During Employee's employment, the Company shall pay Employee a salary at the gross annual rate of $405,603 (less applicable withholding) or such greater amount as the Board or a committee thereof may from time to time establish pursuant to the terms hereof (the "Base Salary"). Such Base Salary shall be reviewed annually and may be increased, but not decreased, by the Board or a committee thereof in its sole discretion. The Base Salary shall be payable in accordance with the Company's customary payroll practices for its senior management personnel.

3.2. Bonus. During Employee's employment, Employee shall be eligible to participate in the Company's bonus programs as may be in effect with respect to senior management personnel. Employee shall be eligible to earn an annual target bonus of 100% of the Base Salary in cash (the "Bonus") such actual amount determined by the Company Compensation Committee in its absolute discretion and at 40% of base salary; provided,



however, that notwithstanding anything to the contrary herein or in any bonus program, Employee must be employed by the Company as of December 31 of the applicable calendar year, in order to be eligible to earn a Bonus for such calendar year. Any Bonus payment to which Employee becomes entitled hereunder shall be paid to Employee in a lump sum (less

applicable withholding) on or before the 15th day of the third month following the end of the calendar year in which the Bonus was earned.

3.3. Equity. Subject to the terms and conditions of the Company's Amended and Restated 2007 Equity Incentive Plan and such other equity plans as the Company may adopt from time to time including, but not limited to, an Employee Stock Purchase Plan, during Employee's employment with the Company, Employee will be eligible to receive stock options, Restricted Stock Units and Performance Restricted Stock Units pursuant to any Award Agreement (as that term is defined in the Company's Equity Incentive Plan) between Employee and the Company. Unless otherwise provided in this Agreement, the terms and conditions of the applicable equity plan will govern all equity grants to Employee (including vesting of options and units), including with regard to the impact of the end of Employee's employment on such equity grants.

3.4. Benefits.

(a) Benefit Plans. During Employee's employment, Employee may participate in any benefit plans (including health and medical insurance) as may be in effect with respect to senior management personnel of the Company, including any equity plan, subject to the eligibility and contribution requirements, enrollment criteria and other terms and conditions of such plans. The Company reserves the right to modify, amend and eliminate any such plans, in its sole and absolute discretion.

(b) Reimbursement of Expenses. During Employee's employment, the Company shall pay or promptly reimburse Employee, upon submission of proper invoices or other documentation in accordance with the Company's policies and procedures, for all reasonable out-of-pocket business, entertainment and travel expenses incurred by Employee in the performance of Employee's duties. Any taxable reimbursement of business or other expenses as specified under this Agreement shall be subject to the following conditions: (i) the expenses eligible for reimbursement in one taxable year shall not affect the expenses eligible for reimbursement in any other taxable year; (ii) the reimbursement of an eligible expense shall be made no later than the end of the calendar year after the year in which such expense was incurred; and (iii) the right to reimbursement shall not be subject to liquidation or exchange for another benefit.

(c) Vacation. During Employee's employment, Employee shall be entitled to vacation in accordance with the policies of the Company applicable to senior management personnel as may be in effect from time to time.

(d) Withholding. The Company shall withhold from all amounts payable or benefits accorded to Employee all federal, state and local income, employment and other taxes, as and in such amounts as may be required by applicable law.

Employee's Initials /s/JC

Section 4. Duration of Employment. Employee's employment with the Company shall begin on the Effective Date and continue until Employee's employment is terminated by either Employee or the Company. At all times, Employee's employment with the Company shall be "at-will," meaning that either Employee or the Company may terminate the employment at any time, for no reason or any lawful reason.

Section 5. Termination; Severance Benefits.

5.1. Notice of Termination. Any termination of Employee's employment by the Company or by Employee (other than on account of death) shall be communicated to the other party by written notice that indicates the specific termination provision in this Agreement relied upon. Except as otherwise expressly provided in this Agreement or the notice, the termination shall take effect immediately. The parties agree that the notice requirements set forth in this Agreement do not alter the "at will" nature of Employee's employment, as described in Section 4.

5.2. Generally. Upon termination of Employee's employment for any reason, Employee shall be deemed simultaneously to have resigned as a member of the Board, if applicable, and from any other position or office Employee may at the time hold with the Company or any of its Affiliates. Employee agrees to cooperate with the Company by signing any necessary documents and taking any other steps necessary to effectuate Employee's resignation from the Board, if applicable, and from any other position or office Employee may hold with the Company or any of its Affiliates. In addition, upon termination of Employee's employment for any reason, the Company shall pay Employee the Accrued Amounts. The Accrued Amounts will be paid within the time required by applicable law. The impact of the termination of Employee's employment on the Employee's participation in the Company's health plans is addressed in Section 5.3 and Section 5.4.

5.3. Termination by Employee.

(a) Resignation Independent of a Change in Control Event. If Employee resigns and a Change in Control Event has not occurred in the prior 12 months, then (irrespective of whether the resignation was with or without Good Reason): (i) Employee shall receive no further compensation or remuneration of any kind other than the Accrued Amounts; and (ii) at the end of the month in which the resignation takes effect, Employee shall cease to be covered under or permitted to participate in or receive any of the benefits described in Section 3.4, except that, if Employee is enrolled and participating in the Company's health benefit plans at the time of termination, the Company will allow Employee to continue as a member of those plans at Employee's expense in accordance with the terms of those plans and the Consolidated Omnibus Budget Reconciliation Act (COBRA) for the legally required benefit continuation period.

(b) Good Reason Resignation Within 12 Months of a Change in Control Event. If Employee resigns for Good Reason within twelve (12) months after a Change in Control Event, Employee will be entitled to receive, in addition to the Accrued Amounts, Change in Control Severance Benefits. All payments and benefits under this section, except for

Employee's Initials /s/JC

the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

5.4. Termination by the Company.

(a) Without Cause Within 12 Months After a Change in Control Event. If the Company terminates Employee's employment without Cause within 12 months after a Change in Control Event, then in lieu of any other payments, rights or benefits under Section 5.4(a), Employee will be entitled to receive Change in Control Severance Benefits in addition to the Accrued Amounts. All payments and benefits under this section, except for the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

(b) Without Cause Not Within 12 Months After a Change in Control Event. If the Company terminates Employee's employment without Cause (other than within 12 months after a Change in Control Event), then Employee will be entitled to receive Severance Benefits in addition to the Accrued Amounts. All payments and benefits under this section, except for the Accrued Amounts, shall: (1) require Employee to execute and return (and not revoke) a separation agreement containing a general release, the form and substance of which are acceptable to the Company; and (2) be subject to Section 5.6 and Section 5.7(b).

(c) For Cause. If the Company terminates Employee's employment for Cause at any time, Employee shall: (i) receive no further compensation or remuneration of any kind (including any Base Salary or Bonus hereunder) other than the Accrued Amounts; and
(ii) at the end of the month in which the termination takes effect, cease to be covered under or be permitted to participate in or receive any of the benefits described in Section 3.4, except that, if Employee is enrolled and participating in the Company's health benefit plans at the time of termination, the Company will allow Employee to continue as a member of those plans at Employee's expense in accordance with the terms of those plans and the Consolidated Omnibus Budget Reconciliation Act (COBRA) for the legally required benefit continuation period.

5.5. Termination upon Death or Inability to Work.

(a) Death. Employee's employment shall terminate immediately upon Employee's death. In the event of Employee's death during the course of Employee's employment with the Company, the Company will pay the Employee's estate the Accrued Amounts.

(b) Inability to Work. Except as otherwise provided by applicable law, the Company may terminate Employee's employment in the event Employee is Unable to Work. In the event of Employee's death or termination by the Company due to Employee being Unable to Work, Employee shall receive: (a) the Accrued Amounts, and (b) in the event that Employee is enrolled in any of the Company's group health benefits plans as of the effective date of Employee's termination, then Employee and Employee's eligible dependents, if any, shall

Employee's Initials /s/JC

remain eligible to continue their participation in such plans for a period of twelve (12) months after Employee's date of termination, subject to the eligibility and other terms and conditions of such plans, except that the Company will pay the full premiums otherwise payable for such coverage during such 12 month period.

5.6. General Release and Compliance Required. Employee's receipt of any right, payment or benefit under Section 5.3(b) or Section 5.4(a) or Section 5.4(b) is subject to and conditioned upon: (a) Employee's execution and delivery to the Company of a separation agreement (that Employee does not revoke) containing a general release, the form and substance of which are acceptable to the Company; and (b) Employee's reaffirmation of and continuing compliance with Employee's contractual and legal obligations to the Company, as expressly set forth in the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A.

5.7. Section 409A.

(a) Purpose. This section is intended to help ensure that compensation paid or delivered to Employee pursuant to this Agreement either is paid in compliance with, or is exempt from, IRC Section 409A. However, the Company does not warrant to Employee that all compensation paid or delivered to Employee for Employee's services will be exempt from, or paid in compliance with, Section 409A.

(b) Amounts Payable On Account of Termination. For the purposes of determining when amounts otherwise payable on account of Employee's termination of employment under this Agreement will be paid, which amounts become due because of Employee's termination of employment, "termination of employment" or words of similar import, as used in this Agreement, shall be construed as the date that Employee first incurs a "separation from service" for purposes of Section 409A on or following termination of employment. Furthermore, if Employee is a "specified employee" of a public company as determined pursuant to Section 409A as of Employee's termination of employment, any amounts payable on account of Employee's termination of employment that constitute deferred compensation within the meaning of Section 409A and that are otherwise payable during the first six months following Employee's termination (or prior to Employee's death after termination) shall be paid to Employee in a cash lump-sum on the earlier of: (i) the date of Employee's death; or (ii) the first business day of the seventh calendar month immediately following the month in which Employee's termination occurs.

(c) Series of Payments. Any right to a series of installment payments shall be treated as a right to a series of separate payments.

(d) Interpretative Rules. In applying Section 409A to amounts paid pursuant to this Agreement, any right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments.

5.8. Participation in Other Severance Plans. Employee agrees and acknowledges that Employee shall not be eligible to participate in or have any right to

Employee's Initials /s/JC

compensation or benefits pursuant to the Company's Change in Control Severance Plan (or any successor plan thereto) or any other Severance Plan issued by the Company.

5.9. Exclusivity. In the event Employee's employment is terminated for any reason, Employee (and Employee's eligible dependents, if any) shall not be entitled to any payments or benefits from the Company or any of its Affiliates except as specifically set forth in this Section 5.

Section 6. Federal Excise Tax.

6.1. General Rule. Employee's payments and benefits under this Agreement and all other arrangements or programs related thereto shall not, in the aggregate, exceed the maximum amount that may be paid to Employee without triggering golden parachute penalties under Section 280G of the Code, and the provisions related thereto with respect to such payments. If Employee's benefits must be cut back to avoid triggering such penalties, such reduction shall be made in the following order: (i) first, any future cash payments (if any) shall be reduced (if necessary, to zero); (ii) second, any current cash payments shall be reduced (if necessary, to zero); (iii) third, all non-cash payments (other than equity or equity derivative related payments) shall be reduced (if necessary, to zero); and (iv) fourth, all equity or equity

derivative payments shall be reduced. If an amount in excess of the limit set forth in this Section is paid to Employee, Employee must repay the excess amount to the Company upon demand, with interest at the rate provided in Section 1274(b)(2)(B) of the Code. Employee and the Company agree to cooperate with each other reasonably in connection with any administrative or judicial proceedings concerning the existence or amount of golden parachute penalties on payments or benefits Employee receives.

6.2. Exception. Section 6.1 shall apply only if it increases the net amount Employee would realize from payments and benefits subject to Section 6.1 after payment of income and excise taxes by Employee on such payments and benefits.

6.3. Determinations. The determination of whether the golden parachute penalties under Section 280G of the Code and the provisions related thereto shall be made by counsel chosen by Employee and reasonably acceptable to the Company. All other determinations needed to apply this Section 6 shall be made in good faith by the Company's independent auditors.

Section 7. Company Computers, Property and Records. Employee agrees to handle all Company property in accordance with the Company's policies and procedures. Employee's authorization to access the Company's computer systems is limited and use of such systems to compete or prepare to compete with the Company constitutes unauthorized access that is strictly prohibited. All records received or created by Employee in the course of employment related to the Company's business (such as but not limited to, email, notes, files, contact lists, agendas, drawings, maps, specifications, and calendars) are the property of the Company.

Section 8. Resolution of Disputes. Employee and the Company hereby agree that, except for disputes regarding alleged or anticipated violations of the Confidentiality, Non-

Disclosure and Non-Competition Agreement attached as Exhibit A, any and all disputes between them shall be resolved solely in accordance with the Mutual Agreement to Arbitrate Disputes on an Individual Basis attached as Exhibit B and, to the greatest extent permitted by law, Employee and the Company expressly waive their respective right to a trial by jury for any and all such disputes between them.

Section 9. General.

9.1. No Conflict. Employee represents and warrants that Employee has not entered, nor will Employee enter, into any other agreements that restrict Employee's ability to fulfill Employee's obligations under this Agreement.

9.2. Governing Law. This Agreement shall be construed, interpreted and governed by the laws of the state of Employee's assigned primary office location during the last six months of Employee's employment with the Company, without regard to the conflicts of law principles.

9.3. Binding Effect. This Agreement shall extend to and be binding upon Employee, Employee's legal representatives, heirs and distributees and upon the Company, its successors and assigns regardless of any change in the business structure of the Company.

9.4. Assignment. The Company's rights and obligations under this Agreement, including the restrictions in the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A, shall automatically transfer with any sale, transfer or other disposition of all or substantially all of its assets, stock or business. Employee consents to that transfer. Employee may not assign any rights or obligations under this Agreement without the Company's prior written consent.

9.5. Entire Agreement. This Agreement contains the entire agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements, understandings, discussions, negotiations and undertakings, whether written or oral, between the parties with respect thereto**,** including Employee's prior Agreement, dated April 30, 2010, except this Agreement does not supersede the Confidentiality, Non-Disclosure and Non-Competition Agreement attached as Exhibit A or the Mutual Agreement to Arbitrate Disputes on an Individual Basis attached as Exhibit B. Nor does this Agreement supersede any Award Agreement (as that term is defined in the Company's Equity Incentive Plan) between Employee and the Company. No waiver, modification or change of any provision of this Agreement shall be valid unless in writing and signed by both parties.

9.6. Waiver. The waiver of any breach of any duty, term or condition of this Agreement shall not be deemed to constitute a waiver of any preceding or succeeding breach of the same or any other duty, term or condition of this Agreement.

9.7. Severability. If any provision of this Agreement shall be unenforceable in any jurisdiction in accordance with its terms, the provision shall be enforceable to the fullest extent permitted in that jurisdiction and shall continue to be enforceable in accordance with its



terms in any other jurisdiction and the validity, legality and enforceability of the remaining provisions contained herein shall not be affected thereby.

9.8. Notices. All notices pursuant to this Agreement shall be in writing and shall be sent by prepaid certified mail, return receipt requested or by recognized air courier service addressed as follows:

(i) If to the Company to:

Amicus Therapeutics, Inc. 1 Cedar Brook Drive

Cranbury, New Jersey 08512 c/o CEO or General Counsel

(ii) If to Employee to:

Jeffrey Castelli
at the address identified herein or in Employee's personnel records,

or to such other addresses as may hereinafter be specified by notice in writing by either of the parties, and shall be deemed given three (3) business days after the date so mailed or sent.

9.9. Compliance. If reasonably requested in writing, Employee agrees within fifteen (15) business days to provide the Company with an executed IRS Form 4669 (Statement of Payments Received) with respect to any taxable amount paid to Employee by the Company.

9.10. Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original but all of which shall together constitute one and the same agreement.

9.11. Knowing and Voluntary Nature of Agreement. Employee acknowledges and agrees that Employee is executing this Agreement knowingly and voluntarily and without any duress or undue influence by the Company or anyone else. Employee further acknowledges and agrees that Employee has carefully read this Agreement and fully understands it. Employee further agrees that Employee has been provided an opportunity to seek, and has received, the advice of an attorney of Employee's choice (at Employee's expense) before signing this Agreement.

*[Signature Page Follows]*

Employee's Initials /s/JC

IN WITNESS WHEREOF, the parties have executed this Agreement on the date first above written.

/s/ JC

Jeffrey Castelli

AMICUS THERAPEUTICS, INC.

By: /s/ DC Name: David Clark
Title: Chief People Officer

Employee’s Initials /s/JC

**EXHIBIT A**

CONFIDENTIALITY, NON-DISCLOSURE AND NON-COMPETITION AGREEMENT

**EXHIBIT B**

MUTUAL AGREEMENT TO ARBITRATE DISPUTES ON AN INDIVIDUAL BASIS

**EXHIBIT C**

JOB DESCRIPTION

**PORTIONS HEREIN IDENTIFIED BY [***] HAVE BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE THE EXCLUDED INFORMATION IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.**

# LICENSE AGREEMENT

**DATED AS OF DECEMBER 22, 2022**

**BY AND BETWEEN**

**THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA**

**AND**

**AMICUS THERAPEUTICS, INC.**

**TABLE OF CONTENTS**

**Page**


ARTICLE 1 DEFINITIONS 1
ARTICLE 2 COLLABORATION PROGRAMS 15
2.1 Overall Project 15
2.2 Research 16
2.3 Funding of the Research Program 17
2.4 Discovery Program 17
2.5 Data Ownership 17
2.6 Manufacturing Technology Transfer 18
ARTICLE 3 INFORMATION SHARING AND IP GOVERNANCE. 18
3.1 Information Sharing Committee 18
3.2 Joint Intellectual Property Committee 19
3.3 Scope of Authority 19
ARTICLE 4 LICENSES AND OTHER RIGHTS 20
4.1 Grant of License 20
4.2 Joint Patent Rights 20
4.3 Research License to Penn 20
4.4 Retained Rights 21
4.5 U.S. Government Rights 21
4.6 Grant of Sublicense by Licensee 21
4.7 No Implied License 23
4.8 DRG Technology License 23
ARTICLE 5 FINANCIAL PROVISIONS 24
5.1 Payments 24
5.2 Milestone Payments 24
5.3 Royalties 25
5.4 Penn Sublicense Income 27
5.5 Discovery Product Proceeds 28
5.6 Mode of Payment and Currency 28
5.7 Royalty and Penn Sublicense Income Reports 29
5.8 Late Payments 30
5.9 Default Payment 30
5.10 Accounting 30
5.11 Books and Records 30
5.12 Audits 30
5.13 Taxes 31
ARTICLE 6 CLINICAL DEVELOPMENT, REGULATORY AFFAIRS; COMMERCIALIZATION 31
6.1 Development Plan 31
6.2 Commercialization 31
6.3 Manufacturing 31

**Page**

6.4 Regulatory 31
6.5 Diligence 32
6.6 Progress Reports 32
ARTICLE 7 INTELLECTUAL PROPERTY 33
7.1 Patent Filing Prosecution and Maintenance 33
7.2 Patent Costs 34
7.3 Infringement 35
7.4 Defense 37
7.5 Patent Marking 37
7.6 Ownership of Inventions 37
7.7 DRG Patent Filing Prosecution and Maintenance, Patent Costs, Infringement 38
ARTICLE 8 CONFIDENTIALITY& PUBLICATION 39
8.1 Confidential Information 39
8.2 Disclosures Required by Law 40
8.3 Penn Intellectual Property 40
8.4 Licensee Intellectual Property 40
8.5 Publications 40
ARTICLE 9 REPRESENTATIONS, WARRANTIES AND COVENANTS 41
9.1 Mutual Representations and Warranties 41
9.2 Representations of Penn 41
9.3 Disclaimer of Representations and Warranties 41
9.4 Covenants of Licensee 42
ARTICLE 10 INDEMNIFICATION; INSURANCE AND LIMITATION OF LIABILITY 42
10.1 Indemnification by Licensee 42
10.2 Insurance 43
10.3 LIMITATION OF LIABILITY 44
ARTICLE 11 TERM AND TERMINATION 44
11.1 Term 44
11.2 Termination of this Agreement for Convenience 45
11.3 Termination For Cause 45
11.4 Effects of Termination 45
ARTICLE 12 ADDITIONAL PROVISIONS 46
12.1 Relationship of the Parties 46
12.2 Expenses 46
12.3 Use of Names 46
12.4 No Discrimination 46
12.5 Successors and Assignment 47
12.6 Further Actions 47
12.7 Entire Agreement of the Parties; Amendments 47

**Page**

12.8 Governing Law 47
12.9 Dispute Resolution 47
12.10 Notices and Deliveries 47
12.11 Waiver 48
12.12 Severability 48
12.13 Interpretation 48
12.14 Counterparts 48

**UNIVERSITY OF PENNSYLVANIA**

**LICENSE AGREEMENT**

This License Agreement (this "**Agreement**") is dated as of December 22, 2022 (the "**Effective Date**") by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), and Amicus Therapeutics, Inc., a corporation organized under the laws of the state of Delaware ("**Licensee**"). Penn and Licensee may be referred to herein as a "**Party**" or, collectively, as "**Parties**".

**RECITALS**:

**WHEREAS**, Licensee is a biopharmaceutical company with expertise in the development, manufacture and commercialization of human therapeutic products for treatment of genetic disorders;

**WHEREAS**, Penn, through Dr. James Wilson and the Wilson Lab, have technology and expertise in the research and development of gene therapy products;

**WHEREAS**, Penn and Licensee were parties to that certain Amended and Restated Research, Collaboration & License Agreement dated as of May 28, 2019, as amended to date, pursuant to which the Parties collaborated regarding the research and development of gene therapy products for certain indications (as amended, the "**First Collaboration Agreement**");

**WHEREAS**, Penn and Licensee were parties to that certain Process Development Research & License Agreement dated March 26, 2020, as amended to date, ("**PD Agreement**") for the development of process technologies relating to manufacturing in gene therapy;

**WHEREAS**, as of the Effective Date, Penn and Licensee have entered into that certain Mutual Termination Agreement (the "**Mutual Termination Agreement**"), pursuant to which the Parties have terminated the First Collaboration Agreement and the PD Agreement; and

**WHEREAS**, Penn and Licensee desire to enter into this Agreement for the grant of rights to Licensee with respect to the further research, development and commercialization of certain gene therapy products and candidates for Fabry and Pompe arising under the First Collaboration Agreement, all in accordance with the terms and conditions set forth herein.

**NOW, THEREFORE**, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows

## Article 1
## DEFINITIONS

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.1 "**AAV**" means adeno-associated virus.

1.2 "**Affiliate**" means with respect to a Person, any corporation or other business entity that controls, is controlled by or is under common control with such Person, but only for so long as such control exists. For the purposes of this Section 1.2, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the affirmative power, either directly or indirectly through one or more intermediaries, to direct the management and policies of such Person or entity, whether by the ownership of more than fifty percent (50%) of the voting stock of such entity, or by contract or otherwise.

1.3 "**BLA**" means (a) a Biologics License Application as defined in the FD&C Act and the regulations promulgated thereunder, (b) a Marketing Authorization Application in the European Union, or (c) any equivalent or comparable application, registration or certification in any other country or region.

1.4 "**Calendar Quarter**" mean the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31 of each Calendar Year.

1.5 "**Calendar Year**" means each successive period of twelve (12) months commencing on January 1 and ending on December 31.

1.6 "**cGMP**" means those current practices, as amended from time to time, related to the manufacture of pharmaceutical products and any precursors thereto promulgated in guidelines and regulations of standard compilations including the GMP Rules of the World Health Organization, the United States Code of Federal Regulations, the Guide to Inspection of Bulk Pharmaceutical Chemicals (established by the United States Department of Health and Human Services), the Pharmaceutical Inspection Convention, and the European Community Guide to Good Manufacturing Practice in the production of pharmaceutical products, and equivalent guidelines, regulations and standards in the Territory, as such guidelines, regulations and standards may be amended from time to time.

1.7 "**Challenge**" means Licensee or a Sublicensee will be deemed to have made a "Challenge" of the Penn Patent Rights if Licensee or a Sublicensee: (a) institutes or voluntarily joins as a party to, or causes its counsel to institute on Licensee's or such Sublicensee's behalf, any interference, opposition, re-examination, post-grant review or similar proceeding with respect to any Penn Patent Right with the U.S. Patent and Trademark Office or any foreign patent office; or (b) files or voluntarily joins as a party to any legal proceeding, or causes its counsel to institute or voluntarily join as a party to any legal proceeding on Licensee's or such Sublicensee's behalf, with a court or other Governmental Body (including, without limitation, the U.S. Patent and Trademark Office or any foreign patent office) having authority to determine the validity, enforceability or scope of the Penn Patent Rights, in which one or more claims in such legal proceeding challenges the validity or enforceability of any Penn Patent Right.

1.8 "**Change of Control**" means the occurrence of any of the following events: (a) any party becomes the owner, directly or indirectly, of more than fifty percent (50%) of the total voting power (on an as converted basis) of the equity units or other interests of Licensee then outstanding that are normally entitled to vote in the election of directors of Licensee other than in connection with a financing or series of financing transactions; (b) the merger, consolidation or amalgamation of Licensee with or into any other party, other than any transaction in which the holders of the outstanding voting securities of Licensee immediately prior to the transaction own, directly or indirectly, not less than fifty percent (50%) of the total voting power (on an as converted basis) of the voting securities of the party surviving such merger, consolidation or amalgamation; or (c) the sale of all or substantially all of the assets of Licensee.

1.9 "**Clinical Study**" means (a) a Phase 1 Study, Phase 1/2 Study, Phase 2 Study, or Phase 3 Study, or (b) such other study in humans that is conducted in accordance with good clinical practices and is designed to generate data in support or maintenance of an application for Regulatory Approval.

1.10 "**Commercially Reasonable Efforts**" means [***].

1.11 "**Compulsory License**" means a compulsory license under Penn Patent Rights obtained by a Third Party through the order, decree, or grant of a competent Governmental Body or court, authorizing such Third Party to develop, make, have made, use, sell, offer to sell or import a Licensed Product in any country.

1.12 "**Confidential Information**" of a Party, means (i) confidential or proprietary information or materials relating to the business, operations, technology or products of a Party or any of its Affiliates, including any know-how, that such Party discloses to the other Party under this Agreement, or otherwise makes available to the other Party under this Agreement, and (ii) the terms of this Agreement; provided that Confidential Information shall not include information that:

(a) is or becomes generally available to the public other than as a result of disclosure by the recipient in breach of this Agreement;

(b) is already known by or in the possession of the recipient at the time of disclosure by the disclosing Party;

(c) is independently developed by recipient without use of or reference to the disclosing Party's Confidential Information; or

(d) is obtained by recipient from a Third Party that has not breached any obligations of confidentiality to the disclosing party.

Information or materials of a Party or any of its Affiliates that was included in the Confidential Information of such Party pursuant to the First Collaboration Agreement shall be deemed Confidential Information of such Party under this Agreement and subject to the terms of Article 8 below.

1.13 "**Controlled**" means, with respect to intellectual property rights, that a Party or one of its Affiliates owns or has a license or sublicense to such intellectual property rights and has the ability to provide to, grant a license or sublicense to, or assign its right, title and interest in and to, such intellectual property rights as provided for in this Agreement without violating the terms of any other agreement or other arrangement with any Third Party.

1.14 "**Designated Product**" means [***].

1.15 "**Discovery Patent Rights**" means [***].

1.16 "**Discovery Product**" means a product that is covered by a Discovery Patent Right and developed or sold by a Third Party, which Third Party has licensed such Discovery Patent Rights directly from Penn.

1.17 "**Discovery Product Proceeds**" means [***].

1.18 "**Discovery Program**" means the discovery research conducted at Penn solely by the Wilson Lab during the Discovery Term to [***].

1.19 "**Discovery Results**" means all any and all ideas, information, inventions, developments, animate and inanimate materials, including live animals, discoveries, software, know-how, methods, techniques, formulae, data, processes, methodologies, techniques, biological materials, software and works of authorship, whether patentable or copyrightable, that are first conceived, discovered, developed, reduced to practice, or generated in the performance of the Discovery Program by the Wilson Lab, including any unpatentable inventions discovered, developed or conceived in the conduct of the Discovery Program. Discovery Results expressly excludes any such items covered by Penn Patent Rights and Joint Patent Rights.

1.20 "**Discovery Term**" means the period beginning January 1, 2016 and ending on May 28, 2024.

1.21 "**DRG Exclusivity Period**" means [***].

1.22 "**DRG Patent Rights**" means [***] and (b) any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals or reissues of any of the Patent Rights in (a), including divisions, but excluding continuations-in-part except to the extent of claims solely supported in the specification and entitled to the priority date of the parent application for any of the foregoing, and (c) any corresponding foreign Patent Rights to the foregoing; provided, however, that the foregoing shall not include [***].

1.23 "**DRG Technology**" means [***].

1.24 "**EMA**" means the European Medicines Agency and any successor entity thereto.

1.25 "**FDA**" means the United States Food and Drug Administration and any successor entity thereto.

1.26 "**FD&C Act**" means the United States Federal Food, Drug and Cosmetic Act, as amended.

1.27 "**Field of Use**" means all research, prophylactic, diagnostic and therapeutic uses in or for humans. For clarity, except for any uses in non-humans intended to support development for prophylactic, diagnostic and/or therapeutic use in humans, any and all uses in non-humans, including any and all veterinary uses in companion animals and livestock species, is excluded from the Field of Use.

1.28 "**First Commercial Sale**" means, on a country-by-country basis, the first commercial transfer or disposition for monetary value of Licensed Product in such country for use or consumption by a Third Party end user by Licensee, or any of its Affiliates or Sublicensees, in each case, after all Regulatory Approvals have been obtained for such country and where such disposition or transfer results in a recordable Net Sale in accordance with Licensee's, or its Affiliate's or Sublicensee's, applicable accounting practices (consistently applied). Sales prior to receipt of Regulatory Approval of a Licensed Product such as so-called "treatment IND sales," "named patient sales," "compassionate use sales" or expanded access programs, shall not be considered a First Commercial Sale.

1.29 "**FPFD**" means, on a Licensed Product-by Licensed Product basis with respect to each Clinical Study, the first dosing of the first patient in such Clinical Study.

1.30 "**Funded Discovery Patent Rights**" means [***].

1.31 "**GAAP**" means United States generally accepted accounting principles applied on a consistent basis.

1.32 "**Gene Editing Technologies**" means nucleic acid polymers that encode proteins whose primary recognized enzymatic activity is to (a) selectively induce double or single stranded breaks in a DNA or RNA sequence, or (b) substitute, replace or delete a particular base or set of bases of a DNA or RNA sequence in the absence of a double or single stranded break in the DNA or RNA. Gene Editing Technologies include, but are not limited to: CRISPR-Cas systems (including different Cas nucleases), Zinc finger nucleases, meganucleases, TALENS or base editors. For clarity, "Gene Editing Technologies" does not include chromosomal integration of a transgene introduced by a parvovirus vector in the absence of exogenous nucleases.

1.33 "**Generic Product**" means, with respect to a particular Licensed Product in a country, a generic or biosimilar pharmaceutical product, that is not licensed or owned by Licensee, any of its Affiliates or Sublicensees, that is approved for use in such country by a Regulatory Authority by referencing the prior approval, in whole or part, or safety and efficacy data submitted in support of the prior approval, of such Licensed Product.

1.34 "**Governmental Body**" means any: (a) nation, principality, state, commonwealth, province, territory, county, municipality, district or other jurisdiction of any nature; (b) federal, provincial, state, local, municipal, foreign or other government; (c) governmental or quasi-governmental authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, board, instrumentality, officer, official, representative, organization, unit, body or entity and any court or other tribunal); (d) multi- national or supranational organization or body; or (e) individual, entity, or body exercising, or entitled to exercise, any executive, legislative, judicial, administrative, regulatory, police, military or taxing authority or power of any nature.

1.35 "**IND**" means an Investigational New Drug Application as defined in the FD&C Act and the regulations promulgated thereunder, or (b) an equivalent application to an equivalent Regulatory Authority in any other regulatory jurisdiction, including a Clinical Trial Authorization to the European

Medicines Agency, the filing of which is necessary to initiate or conduct clinical testing of a pharmaceutical product in humans in such jurisdiction.

1.36 "**Indication**" means each of (a) Pompe disease ("**Pompe Disease**") and (b) Fabry disease ("**Fabry Disease**"), in each case (a) and (b), (i) using a Parvovirus Gene Therapy Product [***] and (ii) [***].

1.37 "**Joint Patent Rights**" means (a) any Patent Rights covering an invention conceived and reduced to practice jointly by the Wilson Lab and Licensee in the conduct of a Research Program, (b) any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals or reissues of any of the Patent Rights in (a), including divisions, but excluding continuations-in-part except to the extent of claims solely supported in the specification and entitled to the priority date of the parent application for any of the foregoing, and (c) any corresponding Patent Rights to the foregoing outside of the United States. Without limiting the foregoing, Joint Patent Rights existing as of the Effective Date are listed in Exhibit 1.37.

1.38 "**Know-How**" means intellectual property, data, results, pre-clinical and clinical protocols and study data, chemical structures, chemical sequences, information, inventions, formulas, techniques, methods, processes, procedures and developments. "Know-How" does not include any of the foregoing claimed in a Penn Patent Right or Patent Right Controlled by Licensee.

1.39 "**Law**" or "**Laws**" means all applicable laws, statutes, rules, regulations, ordinances and other pronouncements having the binding effect of law of any Governmental Body.

1.40 "**Licensed Discovery Know-How**" means all Know-How Controlled by Penn as of the Original Effective Date or during the Discovery Term and developed by the Wilson Lab under the Discovery Program and is necessary or reasonably useful to develop, make, use, sell, offer for sale or import a Designated Product for an Indication. For clarity, Licensed Discovery Know-How does not include any DRG Technology.

1.41 "**Licensed Know-How**" means all Know-How Controlled by Penn as of the Original Effective Date or during the Research Term and (a) developed by the Wilson Lab as of the Original Effective Date, or (b) developed by the Wilson Lab under a Research Program pursuant to the First Collaboration Agreement or this Agreement, and in each case (a) and (b) is necessary or reasonably useful to develop, make, use, sell, offer for sale or import a Licensed Product for an Indication in the Field of Use.

1.42 "**Licensed Product**" means any (a) article, composition, apparatus, substance, chemical or any other material covered by a Program Valid Claim or whose manufacture, import, use, offer for sale or sale would, absent the License, constitute an infringement, inducement of infringement or contributory infringement of any Program Valid Claim or would infringe a Program Valid Claim once issued; (b) article, composition, apparatus, substance, chemical or any other material made, used or sold by or utilizing or practicing a Method; (c) article, composition, apparatus, substance, chemical or any other material that incorporates, uses or is made through the use of any Licensed Know-How and is a parvovirus gene therapy for an Indication; or (d) any parvovirus gene therapy for an Indication conceived during, or test in, a Research Program. Notwithstanding the foregoing, "Licensed Product" shall not include a product, to the extent it would have solely been a Licensed Product pursuant to subsection (c) above, that is, or was prior to the Effective Date, (i) acquired or licensed by Licensee or any of its Affiliates (including pursuant to a Change of Control) or (ii) controlled by a Third Party acquirer of Licensee or any of its Affiliates (whether by merger or acquisition of all or substantially all of the stock or assets of Licensee or its Affiliate or a similar transaction) and, in each case ((i) and (ii)), that has been independently developed by a Third Party and for which [***] prior to the closing of such acquisition or license by Licensee or any of its Affiliates (with respect to clause (i) above) or such merger, acquisition or similar transaction (with respect to clause (ii) above).

1.43 "**Major Markets**" means [***].

1.44 "**Manufacturing Patent Rights**" means, (a) [***] and (b) any corresponding foreign Patent Rights to the foregoing. [***].

1.45 "**Method**" means process or method covered by a Program Valid Claim or whose use or practice would, absent the License, constitute an infringement, inducement of infringement or contributory infringement of any Program Valid Claim, or would infringe a Program Valid Claim once issued.

1.46 "**Net Sales**" means the gross amounts billed, invoiced or received by Licensee or any of its Affiliates or Sublicensees for Sales of Licensed Product (including any cash amounts plus the fair market value of any other forms of consideration), less the following deductions to the extent reasonable customary, and actually deducted:

1.1.1 [***];

1.1.2 [***];

1.1.3 [***];

1.1.4 [***]; and

1.1.5 [***].

Even if there is overlap between any of deductions described above, each individual item shall only be deducted once in the overall Net Sales calculation. Net Sales shall not include sales or other transfers or dispositions of Licensed Products between or among Licensee, Sublicensees or their Affiliates. The provision of a Licensed Product for the purposes of conducting research and development activities, for charitable purposes or for governmental purposes shall be deemed to give rise to a Net Sale solely to the extent Licensee or any of its Affiliates or Sublicensees receives a cash payment for such Licensed Product.

1.47 "**Original Effective Date**" means October 8, 2018, which was the effective date of the initial research, collaboration and license agreement between Licensee and Penn (the "**Original Collaboration Agreement**") relating to the Indications, among other matters.

1.48 "**Parvovirus Gene Therapy Product**" means a product (or proposed or prospective product) that inserts one or more functional genes into a patient's cells using a parvovirus vector to treat an indication, [***].

1.49 "**Patent Rights**" means (a) patents and patent applications, together with any unlisted patents and patent applications claiming priority thereto, and any continuations, continuations-in-part (to the extent related directly to the subject matter of the parent application or containing new information developed pursuant to a Research Program), reissues, reexamination certificates, substitutions, divisionals, supplementary protection certificates, renewals, registrations, extensions including all confirmations, revalidations, patents of addition, Patent Cooperation Treaty applications ("**PCTs**"), and pediatric exclusivity periods and all foreign counterparts thereof, and any patents issued or issuing with respect to any of the foregoing and (b) all official correspondence relating to the foregoing.

1.50 "**Payee**" means the Party owed or receiving a payment under this Agreement.

1.51 "**Payor**" means the Party owing or making a payment under this Agreement.

1.52 "**Penn Patent Rights**" means Penn Patent Rights A (including Penn's interest in the Joint Patent Rights), Discovery Patent Rights (including Penn Patent Rights B), Penn Patent Rights C, and Manufacturing Patent Rights, collectively.

1.53 "**Penn Patent Rights A**" means [***] any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals or reissues of any of the Patent Rights in (a) or (b), including divisions, but excluding continuations-in-part except to the extent of claims solely supported in the specification and entitled to the priority date of the parent application for any of the foregoing, and (d) any corresponding foreign Patent Rights to the foregoing. Without limiting the foregoing, the Penn Patent Rights A that are described in clauses (a) and (b) of this Section 1.53 and are existing as of the Effective Date are listed in Exhibit A.

1.54 "**Penn Patent Rights B**" means [***] any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals or reissues thereof, including divisions, but excluding continuations-in-part except to the extent of claims entirely solely supported in the specification and entitled to the priority date of the parent application for any of the foregoing, and (c) any corresponding foreign Patent Rights to the foregoing. Without limiting the foregoing, Penn Patent Rights B that are existing as of the Effective Date are listed in Exhibit 1.54.

1.55 "**Penn Patent Rights C**" means [***] any continuations, provisionals, continued prosecution applications, substitutions, extensions and term restorations, registrations, confirmations, reexaminations, renewals or reissues thereof, including divisions, but excluding continuations-in-part except to the extent of claims solely supported in the specification and entitled to the priority date of the parent application, and (c) any corresponding foreign Patent Rights to the foregoing. Without limiting the foregoing, Penn Patent Rights C that are existing as of the Effective Date are listed in Exhibit 1.55.

1.56 "**Person**" means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government or agency or political subdivision thereof.

1.57 "**Phase 1 Study**" means a clinical study of a drug candidate in patients with the primary objective of characterizing its safety, tolerability, and pharmacokinetics and identifying a recommended dose and regimen for future studies as described in 21 C.F.R. 312.21(a), or a comparable clinical study prescribed by the relevant regulatory authority in a country other than the United States. The drug candidate can be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.58 "**Phase 1/2 Study**" means a clinical study of a drug candidate in diseased patients that satisfies the requirements of a Phase 1 Study and a Phase 2 Study.

1.59 "**Phase 2 Study**" means a clinical study of a drug candidate in patients with the primary objective of characterizing its activity in a specific disease state as well as generating more detailed safety, tolerability, and pharmacokinetics information as described in 21 C.F.R. 312.21(b), or a comparable clinical study prescribed by the relevant regulatory authority in a country other than the United States including a human clinical trial that is also designed to satisfy the requirements of 21 C.F.R. 312.21(a) or corresponding foreign regulations and is subsequently optimized or expanded to satisfy the requirements of 21 C.F.R. 312.21(b) (or corresponding foreign regulations) or otherwise to enable a Phase 3 Clinical Study (e.g., a phase 1/2 trial). The relevant drug candidate may be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.60 "**Phase 3 Study**" means a clinical study of a drug candidate in patients that incorporates accepted endpoints for confirmation of statistical significance of efficacy and safety in order to obtain Regulatory Approval in any country, as further described in 21 C.F.R. 312.21(c) with respect to the United States, or a comparable clinical study prescribed by the relevant Regulatory Authority in a country other than the United States. The relevant drug candidate may be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.61 "**Pivotal Study**" means Phase 3 Study or other clinical study of a drug candidate in human patients with the disease being studied, in each case, the principal purpose of which is to achieve a determination of efficacy and safety and is designed and intended to provide the basis for obtaining

Regulatory Approval to market the applicable product for patients with the indication being studied or where a Clinical Study subsequently is deemed to achieve efficacy and safety for the applicable product and indication for the purpose of obtaining Regulatory Approval.

1.62 "**Program Valid Claim**" means a claim of (a) an issued and unexpired patent in Penn Patent Rights A or Penn Patent Rights B which claim has not been revoked or held unenforceable or invalid by a decision of a court of governmental agency of competent jurisdiction from which no further appeal can be taken or has been taken within the time allowed for appeal, and has not been abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer; or (b) a pending patent application that is included in Penn Patent Rights A or Penn Patent Rights B which was filed and is being prosecuted, and has not been abandoned or finally disallowed without the possibility of appeal or re-filing of the application and has not been [***].

1.63 "**Regulatory Approval**" means, with respect to a product in any regulatory jurisdiction, approval from the applicable Regulatory Authority sufficient for the manufacture, distribution, use, marketing and sale of such pharmaceutical product in such jurisdiction in accordance with Laws (including, where applicable, any pricing or reimbursement approvals). "Regulatory Approval" does not include authorization by a Regulatory Authority to conduct named patient, compassionate use or other similar activities.

1.64 "**Regulatory Authority**" means any governmental authority, including the FDA or EMA, or any successor agency thereto, that has responsibility for granting any licenses or approvals or granting pricing or reimbursement approvals necessary for the marketing and sale of a pharmaceutical product in any country.

1.65 "**Regulatory Exclusivity**" means with respect to any country or jurisdiction, any exclusive marketing rights or data exclusivity protection conferred by an applicable Regulatory Authority or other Regulatory Authority in such country or jurisdiction with respect to a compound or bio-pharmaceutical product, including any regulatory data protection exclusivity (including any orphan drug designation or pediatric exclusivity).

1.66 "**Research Plan**" means the research plan setting forth the Parties' roles and responsibilities for a Research Program, respectively, conducted pursuant to the First Collaboration Agreement or pursuant to this Agreement. For clarity, "Research Plans" include solely those Research Plans in place pursuant to the First Collaboration Agreement (or the Original Collaboration Agreement) together with the Research Wind-Down Plans, which are set forth in Exhibit B hereto, and any project outline entered into with respect to a New Research Project (if agreed to by the Parties in writing).

1.67 "**Research Program**" means [***].

1.68 "**Research Results**" means all any and all ideas, information, inventions, developments, animate and inanimate materials, including live animals, discoveries, software, know-how, methods, techniques, formulae, data, processes, methodologies, techniques, biological materials, software and works of authorship, whether patentable or copyrightable, that are first conceived, discovered, developed, reduced to practice, or generated in the performance of a Research Program by the Wilson Lab, including any unpatentable inventions discovered, developed or conceived in the conduct of a Research Program. Research Results expressly excludes any such items covered by Penn Patent Rights and Joint Patent Rights.

1.69 "**Research Term**" means the period beginning on the Original Effective Date and ending on the completion of activities under the Research Plan for each Indication [***], whichever occurs earlier [***].

1.70 "**Sale**" means any transaction for which consideration is received or expected by Licensee, its Affiliates or Sublicensees for sale, use, lease, transfer or other disposition of a Licensed Product to or for the benefit of a Third Party. For clarity, sale, use, lease, transfer or other disposition of a Licensed Product by Licensee or any of its Affiliates or Sublicensees to another of these entities for resale by such entity to a Third Party shall not be deemed a Sale.

1.71 "**Service Center Cores**" means the following core laboratories at Penn that report directly to Dr. James Wilson, all science cores, including the Animal Models Core, the Vector Core, the Immunology Core, the Cell Morphology Core, the Biostatistics Core and the Integrated Technology Core.

1.72 "**Sublicensee**" means a Third Party to which a Sublicense is granted pursuant to the terms of Section 4.6.

1.73 "**Sublicense Documents**" means any and all agreements, amendments or written understandings entered into with a Sublicensee (including any of its Affiliates) pertaining to a Sublicense, Penn Patent Rights or Licensed Product. For clarity, a development agreement or distribution agreement for a Licensed Product is a Sublicense Document.

1.74 "**Sublicense Income**" means payments received by Licensee or its Affiliates from a Sublicensee in consideration for a Sublicense or other agreement providing the right to negotiate or obtain a Sublicense. Sublicense Income includes payments received from a Sublicensee in the form of license issue fees, milestone payments and the like, but specifically excludes [***].

1.75 "**Task**" means [***].

1.76 "**Tax**" means all taxes, duties, fees, premiums, assessments, imposts, levies, rates, withholdings, dues, government contributions and other charges of any kind whatsoever, whether direct or indirect, together with all interest, penalties, fines, additions to tax or other additional amounts, imposed by any Governmental Body.

1.77 "**Third Party**" means any Person other than Penn, Licensee or any of their respective Affiliates.

1.78 "**United States**" or "**US**" means the United States of America, its territories and possessions.

1.79 "**USD**" or "**$**" means the lawful currency of the United States of America.

1.80 "**Valid Claim**" means a claim of (a) an issued and unexpired patent in Penn Patent Rights which claim has not been revoked or held unenforceable or invalid by a decision of a court of governmental agency of competent jurisdiction from which no further appeal can be taken or has been taken within the time allowed for appeal, and has not been abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer; or (b) a pending patent application that is included in Penn Patent Rights which was filed and is being prosecuted, and has not been abandoned or finally disallowed without the possibility of appeal or re-filing of the application and has not [***].

1.81 "**Vector Core**" means the performance of the following activities by Vector Operations for and on behalf of personnel and departments of Penn (including the Wilson Lab) and/or for other Third Parties: (a) vector production services, and (b) characterization, release and stability testing of vectors, small scale through large scale, including for use in support of toxicology studies.

1.82 "**Vector Operations**" means a laboratory at Penn that reports to Dr. James M. Wilson and focuses on the development of AAV and other parvovirus vector manufacturing processes.

1.83 "**Wilson Lab**" means Dr. James M. Wilson and all individuals who are under the direct supervision or control of Dr. James M. Wilson or his successor as Director of the Wilson Gene Therapy Program at Penn, provided that the Service Center Cores are not included in the Wilson Lab, including any personnel of the Service Center Cores. For clarity, and notwithstanding the foregoing sentence, Vector Operations is a department of the Wilson Lab and is included in the Wilson Lab, but the performance of Vector Core activities is specifically excluded from the Wilson Lab. It is understood that the activities of the Wilson Lab and/or Vector Operations in the performance of a Research Program are not Vector Core activities. For clarity, references to the Wilson Lab herein shall be deemed to refer to the Wilson Lab and/or Vector Operations.

1.84 **Other Terms**. The definition of each of the following terms is set forth in the section of this Agreement indicated below:

| Defined Term | Section |
|---|---|
| Abandoned Discovery Rights | 7.1.5 |
| Advance Payment | 7.2.3 |
| Agreement | Introductory Clause |
| Amicus Technology | 4.3 |
| Commercial Milestone | 5.2.2 |
| Commercial Milestone Payment | 5.2.2 |
| Development Milestone | 5.2.1 |
| Development Milestone Payment | 5.2.1 |
| Disclosing Party | 8.1 |
| Discovery Product Licenses | 1.17 |
| DRG Election Notice | 7.7.2.4 |
| DRG Patent Costs | 7.7.2.1 |
| DRG Technology Improvement | 7.7.1(b) |
| DRG Technology License | 4.8.1 |
| Effective Date | Introductory Clause |
| Election Notice | 7.1.4 |
| Excluded Penn IP | 1.15 |
| Existing Research Programs | 2.2.1 |
| Fabry Disease | 1.36 |
| First Collaboration Agreement | Recitals |
| Historic DRG Patent Costs | 7.7.2.1 |
| Historic Patent Costs | 7.2.1 |
| Information Sharing Committee (“ISC”) | 3.1.1 |
| Infringement Notice | 7.3.1 |
| Joint Intellectual Property Committee (“JIPC”) | 3.2.1 |
| Liabilities | 10.1.1 |
| License | 4.1 |
| License Maintenance Fee | 5.1.1 |
| Licensee | Introductory Clause |
| Licensee Data | 2.5 |
| Licensee Financial Report | 5.7 |
| Manufacturing Process | 2.6 |
| Mutual Termination Agreement | Recitals |
| New Research Project | 2.2.2 |
| Ongoing DRG Patent Costs | 7.7.2.2 |
| Ongoing Patent Costs | 7.2.2 |
| Paid Research Funding | 2.3.1 |
| Party or Parties | Introductory Clause |
| Patent Costs | 7.2.1 |
| Patent Counsel | 7.1.1 |
| PCT | 1.49 |
| PD Agreement | Recitals |

| | |
|---|---|
| Penn | Introductory Clause |
| Penn Data | 2.5 |
| Penn Discovery Results | 2.4 |
| Penn Financial Report | 5.5.3 |
| Penn Indemnitees | 10.1.1 |
| Penn Sublicense Income | 5.4.1 |
| Pompe Disease | 1.36 |
| Progress Report | 6.6.1 |
| Prosecution Request | 7.1.2 |
| Receiving Party | 8.1 |
| Research Wind-Down Plans | 2.2.1 |
| Royalty | 5.3.1 |
| Royalty Period | 5.3.2 |
| Sale Transaction | 1.74 |
| Service Provider Sublicensee | 4.6.4 |
| Sublicense | 4.6.1 |
| Term | 11.1 |
| Third Party Candidate Patent Right | 7.7.1(b) |
| Third Party IP | 5.3.3(b) |
| Wilson Lab | 1.83 |

## Article 2
## COLLABORATION PROGRAMS

1.1 **Overall Project**. Pursuant to the First Collaboration Agreement, the Parties desired to, and did, collaborate with respect to the pre-clinical development of a parvovirus gene therapy product, for each Indication within the Field of Use, with the goal of designating one Licensed Product for clinical development and commercialization for each Indication in the Field of Use. From and after the Effective Date and during the Research Term, the Parties desire to collaborate with the goal of the Wilson Lab completing those activities allocated to Penn and set forth in the Research Wind-Down Plan for the applicable Research Program for an Indication within the Field of Use [***] in order to enable a smooth and effective transition to Licensee (or its designee) of activities with respect to the further research, development, manufacture, and commercialization of Licensed Products for the relevant Indication. After the Effective Date, Licensee will be responsible for those activities allocated to Licensee in a Research Plan and for any development activities performed outside of the Research Program during the Research Term as contemplated by this Agreement and/or after expiration of the Research Term, as well as regulatory strategy and operations, clinical development, cGMP manufacture, and commercialization of all Licensed Product(s).

1.2 **Research**.

1.1.1 The Parties hereby acknowledge and agree that, as of the Effective Date, Penn is conducting certain Research Programs with respect to the Indications which commenced under the Original Collaboration Agreement and the First Collaboration Agreement (as amended through the Effective Date, the "**Existing Research Programs**"). Penn will wind-down the Existing Research Programs by conducting the activities allocated to Penn with respect to each Existing Research Program to completion in accordance with the Research Plan attached as Exhibit B (the "**Research Wind-Down Plans**") and the other terms and conditions of this Agreement.

1.1.2 After the Effective Date, Penn will conduct each Research Program in accordance with the Research Wind-Down Plan for such Research Program and the other terms and conditions of this Agreement. [***]. In the event Licensee desires that Penn conduct new or further

research for an Indication not covered by a Research Plan then in effect for such Indication, the Parties may agree in writing to a new project outline (including a budget therefor) (a "**New Research Project**") for such new or further research, and Penn shall conduct such research in accordance with such project outline and the other terms and conditions of this Agreement. It is understood that Penn's fees for any activities conducted by the Wilson Lab or Penn in connection with a New Research Project shall [***]. In the event a New Research Project is implemented by the Parties, then the activities conducted under such New Research Project will be deemed to be activities under a Research Program and the Research Term will be deemed to recommence as of the date such project outline for such New Research Project was executed by both Parties and remain in effect until completion of the activities under such New Research Project.

1.1.3 Penn shall maintain records of the activities conducted under and the results of each Research Program (including the Research Results) in sufficient detail and in good scientific manner appropriate for patent purposes to properly reflect all work done and results achieved. Penn will provide task-based, scientific reports of the progress and results of each Research Program on the schedule specified in the Research Plan for such Research Program or on another schedule to be agreed in writing by the Parties; provided that, in any event, Penn shall have provided to Licensee the information and results included in the Final Deliverables (as defined in Section 3.2 of the Mutual Termination Agreement) by no later than [***]. Penn shall maintain reasonable and accurate records of the use of the funds provided by Licensee under this Agreement and shall make such records available to Licensee (or its designee) upon reasonable notice during Penn's normal business hours, but not more frequently once each Calendar Year. All Research Results shall be solely and exclusively owned by Penn. For the avoidance of doubt, Research Results will constitute Licensed Know-How and will be included within the scope of the Licenses granted by Penn to Licensee under this Agreement.

1.1.4 Each Party will have the right to engage Third Party subcontractors to perform certain of its obligations under this Agreement. Any subcontractor to be engaged by a Party to perform a Party's obligations set forth in this Agreement will meet the qualifications typically required by such Party for the performance of work similar in scope and complexity to the subcontracted activity and will enter into an appropriate agreement with such Party consistent with such Party's standard practices which agreement shall be as least as protective as the nondisclosure and nonuse of confidential information obligations set forth herein and requiring the assignment or license of Know-How and other intellectual property generated in the course of the subcontracted work (including, with respect to any such Know-How and other intellectual property licensed to Penn, the right to grant and authorize Sublicenses under such Know-How and other intellectual property as contemplated herein in the same manner and of the same scope as required for intellectual property generated solely by the Wilson Lab). Any Party engaging a subcontractor hereunder will remain responsible and obligated for the acts and omissions of such subcontractor and will not grant rights to such subcontractor that would interfere with, limit or diminish the rights of the other Party under this Agreement.

1.3 **Funding of the Research Program**.

1.1.1 The Parties acknowledge and agree that those portions of the Research Support Amount (as defined in the First Collaboration Agreement) provided by Licensee to Penn pursuant to the First Collaboration Agreement and the Research Program Wind-Down Payment (as defined in the Mutual Termination Agreement) to be provided by Licensee to Penn pursuant to the Mutual Termination Agreement, shall fund Penn's conduct of the Existing Research Program in accordance with the Research Wind-Down Plans in effect as of the Effective Date (the "**Paid Research Funding**"). Notwithstanding anything in this Agreement to the contrary and for the avoidance of doubt, such funds shall be non-refundable and non-creditable and, subject to Penn using such funds first to support and fund each of the Research Wind-Down Plans, may be utilized and allocated by Penn in its sole discretion. For clarity, other than payment of the Research Program Wind-Down Payment (as defined in the Mutual Termination Agreement) in accordance with the terms of the Mutual Termination Agreement, no additional amounts shall be paid by Licensee to Penn for Penn's conduct of the Existing Research Program.

1.1.2 Title to any equipment, laboratory animals, or any other tangible materials made or acquired with funds provided under this Agreement will vest in Penn, and such equipment, animals, or

tangible materials will remain the property of Penn following termination or expiration of this Agreement (but subject to any license grants to Licensee hereunder).

1.4 **Discovery Program**. The Parties acknowledge and agree that, as of the Effective Date, Licensee has provided, or is obligated to provide, pursuant to the Mutual Termination Agreement, the Remaining Discovery Support Amount (as defined in the Mutual Termination Agreement) to Penn which will be utilized by Penn to fund Penn's performance of the Tasks. For clarity, other than payment of the Remaining Discovery Support Amount (as defined in the Mutual Termination Agreement) and outstanding patents costs (as described in Section 3.4 of the Mutual Termination Agreement) in accordance with the terms of the Mutual Termination Agreement, no additional amounts shall be paid by Licensee to Penn for Penn's conduct of the Discovery Program. Notwithstanding anything in this Agreement to the contrary and for the avoidance of doubt, such funds are non-refundable and non-creditable and, subject to Penn using such funds for the Discovery Program, may be utilized and allocated by Penn in its sole discretion. Penn shall maintain records of the activities conducted under and the results of the Discovery Program (including the Discovery Results) in sufficient detail and in good scientific manner appropriate for patent purposes to properly reflect all work done and results achieved. At least once every [***] during the period beginning on the Effective Date and thereafter for the remainder of the Discovery Term, Penn will notify Licensee (via the ISC) of any available Discovery Patent Rights and/or Discovery Results and will provide to Licensee updates and scientific reports of the progress and results of the Discovery Program for Tasks. All Discovery Results shall be solely and exclusively owned by Penn ("**Penn Discovery Results**"). For the avoidance of doubt, Penn Discovery Results will constitute Licensed Discovery Know-How and will be included within the scope of the Licenses granted by Penn to Licensee under this Agreement.

1.5 **Data Ownership**. All data generated by Penn under a Research Program or the Discovery Program shall be owned by Penn including all rights, title and interest ("**Penn Data**"). All data generated by Licensee under a Research Program shall be owned by Licensee ("**Licensee Data**"). For the avoidance of doubt, Penn Data will constitute Research Results and Licensed Know-How and will be included within the scope of the License.

1.6 **Manufacturing Technology Transfer**. On or prior to [***], the Wilson Lab will transfer to Licensee additional Penn Know-How that has been qualified and undergone approval by and through the Wilson Lab PD Know-How (as defined in the PD Agreement immediately prior to the Effective Date) or Licensed Know-How, in each case, that is reasonably necessary to manufacture the Licensed Product for each Indication ("**Manufacturing Process**") and that is existing as of the date of such transfer, including by providing copies or samples of relevant documentation and other embodiments of such Know-How (i.e. standard operating procedures and methods and training materials) to the extent reasonably necessary to perform the Manufacturing Process.

## Article 3
## INFORMATION SHARING AND IP GOVERNANCE.

1.1 **Information Sharing Committee**.

1.1.1 **Formation; Composition**. Within [***] after the Effective Date, the Parties shall establish and maintain (subject to Section 3.1.6 below), an information sharing committee (the "**Information Sharing Committee**" or "**ISC**") comprised of at least one (1) representative from each Party. Penn's representative shall have sufficient knowledge of the Research Program and Discovery Program activities to share information regarding Penn's activities, including any results and data obtained, with respect to the Research Program and/or Discovery Program being conducted by Penn. The ISC may change its size from time to time by mutual consent of the Parties, provided that the ISC will consist at all times of an equal number of representatives of each of Penn and Licensee. Each Party may replace its ISC representatives at any time upon written notice to the other Party.

1.1.2 **Specific Responsibilities**. The ISC will:

(a) oversee the activities under the Research Wind-Down Plans;

(b) establish appropriate reporting procedures for the activities being conducted pursuant to the Research Wind-Down Plans and Penn's performance of the Tasks, including the scope and content of reports to be provided by Penn to Licensee (including under Sections 2.2.3and 2.4) and in order to provide Licensee with sufficient information regarding the Research Results for each Indication, Discovery Results and the Discovery Program for Tasks;

(c) serve as a forum for Penn to share and the Parties to review and discuss any activities being conducted pursuant to the Research Wind-Down Plans; and

(d) serve as a forum for Penn to share and the Parties to review and discuss Discovery Results and any available Discovery Patent Rights, provided by Penn to Licensee pursuant to Section 2.4.

1.1.3 **Reporting**. Each Party shall keep the ISC informed on the status and progress of the activities under each Research Program then currently ongoing under a Research Plan, including delivering quarterly written updates of its progress under each Research Program to the ISC at least one (1) week in advance of each ISC meeting. Penn shall also keep the ISC informed of the status and progress of the activities under the Discovery Program as provided in Section 2.4.

1.1.4 **Meetings**. During the performance of a Research Program by Penn, the ISC will meet at least monthly. Following the Research Term and until the expiration of the Discovery Term, the ISC will meet at least quarterly. Following the completion of Penn's performance of all of the Research Programs, the Parties may agree to meet to discuss items with respect to a Research Plan or the Research Program previously addressed by the ISC. The ISC may meet in person, by videoconference or by teleconference. In-person ISC meetings (if any) will be held at locations alternately selected by Penn and by Licensee.

1.1.5 **No Decision-Making**. The ISC shall be a forum for sharing information only and shall have no decision-making power.

1.1.6 **Termination of ISC**. The ISC shall terminate effective as of the expiration of the Discovery Term. Upon termination, the ISC shall disband and have no further obligations under this Agreement.

1.2 **Joint Intellectual Property Committee**.

1.1.1 **Formation; Composition**. As of the Effective Date, the Parties have established, and hereafter shall maintain, a joint intellectual property oversight committee (the "**Joint Intellectual Property Committee**" or "**JIPC**") comprised of an equal number of representatives from each Party. The JIPC may change its size from time to time by mutual consent of its members, provided that the JIPC will consist at all times of an equal number of representatives of each of Penn and Licensee, with at least one representative of Penn from the Penn Center for Innovation. Each Party may replace its JIPC representatives at any time upon written notice to the other Party.

1.1.2 **Specific Responsibilities**. The JIPC will (a) discuss and make recommendations with respect to the intellectual property activities of the Parties related to Licensed Product research and development under each Research Plan in a manner that is consistent with the other terms of this Agreement, specifically with respect to the prosecution, maintenance, defense and enforcement of the Penn Patent Rights A and Joint Patent Rights, and prosecution and maintenance of Penn Patent Rights B (excluding Patent Rights listed on Exhibit D) and (b) conduct such other activities as specifically assigned to the JIPC under this Agreement.

1.1.3 **Meetings**. The JIPC will meet at least quarterly, unless the Parties mutually agree in writing to a different frequency. The JIPC may meet in person, by videoconference, or by teleconference. In-person JIPC meetings (if any) will be held at locations alternately selected by Penn and by Licensee. Meetings of the JIPC will be effective only if at least one representative of each Party is present or participating in such meeting.

1.1.4 **Decision-Making**. The representatives from each Party on the JIPC will have, collectively, one (1) vote on behalf of that party, and all decision making will be by unanimous consent by the Parties. In the event of a dispute at the JIPC, such dispute will be escalated to Licensee's Chief Executive Officer and Penn's Dean of Medicine or his designee, for discussion in good faith; provided, however, that, [***].

1.3 **Scope of Authority**. Each Party shall retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion shall be delegated or vested in the ISC (or the JIPC) unless expressly provided in this Agreement or otherwise agreed by the Parties in writing. The ISC (and JIPC), including pursuant to any Party's exercise of its final decision making authority, shall not have the power to amend, modify or waive this Agreement or compliance with the terms of this Agreement. No decision of the JIPC shall conflict with the terms of this Agreement nor be in contravention of applicable law in any material respect.

## Article 4
## LICENSES AND OTHER RIGHTS

1.1 **Grant of License**. Subject to the terms and conditions of this Agreement, Penn hereby grants to Licensee (the below rights under (a) through (d), the "**License**").

(a) (i) an exclusive, worldwide, royalty-bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6), under Penn Patent Rights A and (ii) a non-exclusive, world-wide royalty-bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6), under Licensed Know-How, in each case ((i) and (ii)), to make, have made, use, sell, offer for sale, and import Licensed Products for the Indications in the Field of Use during the Term;

(b) (i) an exclusive, worldwide, royalty-bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6), under Penn Patent Rights B and (ii) a non-exclusive, world-wide royalty-bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6), under Licensed Discovery Know-How, in each case ((i) and (ii)), to make, have made, use, sell, offer for sale, and import Designated Products for the Indications in the Field of Use during the Term;

(c) a non-exclusive, world-wide, royalty bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6) under Penn Patent Rights C and Manufacturing Patent Rights, in each case, to make, have made, use, sell, offer for sale, and import Designated Products for the Indication (on an Indication-by-Indication basis) in the Field of Use during the Term; and

(d) an exclusive, world-wide, royalty-bearing right and license, with the right to sublicense (subject to the provisions of Section 4.6) under Penn's interest in Joint Patent Rights to make, have made, use, sell, offer for sale, and import products for any purposes within the Indications in the Field of Use during the Term.

1.2 **Joint Patent Rights**. Each Party hereby grants to the other Party a non-exclusive, world-wide, royalty-free, fully paid up, perpetual, irrevocable right and license, with the right to freely sublicense under the Joint Patent Rights, to make, have made, use, sell, offer for sale and import products and services, other than products and services for the Indications in the Field of Use.

1.3 **Research License to Penn**. Licensee will grant to Penn a non-exclusive, non-transferable, non- sublicensable license (a) under [***], the "**Amicus Technology**") solely for purposes of performing Penn's obligations under a Research Program in accordance with the Research Plan for such Research Program and the terms of this Agreement and (b) under (i) the Licensee Data and (ii) new inventions reduced to practice by Licensee in the performance of a Research Program, in the case of each of (i) and (ii), to the extent Controlled by Licensee and solely during the Research Term and solely for purposes of performing internal, non-commercial research in the Wilson Lab. Notwithstanding the foregoing, Amicus Technology expressly excludes any Joint Patent Rights. For clarity, internal, non-

commercial research includes performance of activities funded by a government entity or non- commercial Third Party (so long as such non-commercial Third Party does not obtain any commercial right in or to any data, results, inventions or other intellectual property arising in connection with the relevant funded activities). Amicus Technology will remain the exclusive property of Licensee. Penn shall use the Amicus Technology solely in the conduct of the Research Program for which such Amicus Technology is provided in accordance with the Research Plan for such Research Program and the terms of this Agreement and, for clarity, shall not use any Amicus Technology in the conduct of the Discovery Program. Penn shall not reverse engineer, decompile or disassemble any Amicus Technology, nor attempt or assist any Third Party to do the foregoing. Amicus Technology is provided "as is" with no warranty, express, implied or statutory, including without limitation warranties of merchantability, title, non- infringement, exclusivity or fitness for a particular purpose.

1.4 **Retained Rights**. Notwithstanding the License or DRG Technology License, Penn retains the right under the Penn Patent Rights and the DRG Patent Rights to (a) conduct educational, research and clinical / patient care activities itself (including sponsored research) and (b) authorize non-commercial third parties to conduct education, non- commercial research and clinical / patient activities, in each case of subpart (a) and (b) related to the Indications in the Field of Use; provided however that Penn shall not have the right to use or authorize the use of any Licensed Product for an Indication that is under active clinical testing or being sold by Licensee in the conduct of clinical or patient care activities without Licensee's consent.

1.5 **U.S. Government Rights**. The License and the DRG Technology License are expressly subject to all applicable provisions of any license to the United States Government executed by Penn and is subject to any overriding obligations to the United States Federal Government under 35 U.S.C. §§200-212, applicable governmental implementing regulations, and the U.S. Government sponsored research agreement or other guidelines, including that products that result from intellectual property funded by the United States Federal Government that are sold in the United States be substantially manufactured in the United States. If so requested by Licensee, Penn shall reasonably cooperate with and assist Licensee to seek and obtain a waiver from the appropriate Regulatory Authorities with respect to such manufacturing requirement.

1.6 **Grant of Sublicense by Licensee**.

1.1.1 Penn grants to Licensee the right to grant and authorize sublicenses in whole or in part, under the License and, solely in connection with a sublicense under a License grant, the DRG Technology License (each, a "**Sublicense**") subject to the terms and conditions of this Agreement and specifically this Section 4.6. The term Sublicense shall include any grant of rights under the License and, solely in connection with a sublicense under a License grant, the DRG Technology License by a Sublicensee to any downstream Third Party to develop, manufacture, use or sell a Licensed Product, such downstream Third Party shall also be considered a Sublicensee for the purposes of this Agreement.

1.1.2 Licensee will have the right to extend any and all of its rights under this Agreement to its Affiliate (subject to such Affiliate agreeing in writing with Licensee to be bound by the terms and conditions of this Agreement to the extent applicable to such Affiliate) without the consent of Penn; provided that Licensee will be responsible for the conduct of any such Affiliate under this Agreement to the same extent as if such activities had been undertaken by Licensee itself.

1.1.3 Licensee will have the right to grant and authorize Sublicenses to Third Parties (and their Affiliates), without the consent of Penn. For clarity, except for Sublicenses granted to Service Provider Sublicensees pursuant to Section 4.6.4 below, this provision permits only a single-tier of sublicensing to a Third Party (and its Affiliates) for Sale of a Licensed Product.

1.1.4 Licensee, Sublicensee and each of their respective Affiliates may also, without Penn's consent, engage Third Party service providers (and grant Sublicenses within the scope of the License and/or DRG Technology License to such Persons) solely to perform activities for the benefit of or on behalf of Licensee or such Sublicensee or Affiliate, as the case may be (each a "**Service Provider Sublicensee**"). Licensee shall remain responsible to Penn for all activities of such Service Provider Sublicensee to the same extent as if such activities had been undertaken by Licensee itself.

1.1.5 Each Sublicense Document will (a) be issued in writing, (b) to the extent applicable, include all of the rights of Penn and require the performance of obligations due to Penn (and, if applicable, the U.S. Government under 35 U.S.C. §§200-212) contained in this Agreement and (c) to the extent applicable, include the following terms and conditions:

(a) Reasonable record keeping, audit and reporting obligations sufficient to enable Licensee and Penn to reasonably verify the payments due to Penn (if any) as a result of such Sublicense and to enable Licensee to reasonably monitor such Sublicensee's progress in developing and/or commercializing Licensed Product.

(b) Infringement and enforcement provisions that do not conflict with the restrictions and procedural requirements imposed on Licensee and do not provide greater rights to Sublicensee than as provided in Sections 7.3 and 7.7.3.

(c) Confidentiality provisions with respect to Confidential Information of Penn provided to a Sublicensee consistent with the obligations on Licensee in Article 8 of this Agreement.

(d) Covenants by Sublicensee that are equivalent to those made by Licensee in Section 9.4.

(e) A requirement of indemnification of Penn by Sublicensee that is equivalent to the indemnification of Penn by Licensee under Section 10.1 of this Agreement.

(f) A requirement of obtaining and maintaining insurance by Sublicensee that is equivalent to the insurance requirement of Licensee under Section 10.2 of this Agreement, including coverage under such insurance of Penn as provided in Section 10.2.

(g) Restriction on use of Penn's names etc. consistent with Section 12.3 of this Agreement.

(h) A requirement of antidiscrimination by Sublicensee no less stringent than that provided in Section 12.4 of this Agreement.

(i) A requirement that Penn is a third party beneficiary of such Sublicense solely with respect to the rights of Penn and the performance obligations owed to Penn as required hereunder.

Notwithstanding the foregoing, with respect to Service Provider Sublicensees, the items set forth in subsections (a), (b), (d), (e), (f), (g), (h) and (i) may need not be included in the relevant Sublicense Document to the extent such is not applicable.

1.1.6 Within thirty (30) days after of the execution of a Sublicense Document, Licensee shall provide a complete and accurate copy of such Sublicense Document (which may be redacted with respect to matters unnecessary to show compliance herewith, provided that in no event will any financial information be redacted) to Penn, in the English Language; provided that Licensee shall not be required to provide any Sublicense Document solely with a Service Provider Sublicensee. Penn's receipt of a Sublicense Document, however, will constitute neither an approval nor disapproval of the Sublicense Document nor a waiver of any right of Penn or obligation of Licensee under this Agreement. Notwithstanding the foregoing, upon Penn's request, Licensee will provide an unredacted copy of any Sublicense Document to Penn's outside counsel to confirm compliance herewith, and such outside counsel shall not provide such Sublicense Document to Penn.

1.7 **No Implied License**. Each Party acknowledges that the rights and licenses granted in this Agreement are limited to the scope expressly granted. Accordingly, except for the rights expressly granted under this Agreement, no right, title, or interest of any nature whatsoever is granted whether by implication, estoppel, reliance, or otherwise, by either Party to the other Party. All rights with respect to

any know-how, patent or other intellectual property right rights that are not specifically granted herein are reserved to the owner thereof.

1.8 **DRG Technology License**.

1.1.1 **Grant of DRG Technology License**. Subject to the terms and conditions of this Agreement, Penn hereby grants to Licensee (the below rights, the "**DRG Technology License**"):

(a) (i) an exclusive, worldwide, royalty-bearing (solely to the extent provided in Section 5.3) right and license, with the right to sublicense only in conjunction with a Designated Product for such Indication subject to the provisions Section 4.6, under the DRG Patent Rights and (ii) a non-exclusive, worldwide, royalty-bearing right and license, with the right to sublicense only in conjunction with a Designated Product subject to the provisions Section 4.6 under the DRG Technology, in each case ((i) and (ii)), to make, have made, use, sell, offer for sale, and import Designated Products for the Indications in the Field of Use for the DRG Exclusivity Period. Following the expiration of the DRG Exclusivity Period, the DRG Technology License granted under this Section 4.8.1(a) shall convert to a non-exclusive, worldwide, royalty-bearing right and license with the right to sublicense only in conjunction with a Designated Product subject to the provisions Section 4.6;

(b) a non-exclusive, worldwide, royalty-bearing (solely to the extent provided in Section 5.3) right and license, with the right to sublicense only in conjunction with a Licensed Product for such Indication subject to the provisions of Section 4.6, under DRG Patent Rights and the DRG Technology to make, have made, use, sell, offer for sale, and import Licensed Products for the Indications; and

1.1.2 **Limited Exclusivity**. [***].

1.1.3 **Diligence**. In the event an IND is filed for a Designated Product for an Indication and such Designated Product does not utilize the DRG Technology, upon written notification by Penn, the exclusive license grant under Section 4.8.1(a) with respect to such Indication shall convert to a non-exclusive, worldwide, royalty-bearing right and license without the right to sublicense (except for sublicenses granted in conjunction with a sublicense to a Licensed Product subject to the provisions Section 4.6).

1.1.4 **Indication Restriction**. Subject to Section 4.8.3 and Penn's retained rights set forth in Section 4.4 and Section 4.8.2, during the DRG Exclusivity Period, Penn shall not license to any Third Party the DRG Patent Rights for a product for an Indication.

## Article 5
## FINANCIAL PROVISIONS

1.1 **Payments**.

5.1.1 **License Maintenance Fee**. Following expiration of the Research Term and until the expiration of the first Royalty Period in the first Major Market for a Licensed Product, Licensee shall pay Penn a non-refundable annual maintenance fee of [***] beginning on the [***] anniversary of the Research Term expiration date and on each anniversary thereafter ("**License Maintenance Fee**"). The License Maintenance Fee payment obligation shall only be creditable against royalties owed to Penn in the year such License Maintenance Fee was paid (there shall be no carry forward credit on License Maintenance Fees paid). For clarity, the amount of the License Maintenance Fee will be paid only once per year (not once per Indication) and such payment obligation shall only commence on the [***] anniversary of the expiration date of Research Term (so long as this Agreement has not been terminated prior to such date).

1.2 **Milestone Payments**.

1.1.1 **Development Milestones**.

(a) As partial consideration for the License, Licensee will pay Penn the following milestone payments (each, a "**Development Milestone Payment**") upon the achievement of the first Licensed Product to achieve the corresponding milestone for each Indication (each, a "**Development Milestone**"), whether achieved by Licensee or an Affiliate or Sublicensee. Licensee shall promptly notify Penn in writing of the achievement of any such Development Milestone and Licensee shall pay Penn in full the corresponding Development Milestone Payment within [***] of such achievement. For clarity, each Development Milestone Payment is non-refundable, non-creditable and is not an advance against Royalties due to Penn or any other amounts due to Penn.

| **Development Milestone (payable once per Indication)** | **Milestone Payment (in U.S. dollars)** |
|---|---|
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |
| [***] | [***] |

(b) Each time a Development Milestone [***] in the table above is achieved for a Licensed Product for an Indication, then any other Development Milestone Payments with respect to earlier Development Milestones (i.e., Development Milestones [***] in the table above, as applicable) for that Indication that have not yet been paid will be due and payable together with the Development Milestone Payment for the relevant Development Milestone that is actually achieved. If Development Milestone [***] is achieved prior to the achievement any of Development Milestones [***], then Milestone Payments for Development Milestones [***] shall be due to the extent not previously paid.

1.1.2 **Commercial Milestone Payments**.

(a) As additional consideration for the License, Licensee will pay Penn the following commercial milestone payments (each, a "**Commercial Milestone Payment**") upon the achievement of the corresponding milestone (each, a "**Commercial Milestone**"), whether achieved by Licensee or an Affiliate or Sublicensee, or a combination of Licensee, Affiliate or Sublicensee, when cumulative worldwide Net Sales of Licensed Product(s) for an Indication reach the respective thresholds indicated below. Licensee shall notify Penn in writing of the achievement of any such Commercial Milestone within [***] following [***] in which such Commercial Milestone is achieved and Licensee shall pay Penn in full the corresponding Commercial Milestone Payment together with such notice. For clarity, each Commercial Milestone Payment is non-refundable, non-creditable and is not an advance against Royalties due to Penn or any other amounts due to Penn.

| **Commercial Milestone (payable once per Indication)** | **Milestone Payment** |
|---|---|
| Cumulative Net Sales of Licensed Product for an Indication reaches [***] | [***] |
| Cumulative Net Sales of Licensed Product for an Indication reaches [***] | [***] |
| Cumulative Net Sales for Licensed Product for an Indication reaches [***] | [***] |
| **Total Commercial Milestone Payments to Penn for each Indication** | [***] |

1.3 **Royalties**.

1.1.1 **Royalty**. As further consideration for the License, on a Licensed Product-by-Licensed Product basis, during the applicable Royalty Period, Licensee shall pay to Penn a non-refundable, non-creditable royalty on worldwide Net Sales of Licensed Product ("**Royalty**") as set forth below:

| **Annual Worldwide Net Sales of a Licensed Product** | **Royalty Rate** |
|---|---|
| Less than [***] | [***] |
| Greater than or equal to [***] and less than or equal to [***] | [***] |
| Greater than [***] | [***] |

For such purposes, "Annual Worldwide Net Sales" means the total Net Sales of the applicable Licensed Product in all countries in a particular Calendar Year.

1.1.2 **Royalty Term**. Licensee's obligation to pay Penn the Royalty will continue on a country-by-country and Licensed Product-by-Licensed Product basis from the date of First Commercial Sale of such Licensed Product in a country until the latest of (a) the expiration or abandonment of the last Valid Claim within the Penn Patent Rights and, if applicable, DRG Patent Rights covering such Licensed Product in such country, (b) [***] after First Commercial Sale of such Licensed Product in such country, (c) the expiration of the Regulatory Exclusivity with respect to such Licensed Product; provided that if both the [***] period described in subpart (b) and the applicable Regulatory Exclusivity described in subpart (c) have both expired and there are only pending Valid Claims, but not any issued Valid Claim, in such country covering such Licensed Product on the date that is [***] after the First Commercial Sale of such Licensed Product in such country, the royalty term with respect to such Licensed Product shall expire on such date (such royalty period, the "**Royalty Period**").

1.1.3 **Royalty Reductions**.

(a) [***]

(b) [***]

(i) [***].

(ii) [***].

(iii) [***].

(iv) [***].

1.1.4 **Calculations.** Licensee must pay Royalties owed to Penn on a Calendar Quarter basis on or before the following dates:

(a) [***] for any Sales that took place on or before the last day of the Calendar Quarter ending December 31, of the prior Calendar Year;

(a) [***] for any Sales that took place on or before the last day of the Calendar Quarter ending March 31 of such Calendar Year;

(b) [***] for any Sales that took place on or before the last day of the Calendar Quarter ending June 30 of such Calendar Year; and

(c) [***] for any Sales that took place on or before the last day of the Calendar Quarter ending September 30.

1.4 **Penn Sublicense Income**.

1.1.1 Subject to the terms and conditions of this Agreement, on a Licensed Product-by-Licensed Product basis, Licensee will pay to Penn the following percentage of Sublicense Income ("**Penn Sublicense Income**") received by Licensee from a Sublicensee:

| **Stage in Licensed Product development for the applicable Indication at which Sublicense is granted by Licensee** | **Percent of Sublicense Income payable to Penn** |
|---|---|
| Prior to [***] for the first Licensed Product for such Indication | [***] |
| After [***] for the first Licensed Product for such Indication and prior to [***] for the first Licensed Product for such Indication | [***] |
| After [***] for the first Licensed Product for an Indication | [***] |

[***].

1.1.2 Licensee will make such payment to Penn on or before the following dates:

(a) [***] for any Sublicense Income received by Licensee on or before the last day of the Calendar Quarter ending December 31, of the prior Calendar Year;

(b) [***] for any Sublicense Income received by Licensee on or before the last day of the Calendar Quarter ending March 31 of such Calendar Year;

(c) [***] for any Sublicense Income received by Licensee on or before the last day of the Calendar Quarter ending June 30 of such Calendar Year; and

(d) [***] for any Sublicense Income received by Licensee on or before the last day of the Calendar Quarter ending September 30 of such Calendar Year.

1.5 **Discovery Product Proceeds**.

1.1.1 During the Term of this Agreement and thereafter, [***].

1.1.2 [***] on or before the following dates:

(a) [***] for any Discovery Product Proceeds received by Penn that took place on or before the last day of the Calendar Quarter ending December 31, of the prior Calendar Year;

(a) [***] for any Discovery Product Proceeds received by Penn that took place on or before the last day of the Calendar Quarter ending March 31 of such Calendar Year;

(b) [***] for any Discovery Product Proceeds received by Penn that took place on or before the last day of the Calendar Quarter ending June 30 of such Calendar Year; and

(c) [***] for any Discovery Product Proceeds received by Penn that took place on or before the last day of the Calendar Quarter ending September 30.

1.1.3 Within [***] after [***] in which Penn receives Discovery Product Proceeds, Penn shall deliver to Licensee a report ("**Penn Financial Report**") setting out sufficient details necessary to calculate the Discovery Product Proceeds received by Penn under this Article 5 in such Calendar Quarter, [***].

1.6 **Mode of Payment and Currency**.

1.1.1 All payments to Penn hereunder shall be made by deposit of USD in the requisite amount to the "The Trustees of the University of Pennsylvania" and will be made by delivery to any one of the following:

For funding of the performance of a Research Program by Penn (if applicable):

**By ACH/Wire**:

[***]
[***] (domestic wires)
[***]
(international wires only)
Account Number:
[***]

For all other payments to Penn under this Agreement:

**By ACH/Wire**:

[***]
[***] (domestic wires)
[***]
(international wires only)
Account Number:
[***]

**By Check (direct mail)**:

The Trustees of the University of Pennsylvania
c/o Penn Center for Innovation
Attention: Financial Coordinator
3600 Civic Center Blvd.
9th Floor
Philadelphia, PA 19104

**By Check (lockbox)**:

The Trustees of the University of Pennsylvania
c/o Penn Center for Innovation
PO Box 785546
Philadelphia, PA 19178-5546

1.1.2 All payments to Licensee hereunder shall be made by deposit of USD in the requisite amount to such bank account as Licensee may from time to time designate by written notice to Penn.

1.1.3 All amounts stated in and payments due under this Agreement shall be in USD. All Royalties, Sublicense Income and/or [***] payable shall be calculated first in the currency of the jurisdiction in which payment was made, and if not in the United States, then converted into USD. The exchange rate for such conversion shall be the average of the rate quoted in The Wall Street Journal for the last business day of each month in the Calendar Quarter for such Royalty, Sublicense Income and/or [***] payment made.

1.7 **Royalty and Penn Sublicense Income Reports**. Within [***] after the end of each Calendar Quarter, Licensee shall deliver to Penn a report ("**Licensee Financial Report**") setting out sufficient details necessary to calculate the Royalty and Penn Sublicense Income due under this Article 5 for such Calendar Quarter, including:

1.1.1 Number of each Licensed Product Sold by Licensee, its Affiliates and Sublicensees in each country, the corresponding name of each such Licensed Product;

1.1.2 Gross sales, Net Sales of each Licensed Product made by Licensee, its Affiliates and Sublicensees;

1.1.3 Royalties due for the applicable period pursuant to Section 5.3;

1.1.4 Sublicense Income due for the applicable period pursuant to Section 5.4 and the calculation of Penn Sublicense Income;

1.1.5 The method and currency exchange rates (if any) used to calculate the Royalties and Penn Sublicense Income;

1.1.6 [***];

1.1.7 [***]; and

1.1.8 Date of First Commercial Sale of each Licensed Product in the United States (this need only be reported in the first royalty report following such First Commercial Sale in the United States).

1.8 **Late Payments**. In addition to any other remedies available to Penn, including the right to terminate this Agreement, any failure by Licensee to make a payment within [***] after the date when due shall obligate Licensee to pay computed interest, the interest period commencing on the due date and ending on the actual payment date, to Penn at a rate per annum equal to [***], or the highest rate allowed by Law, whichever is lower.

1.9 **Default Payment**. In the event of default in payment of any payment owing to Penn under the terms of this Agreement, and if it becomes necessary for Penn to undertake legal action to collect said payment, Licensee shall pay reasonable, documented legal fees and costs incurred in connection therewith.

1.10 **Accounting**. Each Party shall calculate all amounts, and perform other accounting procedures required, under this Agreement and applicable to it in accordance with GAAP.

1.11 **Books and Records**. Licensee will keep accurate books and records of all Licensed Products developed, manufactured, used or sold and all Sublicenses entered into by Licensee with respect to Penn Patent Rights. Licensee will preserve these books and records for at least [***] from the date of the Licensee Financial Report to which they pertain. Penn will keep accurate books and records of all Discovery Product Licenses entered into by Penn and all Discovery Product Proceeds in connection therewith. Penn will preserve these books and records for at least [***] from the date of the Penn Financial Report to which they pertain. Upon reasonable notice, not less than [***] prior to the proposed date of review, books and records pertaining to the calculation of any Milestones, Royalties and Penn Sublicense Income due to Penn or (with respect to Penn as Payor) any Discovery Product Proceeds due to Licensee under this Agreement will be made reasonably available and will be open to examination by up to two (2) representatives or agents of Penn reasonably acceptable to Licensee (and, to the extent such are not employees of Penn, each of whom has executed an appropriate confidentiality agreement reasonably acceptable to Licensee that requires the representative or agent to keep any information learned by it confidential except as needed to report its audit conclusions to Penn) for no longer than [***] during regular office hours to determine the accuracy of such books and records and assess Licensee's compliance with the terms of this Agreement, provided that Licensee shall not have an obligation to provide such access more than once in any given twelve (12) month period nor more than [***] after the date of any record to be audited.

1.12 **Audits**. Payee, at its own cost, through an independent auditor reasonably acceptable to Payor (and who has executed an appropriate confidentiality agreement reasonably acceptable to Payor that requires the auditor to keep any information learned by it confidential except as needed to report its audit conclusions to Payee), may inspect and audit the relevant records of Payor pertaining to the calculation of [***] any Milestones, Royalties and Penn Sublicense Income due to Penn [***]. Payor shall provide such auditors with access to the records at Payor's principal place of business during reasonable business hours. Such access need not be given to any such set of records more often than once each Calendar Year nor more than [***] after the date of any report to be audited. Payee shall provide Payor with written notice of its election to inspect and audit the records related to [***] the Milestones and Royalties [***] due hereunder not less than [***] prior to the proposed date of review of Payor's records by Payee's auditors. Should the auditor establish any underpayment of Milestones, Royalties or Penn Sublicense Income by Licensee [***] Payor shall (a) promptly pay Payee the amount of such underpayment; and (b) reimburse Payee for the cost of the audit, if such underpayment equals or exceeds [***] of amounts paid to Payee hereunder during the time period audited. If the auditor finds

overpayment by Payor, then Payor shall have the right to deduct the overpayment from any future milestones or royalties due to Penn by Licensee [***] or deduct the overpayment from [***] or, if no such future milestones or royalties [***], as applicable, are payable, then Payee shall refund the overpayment to Payor within [***] after Payee receives the audit report. Payor may designate competitively sensitive information which such auditor may see and review but which it may not disclose to Payee; provided, however, that such designation shall not restrict the auditor's investigation or conclusions.

1.13 **Taxes**. All payments made by Licensee to Penn under this Agreement shall be made free and clear of and without any deduction for or on account of any Taxes on or with respect to such payments.

1.14 In the event that a Licensed Product is Covered by a Penn PD Patent Right or a Joint PD Patent Right (each, as defined in the PD Agreement) in a particular country, and such Licensed Product is not Covered by any Penn Patent Rights, Joint Patent Rights, or Licensed Know-How, the royalty and milestone payments under this Agreement shall apply to such Licensed Product as follows:

(a) Solely with respect to such Licensed Product and such country and solely for purposes of subsections (b) and (c) below, the definition of "Program Valid Claim" shall be deemed to refer to such Penn PD Patent Rights or Joint PD Patent Rights (each, as defined in the PD Agreement immediately prior to the termination of such Agreement) instead of Penn Patent Rights A or Penn Patent Rights B;

(b) Licensee will pay Penn milestone payments in accordance with the terms of Section 5.2 upon the achievement of the corresponding milestone event by such Licensed Product; provided that such milestones have not previously been achieved by a Licensed Product for the same Indication;

(c) Licensee will pay Penn royalties in accordance with the terms of Section 5.3 on Net Sales of such Licensed Product.

## Article 6
## CLINICAL DEVELOPMENT, REGULATORY AFFAIRS; COMMERCIALIZATION

1.1 **Development Plan**. Until the First Commercial Sale in a Major Market of the first Licensed Product for each Indication, Licensee shall provide Penn with a development plan for a Licensed Product for such Indication no later than December 1st of each year during the Term, commencing with the Calendar Year after the expiration of the Research Term. The development plan shall include a good faith estimate of the timeline for material clinical activities to be conducted by Licensee, its Affiliates and Sublicensees to support obtaining Regulatory Approvals for a Licensed Product in the Major Markets in each Indication.

1.2 **Commercialization**. As between the Parties, Licensee will have sole responsibility for and sole decision-making over all commercialization activities of the Licensed Products for the Indications in the Field of Use, and will be solely responsible for the associated costs of such commercialization activities.

1.3 **Manufacturing**. Except as otherwise provided in this Agreement or in a Research Plan, as between the Parties, Licensee will have responsibility for and decision-making authority over all manufacturing activities and associated costs for the clinical development (including cGMP manufacturing for clinical trials) and commercialization of the Licensed Products for the Indications in the Field of Use for each such Licensed Product.

1.4 **Regulatory**.

1.1.1 As between the Parties, Licensee will have responsibility for and decision-making over regulatory activities for the Licensed Products for the Indications in the Field of Use. As between the Parties, Licensee will have the right to conduct all communications with Regulatory

Authorities, including all meetings, conferences and discussions (including advisory committee meetings), with regard to Licensed Products for the Indications in the Field of Use. Licensee will lead and have control over preparing and submitting all INDs, BLAs and other material regulatory filings related to the Licensed Products for the Indications in the Field of Use, including all applications for Regulatory Approval, provided, however, that, Licensee shall notify Penn in writing of any such application for Regulatory Approval reasonably in advance of filing to allow for Penn to request and, upon any such request, review such application. Promptly following any such review request from Penn, Licensee shall provide Penn with a copy of such application for Regulatory Approval; provided, however, that Licensee shall not be obligated to provide any particular application for Regulatory Approval more than once (unless Licensee materially changes such application other than to incorporate any comments provided by Penn). As between the Parties, Licensee will own any and all applications for Regulatory Approvals (including INDs), Regulatory Approvals, and other regulatory filings related to the Licensed Products for the Indications in the Field of Use which will be held in the name of Licensee (or its designees).

1.1.2 At Licensee's reasonable request and expense, Penn (through Dr. Wilson and other Wilson Lab personnel) shall reasonably cooperate with and assist Licensee (or its designee) in connection with interactions with Regulatory Authorities relating to Licensed Products for the Indications in the Field of Use. In addition, Licensee will keep Penn reasonably informed of the progress of such regulatory interactions and, upon request but not more than twice per Calendar Year, Licensee will provide to Dr. Wilson (or another designated Wilson Lab personnel), on a confidential basis, a copy of any material regulatory filings or correspondence to or from the FDA or EMA with respect to a Licensed Product for an Indication. Licensee will consider any reasonable comments provided on a timely basis by Dr. Wilson (or such Wilson Lab personnel) with respect to such regulatory interactions.

1.5 **Diligence**. Licensee (itself and/or through its Affiliates or Sublicensees) shall use Commercially Reasonable Efforts to develop and, following Regulatory Approval, to commercialize, in the Major Markets one Licensed Product for each Indication in the Field of Use.

6.6 **Progress Reports**.

6.6.1 Prior to the First Commercial Sale of a Licensed Product for an Indication, Licensee on an annual basis, but in no event later than June 1st of each Calendar Year, shall submit to Penn a progress report (each, a "**Progress Report**") summarizing Licensee's (and any Affiliates' and Sublicensees') material activities related to the development of all Licensed Products for each Indication directed to obtaining Regulatory Approvals necessary for commercialization of Licensed Products in the Major Markets.

6.6.2 Each Progress Report must include all of the following for each annual period:

(a) Update on the status of material pre-clinical work and Clinical Studies involving a Licensed Product, as well as the status of any IND and/or BLA filings for a Licensed Product; and

(b) If known and relevant, anticipated dates for receipt of Regulatory Approval for a Licensed Product in the Major Markets.

## Article 7
## INTELLECTUAL PROPERTY

1.1 **Patent Filing Prosecution and Maintenance**.

1.1.1 Penn will use diligent efforts to file, and thereafter prosecute in good faith and maintain, a Patent Right(s), which would be included in Penn Patent Rights A, claiming the Designated Product for each Indication and the use of such Designated Product for the Indication. Penn Patent Rights will be held in the name of Penn and obtained with counsel selected by Penn and reasonably acceptable to Licensee ("**Patent Counsel**"). Penn shall control all actions and decisions with respect to the filing, prosecution and maintenance of Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on

Exhibit D) and Joint Patent Rights in close coordination with Licensee via discussions at the JIPC and, in any event, Penn will consider any reasonable comments or suggestions by Licensee with respect to same; provided, however, that with respect to Penn Patent Rights A claiming solely a Designated Product applicable to the Indications in the Field of Use, Joint Patent Rights, and Discovery Patent Rights for which there is no Third Party licensee, Penn shall have an obligation to consider in good faith and implement any reasonable comments provided by Licensee. Penn will instruct Patent Counsel to copy Licensee on all correspondence related to Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D), Joint Patent Rights and any other Discovery Patent Rights for which there is no Third Party licensee (including copies of each patent application, office action, response to office action, request for terminal disclaimer, and request for reissue or reexamination of any patent or patent application) and to interact with Licensee with respect to the preparation, filing, prosecution and maintenance of Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D) and Joint Patent Rights. Penn has the right to take action to preserve rights and minimize cost whether or not Licensee has commented, and will use reasonable efforts to not abandon or allow to lapse (a) any Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D) or Joint Patent Rights for which Licensee is licensed and is underwriting its share of the Patent Costs nor (b) any other Discovery Patent Rights for which Licensee is underwriting its share of the Patent Costs, if any, in each case ((a) and (b)) without Licensee's written authorization under this Agreement, except for filing of continuations, divisionals, or the like that substitute for the lapsed application, provided that, Penn shall have no requirement to file, prosecute, or maintain Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D) or Joint Patent Rights if Licensee is not current with its Patent Cost obligations with respect to such Patent Right as set forth in this Agreement. Upon Licensee's reasonable request, the Parties shall cooperate and shall prepare updated versions of each of the exhibits pertaining to Penn Patent Rights. For the purposes of this Agreement, "maintenance" of the Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D) and Joint Patent Rights includes inter parties patent review proceedings before the USPTO or a similar patent administration outside the US. For further clarity, validity challenges raised in infringement litigation will be handled per Section 7.3, Infringement.

1.1.2 The Parties shall discuss and agree at the JIPC the countries in which Patent Rights within the Penn Patent Rights A, Penn Patent Rights B (excluding Patent Rights on Exhibit D) and Joint Patent Rights will be filed. Licensee has the right to request any additional country filing for Penn Patent Rights A, Penn Patent Rights B and Joint Patent Rights via a written request to Penn [***] prior to the deadline set by the patent office in the territory in which filing is to take place ("**Prosecution Request**"). The absence of a given Prosecution Request by such deadline will be considered an election not to secure the Patent Rights associated with the specific phase of patent prosecution in such country, and such patent application(s) and patent(s) in such country will not be part of Penn Patent Rights and therefore not subject to this Agreement, including the License, and Licensee will have no further rights or license to them.

1.1.3 For Penn Patent Rights B listed on Exhibit D and any other Discovery Patent Rights for which there is a Third Party licensee, Penn Patent Rights C and Manufacturing Patent Rights, Penn will instruct Patent Counsel to copy Licensee on all correspondence (including copies of each patent application, office action, response to office action, request for terminal disclaimer, and request for reissue or reexamination of any patent or patent application), to interact with Licensee with respect to the preparation, filing, prosecution and maintenance, and to consider any reasonable comments or suggestions by Licensee with respect to same.

1.1.4 Licensee shall also have the right, on a Penn Patent Right-by-Penn Patent Right and country-by-country basis, to (i) elect not to fund at the time of disclosure, or (ii) elect not to continue to fund, in each case (i) and (ii), its pro rata share (as determined pursuant to Section 7.2) of the Patent Costs with respect to any Penn Patent Right(s) in a particular country, which election may be made by Licensee upon [***] prior written notice to Penn ("**Election Notice**"). Within [***] after receipt of an Election Notice from Licensee, Penn shall notify Licensee in writing whether (a) any Third Party is obligated to fund any portion of the Patent Costs with respect to any Penn Patent Right identified in such Election Notice in any country identified in such Election Notice or (b) Penn and/or Dr. James Wilson will fund such Patent Costs or will allow such Penn Patent Right to lapse or become abandoned in such country. Within [***] after receipt of any such notice from Penn, Licensee shall have the right to cancel its Election Notice and fund or continue to fund, as applicable, its pro rata share of the Patent Costs with

respect to such Penn Patent Right in such country. If Licensee delivers an Election Notice to Penn (and does not cancel such Election Notice, pursuant to the preceding sentence), following the expiration of such [***] period, Licensee shall have no further obligation to pay Ongoing Patent Costs with respect to any Penn Patent Right identified in such Election Notice in any country identified in such Election Notice and any such Patent Right in any such country shall thereafter be excluded from the Penn Patent Rights.

1.1.5 Notwithstanding the foregoing, on a Funded Discovery Patent Right-by-Funded Discovery Patent Right and country-by-country basis, if any Patent Right for which Licensee elects not to fund its share of Patent Costs in a country pursuant to Section 7.1.4, is a Funded Discovery Patent Right and Licensee has funded its share of the Patent Costs for such Funded Discovery Patent Right in such country through the expiration of the Discovery Term, such Patent Right in such country shall be treated as a Funded Discovery Patent Right in such country for the purpose of revenue sharing. If Licensee chooses (pursuant to Section 7.1.4) not to fund its share of the Patent Costs for a Funded Discovery Patent Right in a country following completion of the Discovery Term ("**Abandoned Discovery Rights**"), [***].

1.2 **Patent Costs**.

1.1.1 Subject to Section 7.2.3, within [***] after the Effective Date, Licensee will reimburse Penn for all documented out-of-pocket costs for the filing, prosecution and maintenance of Penn Patent Rights and Joint Patent Rights, including all accrued and documented attorney fees, expenses, official and filing fees ("**Patent Costs**"), incurred prior to the Effective Date or the date at which such Patent Rights are added to the License (as applicable), which have not otherwise been reimbursed by Licensee or other licensees of such Penn Patent Rights ("**Historic Patent Costs**"). Historic Patent Costs for the Discovery Patent Rights that were incurred prior to the Effective Date shall be excluded from Licensee's reimbursement obligation to Penn. Notwithstanding the first sentence of this Section 7.2.1, for Penn Patent Rights or Joint Patent Rights licensed by Penn to more than one licensee, Licensee shall be responsible for payment to Penn of a pro rata share of such documented Historic Patent Costs based on the number of licensees for such Penn Patent Rights or Joint Patent Rights.

1.1.2 Licensee will bear (a) all Patent Costs incurred during the Term, for Penn Patent Rights (other than Discovery Patent Rights) and Joint Patent Rights, (b) for Discovery Patent Rights, all Patent Costs incurred during the period beginning on the Effective Date and thereafter until the expiration of the last Discovery Patent Right (collectively, "**Ongoing Patent Costs**"). Notwithstanding the foregoing, for Penn Patent Rights or Joint Patent Rights licensed by Penn to more than one licensee, Licensee shall be responsible for payment to Penn of a pro rata share of such documented Ongoing Patent Costs based on the number of licensees for such Penn Patent Rights or Joint Patent Rights. No later than [***] prior to the end of each Calendar Year during the Term, Penn shall provide to Licensee, a good faith estimate and budget for the Ongoing Patent Costs anticipated to be incurred for the next Calendar Year and, to the extent applicable, Licensee's proportionate share of such Ongoing Patent Costs. This Section 7.2.2 is subject to Section 7.1.4 above.

1.1.3 Licensee shall pay in advance the Patent Counsel's estimated costs for undertaking material patent actions with respect to Penn Patent Rights and Joint Patent Rights before Penn authorizes the Patent Counsel to proceed ("**Advance Payment**"). Notwithstanding whether Licensee makes an Advance Payment for any patent action, Licensee shall bear its pro rata share (based on the number of licensees for such Penn Patent Rights or Joint Patent Rights) of all Patent Costs with respect to Penn Patent Rights and Joint Patent Rights as set forth in Section 7.2.1 or Section 7.2.2 and shall pay such amounts within [***] of receipt of invoice for such patent actions. For clarity, the term "Patent Costs" means and includes Historic Patent Costs and Ongoing Patent Costs.

1.3 **Infringement**.

1.1.1 If either Party believes that an infringement by a Third Party with respect to any Penn Patent Right is occurring or may potentially occur, the knowledgeable Party will provide the other Party with (a) written notice of such infringement or potential infringement and (b) evidence of such infringement or potential infringement (the "**Infringement Notice**"). During the period in which, and in the jurisdiction where, Licensee has exclusive rights under this Agreement, subject to Licensee's right to

institute suit for patent infringement pursuant to Section 7.3.2 if infringing activity of potential commercial significance has not been abated within [***] following the date the Infringement Notice for such activity was provided, neither Penn or Licensee will notify such a Third Party (including the infringer) of infringement or put such Third Party on notice of the existence of Penn Patent Rights without first obtaining the written consent of the other Party. If Licensee puts such infringer on notice of the existence of any Penn Patent Right without the prior written consent of Penn prior to the expiration of such [***] period, then Licensee's right to initiate a suit under Section 7.3.2 below will terminate immediately without the obligation of Penn to provide notice to Licensee. Both Penn and Licensee will use their diligent efforts to cooperate with each other to terminate any such infringement without litigation.

1.1.2 With respect to Penn Patent Rights A, if infringing activity of potential commercial significance has not been abated within [***] following the date the Infringement Notice for such activity was provided, then during the period in which, and in the jurisdiction where, Licensee is the sole licensee for certain Penn Patent Rights A and the infringement is a competing product to a Licensed Product for an Indication, Licensee may institute suit for patent infringement of such Penn Patent Rights A against the infringer. With respect to Penn Patent Rights B, if infringing activity of potential commercial significance has not been abated within [***] following the date the Infringement Notice for such activity was provided, then during the period in which, and in the jurisdiction where, Licensee is the sole licensee for certain Penn Patent Rights B and the infringement is a competing product to a Designated Product for an Indication, the JIPC shall discuss and recommend how to handle such infringement, including whether to institute suit for patent infringement of such Penn Patent Rights B against the infringer, which Party shall have the right to initiate and control such suit and making decisions with respect to litigation strategy. If the JIPC (after escalation pursuant to Section 3.2.4) is unable to reach agreement, Penn shall have the final decision-making authority with respect to handling any infringement action related to Penn Patent Rights B; provided that in any event, Penn will consider any reasonable comments or suggestions by Licensee with respect to same.

1.1.3 Penn may voluntarily join such suit at its own expense, but may not thereafter commence suit against the infringer for the acts of infringement that are the subject of Licensee's suit or any judgment rendered in such suit. If in a suit initiated by Licensee, Penn is involuntarily joined other than by Licensee, then Licensee will pay any documented costs incurred by Penn arising out of such suit, including any documented legal fees of counsel that Penn selects and retains to represent it in the suit. In any suit initiated by Licensee, Licensee shall be free to enter into a settlement, consent judgment or other voluntary disposition, provided that any settlement, consent judgment or other voluntary disposition that (i) limits the scope, validity or enforcement of Penn Patent Rights A or Penn Patent Rights B or (ii) admits fault or wrongdoing on the part of Penn must be approved in advance by Penn in writing (such approval not to be unreasonably withheld or delayed). Licensee's request for such approval shall include complete copies of proposed settlement documents, a summary of such settlement, and any other information material to such settlement that is reasonably requested by Penn. Penn shall provide Licensee notice of its approval or denial within [***] of any request for such approval by Licensee, provided that (x) in the event Penn wishes to deny such approval, such notice shall include a detailed written description of Penn's reasonable objections to the proposed settlement, consent judgment, or other voluntary disposition and (y) Penn shall be deemed to have approved of such proposed settlement, consent judgment, or other voluntary disposition in the event it fails to provide such notice within such [***] period in accordance herewith.

1.1.4 If, within [***] following the date of a request to do so from Penn, infringing activity of potential commercial significance has not been abated and if Licensee has not brought suit against the infringer, then Penn may institute suit for patent infringement against the infringer. If Penn institutes such suit, then Licensee may not join such suit without the prior written consent of Penn (which consent shall not be unreasonably withheld or delayed) and may not thereafter commence suit against the infringer for the acts of infringement that are the subject of Penn's suit or any judgment rendered in such suit.

1.1.5 Notwithstanding Sections 7.3.2, 7.3.3 and 7.3.4, in the event that any Penn Patent Rights A or Penn Patent Rights B are infringed by a Third Party and any of the infringed Penn Patent Rights A or Penn Patent Rights B are also licensed by Penn to a Third Party, prior to any enforcement

action being taken by either Party regarding such infringement, the JIPC shall discuss and recommend how to handle such infringement by such Third Party.

1.1.6 Any recovery or settlement received in connection with any suit will first be shared by Penn and Licensee equally to cover any litigation costs each incurred (to the extent not previously reimbursed) and next shall be paid to Penn or Licensee to cover any litigation costs it incurred in excess of the litigation costs of the other (to the extent not previously reimbursed). Any remaining recoveries shall be allocated as follows:

For any portion of the recovery or settlement, other than for amounts attributable and paid as enhanced damages for willful infringement:

(a) for any suit that is initiated by Licensee and in which Penn was not a party in the litigation, Penn shall receive [***] of the recovery and the Licensee shall receive the remainder; and

(b) for any suit that is initiated by the Licensee or Penn and that the other Party joins voluntarily (but only to the extent such voluntary joining is allowed under this Agreement or expressly by the other Party in a separate agreement) or involuntarily, the non-initiating party's percentage of the total litigation costs incurred by Penn and Licensee, but in no event shall the non-initiating Party receive less than [***] of such recovery, while the initiating party shall receive the remainder, and in no case shall Penn receive less than [***] of such recovery.

For any portion of the recovery or settlement paid as enhanced damages for willful infringement:

(c) for any suit that is initiated by Licensee or Penn and the other Party voluntarily (but only to the extent such voluntary joining is allowed under this Agreement or expressly by the other Party in a separate agreement) or involuntarily, the initiating party shall receive [***] and the non-initiating shall receive the remainder; and

(d) for any suit that is initiated by Licensee and in which Penn was not a party in the litigation, Penn shall receive [***] and Licensee shall receive the remainder.

For any portion of the recovery or settlement received in connection with any suit that is initiated by Penn and in which Licensee was not a party in the litigation, any recovery in excess of litigation costs will belong to Penn.

1.1.7 Each Party will reasonably cooperate and assist with the other in litigation proceedings instituted hereunder but at the expense of the Party who initiated the suit (unless such suit is being jointly prosecuted by the Parties). For clarity, such requirement does not require a Party to join a suit unless otherwise specifically required under this Agreement. If Penn is subjected to third party discovery related to the Penn Patent Rights or Licensed Products licensed to Licensee hereunder, Licensee will pay Penn's documented out-of- pocket expenses with respect to same.

1.1.8 Penn shall keep Licensee reasonably informed of the initiation and status of any action to enforce any Penn Patent Rights A, Discovery Patent Rights (including Penn Patent Rights B), Penn Patent Rights C or Manufacturing Patent Rights pertaining to the Indications or a Licensed Product.

1.4 **Defense**. Each Party shall have the right to defend any adversarial legal proceeding brought against it, and the Parties shall reasonably cooperate with one another regarding such defense, provided that such right of defense does not include any right to bring infringement actions (including counterclaims) with respect to Penn Patent Rights except as expressly set forth herein or as otherwise agreed by the Parties.

1.5 **Patent Marking**. Licensee shall place in a conspicuous location on any Licensed Product (or its packaging where appropriate and practicable) made or sold under this Agreement a patent

notice in accordance with the Laws concerning the marking of patented articles where such Licensed Product is made or sold, as applicable.

1.6 **Ownership of Inventions**. Ownership of any inventions or other intellectual property generated in the conduct of a Research Program or otherwise under this Agreement will be determined in accordance with United States patent law or other applicable intellectual property law. For clarity, (a) inventions conceived and reduced to practice solely by Penn inventors will be solely owned by Penn, (b) inventions conceived and reduced to practice solely by Licensee inventors will be solely owned by Licensee, and (c) inventions jointly conceived and reduced to practice by both Penn and Licensee inventors will be jointly owned by Penn and Licensee.

1.7 **DRG Patent Filing Prosecution and Maintenance, Patent Costs, Infringement**.

1.1.1 **Patent Filing Prosecution and Maintenance**.

(a) Penn will use diligent efforts to file, and thereafter prosecute in good faith and maintain DRG Patent Right(s). DRG Patent Right(s) will be held in the name of Penn and obtained with Patent Counsel. Penn shall control all actions and decisions with respect to the filing, prosecution and maintenance of DRG Patent Right(s). For the purposes of this Agreement, "maintenance" of the DRG Patent Right(s) includes *inter partes* patent review proceedings before the USPTO or a similar patent administration outside the US. For DRG Patent Rights, Penn will instruct Patent Counsel to provide Licensee copies of patent applications when filed, notices of allowance when received, office actions when issued and office action responses when filed.

(b) In the event that DRG Technology is conceived and reduced to practice by the Wilson Lab and/or Vector Operations during the Discovery Term without the use of any Licensee funding ("**DRG Technology Improvement**") and such DRG Technology Improvement is also incorporated into any clinical candidate of a Third Party with whom the Wilson Lab is collaborating, then Penn may file and prosecute a Patent Right that covers such clinical candidate of a Third Party with whom the Wilson Lab is collaborating incorporating such DRG Technology Improvement ("**Third Party Candidate Patent Right**"); provided, however, that if Penn files a Third Party Candidate Patent Right, Penn shall also separately file and prosecute a patent application specific for such DRG Technology Improvement distinct from such Third Party Candidate Patent Right.

1.1.2 **Patent Costs**.

1.1.1.1 Subject to Section 7.7.2.3, within [***] after the Effective Date, Licensee will reimburse Penn for all documented out-of-pocket costs for the filing, prosecution and maintenance of DRG Patent Right(s) for the filing, prosecution and maintenance of DRG Patent Rights, including all accrued and documented attorney fees, expenses, official and filing fees ("**DRG Patent Costs**"), incurred prior to the Effective Date, which have not otherwise been reimbursed by Licensee or other licensees of such DRG Patent Rights ("**Historic DRG Patent Costs**"). Notwithstanding the first sentence of this Section 7.7.2.1, for DRG Patent Right(s) licensed by Penn to more than one licensee, Licensee shall be responsible for payment to Penn of a pro rata share of such documented Historic DRG Patent Costs based on the number of licensees for such Patent Rights.

1.1.1.2 Licensee will bear (a) all documented out-of-pocket costs for the filing, prosecution and maintenance of DRG Patent Right(s) for the filing, prosecution and maintenance of DRG Patent Rights, including all attorney fees, expenses, official and filing fees incurred during the Term for DRG Patent Right(s) ("**Ongoing DRG Patent Costs**"). Notwithstanding the foregoing, for DRG Patent Rights licensed by Penn to more than one licensee, Licensee shall be responsible for payment to Penn of a pro rata share of such documented Ongoing DRG Patent Costs based on the number of licensees for such DRG Patent Rights. No later than [***] prior to the end of each Calendar Year during the Term, Penn shall provide to Licensee, a good faith estimate and budget for the Ongoing DRG Patent Costs anticipated to be incurred for the next Calendar Year and, to the extent applicable, Licensee's proportionate share of such Ongoing DRG Patent Costs. This Section 7.7.2 is subject to Section 7.7.1 above.

1.1.1.3 With respect to DRG Patent Right(s), Licensee shall be subject to Advance Payment. Notwithstanding whether Licensee makes an Advance Payment for any patent action, Licensee shall bear its pro rata share (based on the number of licensees for such DRG Patent Rights) of all DRG Patent Costs with respect to DRG Patent Right(s) as set forth in this Section 7.7.2, above, and shall pay such amounts within [***] of receipt of invoice for such patent actions.

1.1.1.4 Licensee shall also have the right, on a DRG Patent Right-by-DRG Patent Right and country-by-country basis, to (i) elect not to fund at the time of disclosure, or (ii) elect not to continue to fund, in each case (i) and (ii), its pro rata share (as determined pursuant to this Section 7.7 above) of the DRG Patent Costs with respect to any DRG Patent Right(s) in a particular country, which election may be made by Licensee upon [***] prior written notice to Penn ("**DRG Election Notice**"). If Licensee delivers a DRG Election Notice to Penn, following the expiration of such [***] period, Licensee shall have no further obligation to pay Ongoing DRG Patent Costs with respect to any DRG Patent Right identified in such DRG Election Notice in any country identified in such DRG Election Notice and any such Patent Right in any such country shall thereafter be excluded from the DRG Patent Rights.

1.1.3 **Infringement**.

1.1.1.1 If either Party believes that an infringement by a Third Party with respect to any DRG Patent Right is occurring or may potentially occur, the knowledgeable Party will provide the other Party with (a) written notice of such infringement or potential infringement and (b) evidence of such infringement or potential infringement. With respect to DRG Patent Rights, Penn shall have the exclusive right to enforce such Patent Rights and institute suit for Patent Infringement. If Penn institutes such suit, then Licensee may not join such suit without the prior written consent of Penn.

1.1.1.2 Any recovery or settlement received in connection with any suit will be [***].

1.1.1.3 Licensee will reasonably cooperate and assist Penn in litigation proceedings instituted hereunder at Penn's request and expense.

1.1.1.4 Penn shall keep Licensee reasonably informed of the initiation and status of any action to enforce any DRG Patent Rights to which Licensee has rights hereunder.

## Article 8
## CONFIDENTIALITY& PUBLICATION

1.1 **Confidential Information**. Licensee shall not disclose Confidential Information to Penn unless it is reasonably necessary to the performance of a Research Program or otherwise required to perform Licensee's obligations under this Agreement. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, during the Term and for [***] thereafter, the receiving Party (the "**Receiving Party**") and its Affiliates will keep confidential and will not publish or otherwise disclose or use for any purpose any Confidential Information, which is disclosed to it by the other Party (the "**Disclosing Party**") or its Affiliates or otherwise made available to a Receiving Party in the course of performing its obligations or exercising its rights under this Agreement. A Receiving Party shall also have the right to disclose the disclosing Party's Confidential Information to those of the Receiving Party's and its Affiliates' employees, agents and/or consultants who have a need to know such Confidential Information to perform its obligations or exercise its rights under this Agreement; and who have entered into a written agreement with the Receiving Party (or its relevant Affiliate) to be bound by the obligations of confidentiality and non-use at least as protective of such Confidential Information as set forth in this Article 8. In the case of Licensee as the Receiving Party, Licensee and its Affiliates shall have the right to use and disclose Confidential Information of Penn: for the purpose of developing, seeking and obtaining Regulatory Approval for, making, having made, using, selling, offering for sale and/or otherwise commercializing Licensed Products under the License and, if applicable, also the DRG Technology License; and to actual and potential Third Party service providers, sublicensees, other sources of financing and/or acquirers or others on a need-to-know basis under appropriate conditions of confidentiality.

1.2 **Disclosures Required by Law**. In the event a Party is required to make a disclosure under Law or regulation, the order of a court of competent jurisdiction, or the rules of the U.S. Securities and Exchange Commission or other Governmental Body within or outside the United States (including by reason of any securities offering by Licensee), or any stock exchange or listing entity, a Receiving Party shall provide prompt written notice to the Disclosing Party and take all reasonable steps to limit the extent of the disclosure and obtain confidential treatment for any remaining required disclosure.

1.3 **Penn Intellectual Property**. In order to preserve the patentability of Penn intellectual property and to preserve Penn's publication rights, Licensee shall maintain Penn Patent Rights, Research Results and Confidential Information provided by Penn pursuant to a Research Program (whether oral or written) as confidential and shall not disclose such Confidential Information to any Third Party except as permitted under this Article 8 until the publication of such information by Penn or until Penn provides Licensee with written verification that all desirable patentable inventions have been protected, whichever occurs sooner.

1.4 **Licensee Intellectual Property**. In order to preserve the patentability of Licensee's intellectual property and otherwise to preserve Licensee's rights therein and thereto, Penn shall maintain Amicus Technology and Confidential Information provided by Licensee pursuant to a Research Program or otherwise under this Agreement as confidential and shall not disclose such information to any Third Party except as expressly permitted under this Agreement. For the avoidance of doubt, for purposes of this Agreement, all records maintained by Licensee described in Section 5.11 and all Amicus Technology, Progress Reports and Licensee Financial Reports provided by Licensee to Penn under this Agreement, as well as the sequence of any Designated Product, shall be Confidential Information of Licensee.

1.5 **Publications**. Penn shall have the first right to publish, present or otherwise disclose for any purpose Research Results, or other information and material resulting from a Research Program, to the extent any Research Results or other information to be included in any publication, presentation or disclosure exists or was generated by Penn personnel on or prior to [***]; provided, however, that consistent with the Wilson Lab's standard operating procedures for collaborations with commercial third parties, Penn shall provide Licensee the opportunity to review and comment on any proposed manuscripts or any other proposed public disclosure describing work developed under a Research Program that has not previously been disclosed, [***] prior to its submission for publication or first public disclosure for manuscripts and [***] prior to its submission or first public disclosure for abstracts and speaking engagements to (a) determine whether such contains any Licensee Confidential Information and (a) enable Licensee to identify any Penn intellectual property or joint intellectual property that it wishes Penn to file patent applications on or to seek other intellectual property protection for. If within the [***] or [***] review period (i) Licensee notifies Penn in writing that the Licensee requires deletion from the publication or presentation of Licensee Confidential Information, the Parties will cooperate to modify the disclosure to ensure Licensee Confidential Information is not disclosed or (ii) if Licensee requests in writing that publication or presentation be delayed to allow for patent filings or other intellectual property protection on certain items in the proposed publication or presentation, Penn shall delay the publication or presentation for up to [***] to allow for the filing of applicable patent applications.

## Article 9
## REPRESENTATIONS, WARRANTIES AND COVENANTS

1.1 **Mutual Representations and Warranties**. Each Party represents and warrants to the other Party that, as of the Effective Date:

1.1.1 such Party is duly organized and validly existing under the Laws of the jurisdiction of its incorporation or organization;

1.1.2 such Party has taken all action necessary to authorize the execution and delivery of this Agreement and the performance of its obligations under this Agreement;

1.1.3 this Agreement is a legal and valid obligation of such Party, binding upon such Party and enforceable against such Party in accordance with the terms of this Agreement, except as enforcement may be limited by applicable bankruptcy, fraudulent conveyance, insolvency, reorganization,

moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles; and

1.1.4 such Party has all right, power and authority to enter into this Agreement, to perform its obligations under this Agreement.

1.2 **Representations of Penn**. Except as otherwise disclosed by Penn to Licensee, Penn hereby represents:

1.1.1 as of the Effective Date, to Penn's knowledge, Penn's performance of any Research Program and/or the Discovery Program and/or grant of rights to Licensee under this Agreement does not conflict with any agreement between Penn and a Third Party; and

1.1.2 other than licenses granted under the Excluded Penn IP, rights granted to Patent Rights set forth in Exhibit F or the arrangements with Third Parties described in Exhibit F, to Penn's knowledge, Penn has not entered into any arrangement with any Third Party for any Indication prior to the Effective Date which is still in effect and pursuant to which a Third Party has license rights, or has an option to obtain rights, to any Patent Rights conceived or reduced to practice in the Wilson Lab for such Indication.

1.3 **Disclaimer of Representations and Warranties**.

1.1.1 Other than the representations and warranties provided in Section 9.1 above, **PENN MAKES NO REPRESENTATIONS AND WARRANTIES, WHETHER EXPRESS OR IMPLIED, AND EXPLICITLY DISCLAIMS ANY REPRESENTATION AND WARRANTY, INCLUDING WITH RESPECT TO ANY ACCURACY, COMPLETENESS, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, COMMERCIAL UTILITY, NON-INFRINGEMENT OR TITLE FOR THE INTELLECTUAL PROPERTY, PATENT RIGHTS, LICENSE AND ANY LICENSED PRODUCT**.

1.1.2 Furthermore, nothing in this Agreement will be construed as:

(a) A representation or warranty by Penn as to the validity or scope of any Penn Patent Right;

(b) A representation or warranty that anything made, used, sold or otherwise disposed of under the License is or will be free from infringement of patents, copyrights, trademarks or any other forms of intellectual property rights or tangible property rights of Third Parties;

(c) Obligating Penn to bring or prosecute actions or suits against Third Parties for patent, copyright or trademark infringement; and

(d) Conferring by implication, estoppel or otherwise any license or rights under any Patent Rights of Penn other than Penn Patent Rights as defined herein, regardless of whether such Patent Rights are dominant or subordinate to Penn Patent Rights.

1.4 **Covenants of Licensee**.

1.1.1 Licensee and its Affiliates will not, directly or indirectly (including where such is done by a Third Party on behalf of Licensee or its Affiliates) make any Challenge; provided, however, that if any Penn Patent Right is asserted against Licensee or its Affiliate, then such Licensee or its Affiliates is entitled to all and any defenses available to it including challenging the validity or enforceability of such Patent Right.

1.1.2 Licensee will comply in all material respects with all Laws that apply to its activities or obligations under this Agreement. For example, Licensee will comply with applicable United States export laws and regulations. The transfer of certain technical data and commodities may require a

license from the applicable agency of the United States Government and/or written assurances by Licensee that Licensee will not export data or commodities to certain foreign countries without prior approval of the agency.

1.1.3 Licensee will not grant a security interest in the License or this Agreement.

**Article 10**
**INDEMNIFICATION; INSURANCE AND LIMITATION OF LIABILITY**

1.1 **Indemnification by Licensee**.

1.1.1 Licensee shall defend, indemnify and hold Penn and its respective trustees, officers, faculty, students, employees, contractors and agents (the "**Penn Indemnitees**") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorneys' fees), including, without limitation, bodily injury, risk of bodily injury, death and property damage (collectively, "**Liabilities**") to the extent arising out of Third Party claims or suits [***] including:

(a) the gross negligence, recklessness or wrongful intentional acts or omissions of Licensee, its Affiliates or Sublicensees and its or their respective directors, officers, employees and agents, in the performance of the Licensee's obligations or exercise of Licensee's rights under this Agreement;

(b) any material breach of this Agreement by Licensee;

(c) the development, manufacturing or commercialization of Licensed Products (including commercial manufacturing, packaging and labeling of Licensed Products, and all product liability losses of a Licensed Product by or on behalf of Licensee or its Affiliates or Sublicensees); and

(d) any enforcement action or suit brought by Licensee against a Third Party for infringement of Penn Patent Rights or Joint Patent Rights;

provided that Licensee's obligations pursuant to this Section 10.1 shall not apply to the extent such Liabilities and Third Party claims or suits result or arise from [***].

1.1.2 As a condition to a Penn Indemnitee's right to receive indemnification under this Section 10.1, Penn shall: (a) promptly notify Licensee as soon as it becomes aware of a claim or suit for which indemnification may be sought pursuant hereto; (b) fully cooperate, and cause the individual Penn Indemnitees to fully cooperate, with Licensee in the defense, settlement or compromise of such claim or suit; and (c) permit the Licensee to control the defense, settlement or compromise of such claim or suit, including the right to select defense counsel. In no event, however, may Licensee compromise or settle any claim or suit in a manner which (i) admits fault or negligence on the part of Penn or any other Penn Indemnitee; (ii) commits Penn or any other Penn Indemnitee to take, or forbear to take, any action, without the prior written consent of Penn, or (iii) grant any rights under the Penn Patent Rights except for Sublicenses permitted under Article 4. Penn shall fully cooperate, and cause the individual Penn Indemnitees to fully cooperate, with Licensee and its counsel in the course of the defense or settlement of any such suit, claim or demand, such cooperation to include without limitation providing or making available documents, information and witnesses.

1.1.3 Notwithstanding Section 10.1.2 above, a Penn Indemnitee shall be entitled to participate in, but not control, the defense of a Third Party claim or suit subject to indemnification under Section 10.1.1 above and to engage counsel of its own choice for such purpose; provided that such engagement shall be at such Penn Indemnitee's own expense unless a bona fide conflict exists between Licensee and Penn or any other Penn Indemnitee with respect to a claim or suit subject to indemnification hereunder, such that representation by Licensee and Penn or such other Penn Indemnitee by the same legal counsel due to a misalignment of interests or would be prohibited under applicable law, ethical rules or equitable principles, in which case, Licensee will either pay any reasonable, documented out-of-pocket

attorney's fees and litigation expenses of such Penn Indemnitee directly or reimburse Penn within [***] of Licensee's receipt of invoices for such fees and expenses.

1.1.4 In no event shall Licensee be liable under this Section 10.1 for any settlement, compromise or other disposition of a Third Party claim or suit for which a Penn Indemnitee seeks indemnification hereunder and that is reached without the prior written consent of Licensee, such consent not to be unreasonably withheld, conditioned or delayed.

1.2 **Insurance**.

1.1.1 Licensee, at its sole cost and expense, must insure its activities in connection with the exercise of its rights under this Agreement and keep in force and maintain Commercial Form General Liability Insurance (contractual liability included) with at least the following limits:

(a) Each occurrence [***];

(b) General aggregate [***]

***Prior to the commencement of clinical trials, if applicable, involving Licensed Product***:

(c) Clinical trials liability insurance [***]

***Prior to the First Commercial Sale of a Licensed Product***:

(d) Products liability insurance [***]

Penn may review periodically the adequacy of the minimum amounts of insurance for each coverage required by this Section 10.2.1, and has the right to discuss with Licensee adjustments to such limits.

1.1.2 If the above insurance is written on a claims-made form, it shall continue for three (3) years following termination or expiration of this Agreement. The insurance shall have a retroactive date of placement prior to or coinciding with the Effective Date of this Agreement.

1.1.3 Licensee expressly understands, however, that the coverages and limits in Section 10.2.1 do not in any way limit Licensee's liability or indemnification obligations. Licensee's insurance will:

(a) Be issued by an insurance carrier with an A.M. Best rating of "A" or better;

(b) Provide for thirty (30) day advance written notice to Penn of any modification;

(c) State that Penn is endorsed as an additional insured with respect to the coverages in Section 10.2.1; and

(d) Include a provision that the coverages will be primary and will not participate with nor will be excess over any valid and collective insurance or program of self insurance carried or maintained by Penn.

1.1.4 Licensee must furnish to Penn with (a) valid certificate of insurance evidencing compliance with all requirements of this Agreement and (b) additional insured endorsements for Licensee's applicable policies naming "The Trustees of the University of Pennsylvania" as an additional insured. Licensee must furnish both documents within thirty (30) days of the Effective Date, once per year thereafter and at any time there is a modification in such insurance.

1.3 **LIMITATION OF LIABILITY**. [***], IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER OR ANY OF ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES, INCLUDING LOSS OF PROFITS OR OPPORTUNITY, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE ARISING OUT OF OR RELATING TO THIS AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREIN OR ANY BREACH HEREOF; PROVIDED THAT NOTHING IN THIS SECTION 10.3 SHALL BE DEEMED TO LIMIT LICENSEE'S INDEMNIFICATION OBLIGATIONS UNDER SECTION 10.1.

## Article 11
## TERM AND TERMINATION

1.1 **Term**. The term of this Agreement (the "**Term**") shall commence on the Effective Date and, unless terminated sooner as provided below, shall continue in full force and effect on a country- by-country and Licensed Product-by-Licensed Product basis until [***]. Following expiration of the [***] (but not earlier termination) in a particular country, the license to Licensed Know-How and Licensed Discovery Know-How in such country for Licensed Products for the applicable Indication in the Field of Use as set forth in Section 4.1 will become perpetual and fully paid-up.

1.2 **Termination of this Agreement for Convenience**. Subject to Section 11.4, Licensee may, at its convenience, terminate this entire Agreement or on an Indication-by-Indication basis, by providing at least [***] prior written notice to Penn of such intention to terminate.

1.3 **Termination For Cause**.

1.1.1 In addition to all other remedies available to it, Penn may terminate this Agreement upon [***] written notice if Licensee materially fails to comply with any Laws that apply to its activities or obligations under this Agreement and that can be remedied and Licensee fails to remedy such lack of compliance within such [***] period, (b) upon [***] written notice, if Licensee grants a security interest in this Agreement or any of the rights granted herein and does not revoke such grant prior to the expiration of such [***] period, or (d) upon written notice, if Licensee breaches Section 9.4.1 and does not withdraw or discontinue the applicable Challenge within [***] of such notice.

1.1.2 If either Party materially breaches any of its material obligations under this Agreement, the non-breaching Party may give to the breaching Party a written notice specifying the nature of the default, requiring it to cure such breach, and stating its intention to terminate this Agreement. If such breach is not cured within [***] of such notice (for non-payment), and [***] of such notice for all other material breaches, such termination shall become effective upon a notice of termination by the terminating Party thereafter; provide that if there is a good faith dispute as to the existence of a material breach, such [***] or [***] period may be extended by mutual agreement of the Parties to allow the Parties additional time to continue good faith discussions to resolve the dispute. To the extent Licensee's material breach relates solely to an Indication, Penn's right to terminate the Licensee's rights under this Agreement will be limited to such Indication.

1.1.3 Either Party may terminate this Agreement, upon written notice if, at any time, the other Party files in any court or agency pursuant to any statute or regulation of any state, country or jurisdiction, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of such Party or of its assets, or if such Party proposes a written agreement of composition or extension of its debts, or if such Party is served with an involuntary petition against it, filed in any insolvency proceeding, and such petition is not dismissed within [***] after the filing thereof, or if such Party proposes or is a party to any dissolution or liquidation, or if such Party makes an assignment for the benefit of its creditors of all or substantially all its assets.

1.4 **Effects of Termination**.

1.1.1 Notwithstanding the termination or expiration of this Agreement, the following provisions shall survive: Sections [***] and Articles [***].

1.1.2 Termination of this Agreement shall not relieve the Parties of any obligation or liability that, at the time of termination, has already accrued hereunder, or which is attributable to a period prior to the effective date of such termination. Termination of this Agreement shall not preclude either Party from pursuing all rights and remedies it may have hereunder or at Law or in equity with respect to any breach of this Agreement nor prejudice either Party's right to obtain performance of any obligation.

1.1.3 If this Agreement is terminated for any reason, all outstanding Sublicenses (including all Sublicense Documents for each Sublicense) not in default shall survive, provided that each such Sublicensee agrees in writing to be bound by the applicable terms of this Agreement with respect to the activities of such Sublicensee under such Sublicense. The duties and obligations of Penn under any surviving Sublicenses will not be greater than the duties of Penn under this Agreement, and the rights of Penn under any surviving Sublicenses will not be less than the rights of Penn under this Agreement, including all financial consideration and other rights of Penn.

1.1.4 Upon termination of this Agreement and subject to Section 11.3.2, Licensee, its Affiliates and Sublicensees whose rights do not survive termination of this Agreement will promptly cease selling the Licensed Product(s) subject to such termination. Each Party will return (or destroy, as directed by the other Party) all data, files, records and other materials containing or comprising the other Party's Confidential Information with respect to this Agreement, except to the extent such Confidential Information is necessary or useful to conduct activities in connection with surviving portions of or rights pursuant to this Agreement. Notwithstanding the foregoing, the Parties will be permitted to retain one copy of such data, files, records, and other materials for archival and legal compliance purposes.

## Article 12
## ADDITIONAL PROVISIONS

1.1 **Relationship of the Parties**. Nothing in this Agreement is intended or shall be deemed, for financial, tax, legal or other purposes, to constitute a partnership, agency, joint venture, fiduciary or employer-employee relationship between the Parties. The Parties are independent contractors and at no time will either Party make commitments or incur any charges or expenses for or on behalf of the other Party.

1.2 **Expenses**. Except as otherwise provided in this Agreement, each Party shall pay its own expenses and costs incidental to the preparation of this Agreement and to the consummation of the transactions contemplated hereby.

1.3 **Use of Names**. Licensee, its Affiliates and Sublicensees may not use the name, logo, seal, trademark, or service mark (including any adaptation of them) of Penn or any Penn school, organization, employee, student or representative in any press release, advertising, promotional or sales literature, without the prior written consent of Penn. Notwithstanding the foregoing, Licensee may use the name of Penn in a non-misleading and factual manner solely in (a) executive summaries, business plans, offering memoranda and other similar documents used by Licensee for the purpose of raising financing, including for the operations of Licensee as related to a Licensed Product, or entering into commercial contracts with Third Parties, but in such case only to the extent necessary to inform a reader that the Penn Patent Rights has been licensed by Licensee from Penn, and (b) any securities reports required to be filed with the Securities and Exchange Commission or any other disclosures required under applicable Laws (including securities regulations).

1.4 **No Discrimination**. Neither Penn nor Licensee will discriminate against any employee or applicant for employment because of race, color, sex, sexual orientation, age, religion, national or ethnic origin, handicap, or veteran status.

1.5 **Successors and Assignment**.

1.1.1 The terms and provisions hereof shall inure to the benefit of, and be binding upon, the Parties and their respective successors and permitted assigns.

1.1.2 Neither Party may assign or transfer this Agreement or any of its rights or obligations created hereunder, by operation of law or otherwise, without the prior written consent of the other Party. Notwithstanding the foregoing, without the other Party's consent, either Party shall have the right to assign any of its rights or obligations under this Agreement, or to transfer this Agreement, to: (a) any of its Affiliates, [***]; or (b) a Third Party in connection with a merger, acquisition of all or substantially all of the business or assets of such Party (whether by sale of stock or assets), consolidation, change of control or other similar transaction; provided that such third party is bound by the terms of this Agreement, by operation of law or otherwise.

1.1.3 Any assignment not in accordance with this Section 12.5 shall be null and void.

1.6 **Further Actions**. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

1.7 **Entire Agreement of the Parties; Amendments**. This Agreement, the Exhibits and Appendices or Schedules hereto constitute and contain the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersede any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of this Agreement shall be valid or effective unless made in a writing referencing this Agreement and signed by a duly authorized officer of each Party.

1.8 **Governing Law**. This Agreement shall be governed by and interpreted in accordance with the laws of the Commonwealth of Pennsylvania, excluding application of any conflict of laws principles that would require application of the law of a jurisdiction outside of the Commonwealth of Pennsylvania.

1.9 **Dispute Resolution**. If a dispute arises between the Parties concerning this Agreement, then the Parties will confer, as soon as practicable, in an attempt to resolve the dispute. Prior to initiation of outside dispute resolution or termination of this Agreement for a material breach, each Party shall escalate such issue to the Chief Executive Officer of Licensee and Dean of Medicine for Penn and such parties will engage in good faith discussions with regard to the applicable dispute within fifteen (15) days. If the Parties are unable to resolve such dispute amicably through good faith discussion and such escalation within thirty (30) days, then either Party may submit to the exclusive jurisdiction of, and venue in, the state and Federal courts located in the Eastern District of Pennsylvania.

1.10 **Notices and Deliveries**. Any notice, request, approval or consent required or permitted to be given under this Agreement shall be in writing and directed to a Party at its address or, in the case of Penn providing notice to Licensee, email address shown below or such other address or email address as such Party shall have last given by notice to the other Party. A notice will be deemed received: if delivered personally, on the date of delivery; if mailed, five (5) days after deposit in the United States mail; if sent via courier, one (1) business day after deposit with the courier service; or, in the case of Penn providing notice to Licensee, if sent via email, upon receipt of confirmation of transmission (i.e., a read receipt e-mail is received by the sender) provided that a confirming copy of such notice is sent by certified mail, postage prepaid, return receipt requested.

***For Penn***

Penn Center for Innovation University of Pennsylvania
3600 Civic Center Blvd.
9th Floor Philadelphia, PA 19104
Attention: Managing Director

***with a copy to***:

University of Pennsylvania Office of General Counsel
2929 Walnut St., Suite 400
Philadelphia, PA 19104
Attention: General Counsel

***For Licensee***:

Amicus Therapeutics, Inc.
3675 Market St.
Philadelphia, PA 19104
Attention: Chief Legal Officer
Email: GCOffice@amicusrx.com

***with a copy to***:

Wilson Sonsini Goodrich & Rosati
12235 El Camino Real
San Diego CA 92130
Attention: Miranda Biven
Email: mbiven@wsgr.com

1.11 **Waiver**. A waiver by either Party of any of the terms and conditions of this Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any other term or condition hereof. All rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either Party.

1.12 **Severability**. When possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under law, but if any provision of this Agreement is held to be prohibited by or invalid under law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement. The Parties shall make a good faith effort to replace the invalid or unenforceable provision with a valid one which in its economic effect is most consistent with the invalid or unenforceable provision.

1.13 **Interpretation**. The words “include,” “includes” and “including” shall be deemed to be followed by the phrase “without limitation.” All references herein to Articles, Sections, Schedules and Exhibits shall be deemed references to Articles and Sections of, Schedules and Exhibits to, this Agreement unless the context shall otherwise require. Except as otherwise expressly provided herein, all terms of an accounting or financial nature shall be construed in accordance with GAAP, as in effect from time to time. Unless the context otherwise requires, countries shall include territories. References to any specific Law or article, section or other division thereof, shall be deemed to include the then-current amendments or any replacement Law thereto.

1.14 **Counterparts**. This Agreement may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A facsimile or a portable document format (PDF) copy of this Agreement, including the signature pages, will be deemed an original.

**[SIGNATURE PAGE FOLLOWS]**

**IN WITNESS WHEREOF**, the Parties have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

**AMICUS THERAPEUTICS, INC.**

**THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA**

By: /s/ John Swartley
Name: John Swartley
Title: AVP and Managing Director, PCI

By: /s/ Bradley Campbell
Name: Bradley Campbell
Title: President & CEO

**Read and Acknowledged:**

By: /s/ Jim Wilson
Name: Jim Wilson
Title: Professor

List of Exhibits

[***]

**Exhibit 1.14A**

[***]

**Exhibit 1.14B**

[***]

**Exhibit 1.30**

[***]

**Exhibit 1.37**

[***]

**Exhibit 1.44**

[***]

**Exhibit 1.54**

[***]

**Exhibit 1.55**

[***]

**Exhibit A**

[***]

**Exhibit B**

[***]

**Exhibit C**

[***]

**Exhibit D**

[***]

**Exhibit E**

[***]

**Exhibit F**

[***]

**Exhibit Y**

[***]

**Exhibit Z**

[***]

**PORTIONS HEREIN IDENTIFIED BY [***] HAVE BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE THE EXCLUDED INFORMATION IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.**

# MUTUAL TERMINATION AGREEMENT

THIS MUTUAL TERMINATION AGREEMENT (this "**Termination Agreement**") is made and entered into as of December 22, 2022 (the "**Termination Effective Date**"), by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), and Amicus Therapeutics, Inc., a corporation organized under the laws of the state of Delaware ("**Licensee**"). Penn and Licensee may be referred to herein as a "**Party**" or, collectively, as "**Parties**." Capitalized terms used herein but not otherwise defined shall have the meanings ascribed to them in the Collaboration Agreement (as defined below).

## RECITALS

WHEREAS, the Parties entered into that certain Amended and Restated Research, Collaboration & License Agreement dated May 28, 2019, as amended through the First Amendment dated December 20, 2019, the Second Amendment dated March 26, 2020, the Third Amendment dated December 3, 2020, the Fourth Amendment dated December 23, 2020, the Fifth Amendment dated April 6, 2021, the Sixth Amendment dated August 1, 2021, and the Seventh Amendment effective as of September 28, 2021 (collectively, the "**Collaboration Agreement**"), pursuant to which, among other things, Penn and Licensee were conducting a research program for the pre-clinical development of certain gene therapy products intended to treat certain specified indications;

WHEREAS, the Parties entered into that certain Process and Development Agreement dated March 26, 2020, as amended through the First Amendment dated September 28, 2021 (the "**PD Amendment**") (collectively, the "**PD Agreement**"), pursuant to which, among other things, Penn and Licensee were conducting a research program for the development and/or optimization of manufacturing technology for gene therapy products;

WHEREAS, the Parties hereby agree to terminate the Collaboration Agreement and any further activities pursuant to the PD Agreement, in each case, effective as of the Termination Effective Date; and

WHEREAS, in conjunction with this Termination Agreement, the Parties are entering into that certain License Agreement, dated as of the date hereof, pursuant to which Licensee will have rights to research, develop and commercialize products for Pompe Disease and Fabry Disease ("**License Agreement**").

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants contained herein, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

## ARTICLE 1
## TERMINATION OF THE COLLABORATION AGREEMENT

**1.1 Termination**. Subject to the terms and conditions of this Termination Agreement, the Collaboration Agreement and the PD Agreement are each hereby terminated as of the Termination Effective Date and, as a result of such termination, the Parties hereby acknowledge and agree that, except as expressly provided for under this Termination Agreement, their respective rights and obligations under each of the Collaboration Agreement and the PD Agreement are hereby terminated as of the Termination Effective Date and that both Parties shall have no further liability to each other under the Collaboration

Agreement or the PD Agreement, respectively, nor with respect to the Collaboration Agreement or the PD Agreement, except as set forth in this Termination Agreement.

**1.2 Effect of Termination; Survival**. Upon the Termination Effective Date, all rights and obligations of the Parties under the Collaboration Agreement shall terminate, including all of those referenced in Section 12.4 of the Collaboration Agreement, except those described in the following Articles and Sections of the Collaboration Agreement and, to the extent applicable, for the period of time specified in the applicable provision: Sections [***]. Upon the Termination Effective Date, all rights and obligations of the Parties under the PD Agreement shall terminate, including all of those referenced in Section 10.4 of the PD Agreement, except those rights, licenses and obligations described in the following Articles and Sections of the PD Agreement: Sections [***] and Articles [***]. The Parties acknowledge and agree that no Licensee PD Patent Rights, Licensee PD Know-How, and Joint PD Patent Rights were generated during the term of the PD Agreement.

**1.3 Return of Penn Materials**. Licensee shall deliver to Penn all materials, reports and information listed on Schedule 1.3 by [***] or by such later date as may be specified on Schedule 1.3 with respect to particular items.

## ARTICLE 2
## LICENSES

**2.1 Termination of License Grants under Collaboration Agreement and PD Agreement**. Subject to any licenses granted by Penn to Licensee pursuant to that certain License Agreement, dated as of the Termination Effective Date, by and between the Parties for the completion of certain activities related to Pompe and Fabry diseases and the grant of rights by Penn to Licensee for continued research, development and commercialization of products for Pompe and Fabry, all licenses granted by Penn to Licensee in connection with the Collaboration Agreement and PD Agreement are hereby terminated effective as of the Termination Effective Date; provided that this Section 2.1 shall not be deemed to modify or limit those rights and obligations of each party under the Collaboration Agreement or the PD Agreement specified to survive termination pursuant to Section 1.2 of this Agreement.

**2.2 Pilot Studies Reports and License Grants to Licensee**.

**2.2.1** The Parties acknowledge and agree that, as of the Termination Effective Date, Penn has completed under the Collaboration Agreement certain Pilot Studies (as defined in the Collaboration Agreement) funded by Licensee and related to Duchenne muscular dystrophy ("**DMD**") and Angelman Syndrome (the "**DMD Study**" and the "**Angelman Study**"). Within [***] after the Termination Effective Date, and solely to the extent not already provided, Penn shall deliver to Licensee a complete and accurate, to the knowledge of Penn, copy of all datasets and reports arising out of, and detailing the results of, each of the DMD Study(ies) (the "**DMD Results**") and the Angelman Study(ies) (the "**Angelman Results**"), as further described on Schedule 3.2(a).

**2.2.2** Subject to the terms and conditions of this Termination Agreement (including Section 2.2.4 below), Penn hereby grants to Licensee (a) a non-exclusive, transferable (in accordance with Section 6.4), sublicensable (in accordance with this Section 2.2), royalty-free, fully paid-up right and license under the DMD Results (and any intellectual property rights therein or arising therefrom (including Patent Rights)) for internal research purposes and (b) a non-exclusive, transferable (in accordance with Section 6.4), sublicensable (in accordance with this Section 2.2), royalty-free, fully paid-up right and license under the Angelman Results (and any intellectual property rights therein or arising therefrom (including Patent Rights)) for internal research purposes. Penn acknowledges and agrees that "internal research purposes" shall include the right for Licensee to extend the licenses in clauses (a) and/or (b) of this Section 2.2.2 to Licensee's Affiliates and also to Third Party service providers who are performing activities

for and on behalf of Licensee and/or its Affiliates for the purposes of such Affiliate or Third Party performing any such activities.

**2.2.3** Licensee will have the right to extend any and all of its rights and licenses under Section 2.2.2 above to its Affiliate(s), [***] provided that Licensee shall remain liable for all actions and omissions of its Affiliate and the terms of such extension shall contain a requirement for such Affiliate to comply with the terms contained herein relevant to such license grant. In addition, Licensee will have the right to grant and authorize sublicenses under Licensee's rights and licenses granted pursuant to Section 2.2.2, as follows and [***], to Third Parties (and their Affiliates) that are (i) Service Provider Sublicensees (as defined in the Collaboration Agreement) or (ii) if such Third Parties (and/or their Affiliates) also obtain a license from Licensee or its Affiliate under other intellectual property owned or controlled by Licensee or its Affiliate to research, develop, manufacture and/or commercialize gene therapy products for the treatment and/or prevention of DMD or Angelman Syndrome, as applicable. Each sublicense to a Third Party shall: (x) be in writing; and (y) be subject and subordinate to, and consistent with, the terms and conditions of this Termination Agreement (and Sections 5.6.2, 5.6.3, 5.6.4, 5.6.5, and 5.6.6 of the Collaboration Agreement, as applicable). Licensee shall remain responsible to Penn for all activities of its Affiliates and/or any Third Parties (or their respective Affiliates) that obtain rights to the DMD Results and/or the Angelman Results pursuant to this Section 2.2, to the same extent as if such activities had been undertaken by Licensee itself.

**2.2.4** For clarity, Confidential Information (as such term is defined in the Collaboration Agreement) of Penn included in the DMD Results and the Angelman Results shall be subject to the provisions of Publication and Confidentiality set forth in Article 9 of the Collaboration Agreement; it being understood that references in Article 9 to the Collaboration Agreement shall be deemed to be references to this Agreement and accordingly, Licensee shall have the right to use and disclose the DMD results and Angelman Results for the purposes of exercising its rights and licenses with respect to the same under this Agreement, subject to Section 6.1 below (i.e., subject to the confidentiality and publication obligations set forth in Article 9 of the Collaboration Agreement incorporated herein by reference under Section 6.1). Licensee shall not, and shall require that all sublicensees pursuant to Section 2.2.3 above shall not, include any DMD Results or Angelman Results in any patent application or publication without Penn's review and approval (such approval not to be unreasonably withheld, conditioned or delayed).

**2.2.5 Intentionally Omitted**.

**2.2.6 Indemnity**.

2.2.6.1 Licensee shall defend, indemnify and hold Penn and its respective trustees, officers, faculty, students, employees, contractors and agents (the "**Penn Indemnitees**") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorneys' fees), including, without limitation, bodily injury, risk of bodily injury, death and property damage (collectively, "**Liabilities**") to the extent arising out of Third Party claims or suits arising from (a) the gross negligence, recklessness or wrongful intentional acts or omissions of Licensee, its Affiliates or Sublicensees and its or their respective directors, officers, employees and agents, in the performance of the Licensee's obligations or exercise of Licensee's rights under this Agreement; (b) the material breach of this Agreement by Licensee; and (c) the development, manufacture and/or commercialization by, or under the authority of, Licensee of any gene therapy products that are

intended for use in Angelman Syndrome or DMD and use the DMD Results and/or Angelman Results licensed to Licensee hereunder; provided that [***].

2.2.6.2 As a condition to a Penn Indemnitee's right to receive indemnification under this Section 2.2.6.1, Penn shall: (a) promptly notify Licensee as soon as it becomes aware of a claim or suit for which indemnification may be sought pursuant hereto; (b) fully cooperate, and cause the individual Penn Indemnitees to fully cooperate, with Licensee in the defense, settlement or compromise of such claim or suit; and (c) permit the Licensee to control the defense, settlement or compromise of such claim or suit, including the right to select defense counsel. In no event, however, may Licensee compromise or settle any claim or suit in a manner which (i) admits fault or negligence on the part of Penn or any other Penn Indemnitee; (ii) commits Penn or any other Penn Indemnitee to take, or forbear to take, any action, without the prior written consent of Penn, or (iii) grant any rights under the Research Results except for Sublicenses permitted hereunder. Penn shall fully cooperate, and cause the individual Penn Indemnitees to fully cooperate, with Licensee and its counsel in the course of the defense or settlement of any such suit, claim or demand, such cooperation to include without limitation providing or making available documents, information and witnesses.

2.2.6.3 Notwithstanding the above, a Penn Indemnitee shall be entitled to participate in, but not control, the defense of a Third Party claim or suit subject to indemnification under this Section 2.2.6 and to engage counsel of its own choice for such purpose; provided that such engagement shall be at such Penn Indemnitee's own expense unless a bona fide conflict exists between Licensee and Penn or any other Penn Indemnitee with respect to a claim or suit subject to indemnification hereunder, such that representation by Licensee and Penn or such other Penn Indemnitee by the same legal counsel due to a misalignment of interests or would be prohibited under applicable law, ethical rules or equitable principles, in which case, Licensee will either pay any reasonable, documented out-of-pocket attorney's fees and litigation expenses of such Penn Indemnitee directly or reimburse Penn within [***] of Licensee's receipt of invoices for such fees and expenses.

2.2.6.4 In no event shall Licensee be liable under this Section 2.2.6 for any settlement, compromise or other disposition of a Third Party claim or suit for which a Penn Indemnitee seeks indemnification hereunder and that is reached without the prior written consent of Licensee, such consent not to be unreasonably withheld, conditioned or delayed.

**2.3 Option Grants to Penn**.

**2.3.1** CDKL5. In the event that Licensee does not enter into an agreement granting a license, assignment or other rights to CDKL5 Technology [***] within [***] of the Termination Effective Date, Licensee shall provide written notice to Penn ("**CDKL5 Notice**") and Penn shall have the right to obtain a license, assignment or other rights to such CDKL5 Technology on terms and conditions to be agreed upon; provided that [***]. Penn may exercise such option by providing written notice ("**CDKL5 Exercise Notice**") to Licensee within [***] of receipt of the CDKL5 Notice from Licensee. If applicable, the Parties would negotiate in good faith for a period of [***] from Licensee's receipt of Penn's CDKL5 Exercise Notice ("**CDKL5 Negotiation Period**"). In the event the Parties do not enter

into an agreement with respect to the CDKL5 Technology prior to the expiration of the CDKL5 Negotiation Period, Licensee shall [***].

**2.3.2** MPS IIIA. Licensee hereby grants to Penn, subject to the terms and conditions of this Agreement (including without limitation Section 2.4.5 below), an option to acquire [***] right and license, with the right to grant sublicenses (on equivalent terms to Licensee's rights to sublicense under the License Agreement), under the MPS IIIA Technology to research, have researched, develop, have developed, make, have made, use, sell, offer for sale, import and export an Amicus MPS IIIA Candidate or another gene therapy product that contains the same transgene as the Amicus MPS IIIA Candidate for treatment and/or prevention of MPS IIIA (collectively, the "**MPS IIIA Products**"). Penn may exercise such option by providing written notice ("**MPS IIIA Exercise Notice**") to Licensee no later than the [***]. Upon Penn's exercise of the option in accordance with this Section 2.3.2, the Parties would negotiate [***] in good faith for a period of [***]. If Penn does not issue an MPS IIIA Exercise Notice in accordance with this Section 2.3.2 prior to the expiration of the [***] or, if Penn issues an MPS IIIA Exercise Notice in accordance with this Section 2.3.2 and the Parties do not enter into an MPS IIIA License with respect to the MPS IIIA Technology prior to the expiration of the [***], then Licensee and its Affiliates shall have no further obligations to Penn, and Penn shall have no further rights with respect to, any MPS IIIA Technology. For clarity, (a) certain intellectual property pertaining to the Amicus MPS IIIA Candidate is jointly owned by the Parties and nothing contained in this Section 2.3.2 shall waive, alter, amend or revise any Penn ownership rights in such intellectual property pertaining to the Amicus MPSIIIA Candidate, and (b) such MPS IIIA License shall not be effective until execution of an MPS IIIA Penn Sublicense contemporaneously with, or promptly after, execution of an MPS IIIA License (as such timing may be set forth in the MPS IIIA License).

**2.3.3** Definitions

(a) "**Amicus MPS IIIA Candidate**" means Licensee's gene therapy product as described in Schedule 2.3.3(a).

(b) "**Affiliate**" means with respect to an entity, any corporation or other business entity that controls, is controlled by or is under common control with such entity, but only for so long as such control exists. For the purposes of this Section 2.3.3(b), the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the affirmative power, either directly or indirectly through one or more intermediaries, to direct the management and policies of such entity, whether by the ownership of more than fifty percent (50%) of the voting stock of such entity, or by contract or otherwise.

(c) "**CDKL5 Technology**" means [***]. The [***] included in the CDKL5 Technology are set forth on Schedule 2.3.3(c).

(d) "**Controlled**" means, with respect to intellectual property rights, that Licensee or one of its Affiliates owns or has a license or sublicense to such intellectual property rights and has the ability to provide to, grant a license or sublicense to, or assign its right, title and interest in and to, such intellectual property rights as provided for in this Termination Agreement without violating the terms of any other agreement or other arrangement with any third party.

(e) "**Know-How**" means intellectual property, data, results, pre-clinical and clinical protocols and study data, chemical structures, chemical sequences, information, inventions, formulas, techniques, methods, processes, procedures and developments. "Know-How" does not include any of the foregoing claimed in a Patent Right Controlled by Licensee.

(f) "**MPS IIIA**" means Mucopolysaccharidosis Type IIIA.

(g) "**MPS IIIA Technology**" means [***], as identified on Schedule 2.3.3(g). For clarity, MPS IIIA Technology includes [***].

(h) "**MPS IIIA Upstream Agreement**" means [***].

(i) "**Patent Rights**" means (i) patents and patent applications, together with any unlisted patents and patent applications claiming priority thereto, and any continuations, continuations-in-part (to the extent related directly to the subject matter of the parent application), reissues, reexamination certificates, substitutions, divisionals, supplementary protection certificates, renewals, registrations, extensions including all confirmations, revalidations, patents of addition, PCTs, and pediatric exclusivity periods and all foreign counterparts thereof, and any patents issued or issuing with respect to any of the foregoing and (ii) all official correspondence relating to the foregoing.

**2.1 Representations, Warranties and Covenants**.

**2.4.1** Licensee represents and warrants to Penn that, as of the Termination Effective Date, Licensee has the right, power and authority to grant to Penn the rights granted to Penn pursuant to Section 2.3 with respect to the MPS IIIA Upstream Agreement. In particular, as of the Termination Effective Date, the grant of such rights requires no consent, waiver or other action by any party (other than Licensee) to the MPS IIIA Upstream Agreement and the rights and obligations of Penn set forth in Sections 2.3.1 and 2.3.2 of this Termination Agreement do not contravene nor are they inconsistent with or conflict with the terms of the MPS IIIA Upstream Agreement.

**2.4.2** Licensee represents and warrants to Penn that, as of the Termination Effective Date: (a) the MPSIIIA Upstream Agreement constitutes all agreements between Licensee and a Third Party pursuant to which Licensee has licensed, or otherwise obtained rights with respect to, the Amicus MPS IIIA Candidate (b) Licensee has provided to Penn a redacted copy of the MPS IIIA Upstream Agreement, as amended as of the date hereof, containing those provisions of the MPS IIIA Upstream Agreement relevant to Penn's rights and obligations under Section 2.3 above, (c) the MPS IIIA Upstream Agreement is in full force and effect; (d) Licensee is not in breach or default in the performance of its obligations under the MPS IIIA Upstream Agreement; (e) Licensee has not received any notice from any third party of any breach, default or non-compliance of Licensee under the terms of the MPS IIIA Upstream Agreement relating to the MPS IIIA Technology; and (f) there have been no amendments or other modification to the MPS IIIA Upstream Agreement relating to the MPS IIIA Technology, except as have been disclosed to Penn in writing.

**2.4.3** As of the Termination Effective Date, Licensee represents and warrants to Penn that (a) Licensee does not Control any Know-How or Patent Rights covering the Amicus MPS IIIA Candidate other than Patent Rights included in the MPS IIIA Technology and (b) Licensee is not actually aware of any intellectual property

that is Controlled by Amicus and pertains to the Amicus MPS IIIA Candidate other than the MPS IIIA Technotelogy and any Joint Patent Rights.

**2.4.4** [***].

**2.4.5** To the extent that Penn becomes aware of and/or Licensee identifies, in either case, after the Termination Effective Date, any information or materials [***], Penn will use [***]efforts to provide such information or materials to Licensee promptly following a written request by Licensee to do so.

**2.4.6** It is understood that the [***] may require that particular provisions be incorporated into an agreement pursuant to which [***]. The requirements of any such provisions in the [***] are set out on [***] attached hereto. In the event Licensee and Penn agree to the terms of a license as described in Section 2.3.2, Penn [***].

**2.4.7** Prior to the expiration of Penn's option to the MPS IIIA Technology pursuant to Section 2.3.2 above, Licensee shall not amend or waive, or take any action or omit to taking any action that would alter, in any material respect any of Licensee's rights under the MPS IIIA Upstream Agreement in any manner that materially adversely affects, or would reasonably be expected to materially adversely affect, Penn's rights and benefits under Section 2.3.

**2.2 Mouse License**. Commencing on the Termination Effective Date and continuing until the [***] anniversary thereof, Licensee hereby authorizes Penn and any Third Party acting for, or on behalf of, Penn to use for research purposes [***].

## ARTICLE 3
## FINANCIALS

**3.1 Discovery Support Amount**. In partial consideration for Penn agreeing to enter into this Termination Agreement and in satisfaction in full of Licensee's obligation pursuant to Section 12.4.4(c) of the Collaboration Agreement, Licensee hereby agrees to, and shall, pay to Penn a certain unpaid portion of the Discovery Support Amount (as defined in the Collaboration Agreement) in the total amount of [***] (the "**Remaining Discovery Support Amount**"), which amount shall be payable by Licensee to Penn on or prior to [***].

**3.2 Research Program Wind-Down Payment**. In partial consideration for Penn agreeing to enter into this Termination Agreement and in satisfaction in full of Licensee's obligations pursuant to Section 12.4.4(a)-(b) of the Collaboration Agreement related to the Research Support Amount and wind-down costs related thereto, Licensee hereby agrees to, and shall, make a payment to Penn in the amount of [***] ("**Research Program Wind-Down Payment**") in accordance with the following payment schedule: [***].

**3.3 Payment Procedures**. Sections 6.6, 6.8, 6.9 and 6.13 of the Collaboration Agreement shall govern the payments to be made by Licensee to Penn pursuant to Sections 3.1, 3.2 and 3.4 of this Termination Agreement.

**3.4 Outstanding Patent Costs and Alliance Management Fee**. Licensee shall: (a) within [***] after receipt of applicable invoice(s), pay Penn all unreimbursed Patent Costs incurred from November 1, 2022 through the Termination Effective Date; (b) by [***], pay all Patents Costs under [***]; (c) by [***], pay Penn the [***].

**3.5 No Other Amounts Payable by Penn or Licensee**. Licensee hereby acknowledges and agrees that no amounts are due or payable by Penn to Licensee in connection with the Collaboration Agreement or the PD Agreement, including, without limitation, [***]. Further, [***] except for those

amounts specified in Sections 3.1, 3.2 and 3.4 above and excluding any costs associated with any patent rights due under the License Agreement with respect to Penn Patent Rights pertaining to Fabry Disease or Pompe Disease, no amounts are due or payable by Licensee to Penn in connection with the Collaboration Agreement or the PD Agreement as of the Termination Effective Date. Penn and Licensee mutually agree that this Section 3.5 does not include reference to any payments that come due under the License Agreement.

## ARTICLE 4
## GENERAL REPRESENTATIONS AND WARRANTIES; DISCLAIMERS; LIMITATION OF LIABILITY

**4.1** Each Party represents and warrants to the other Party that, as of the Termination Effective Date:

**4.1.1** such Party is duly organized and validly existing under the laws of the jurisdiction of its incorporation or organization;

**4.1.2** such Party has taken all action necessary to authorize the execution and delivery of this Termination Agreement and the performance of its obligations under this Termination Agreement;

**4.1.3** this Termination Agreement is a legal and valid obligation of such Party, binding upon such Party and enforceable against such Party in accordance with the terms of this Termination Agreement, except as enforcement may be limited by applicable bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles; and

**4.1.4** such Party has all right, power and authority to enter into this Termination Agreement, to perform its obligations under this Termination Agreement.

**4.2** EXCEPT FOR THE EXPRESS REPRESENTATIONS AND WARRANTIES SET FORTH IN SECTION 2.4 AND THIS ARTICLE 4, (A) NEITHER PARTY HERETO NOR ANY PERSON ON SUCH PARTY'S BEHALF HAS MADE OR MAKES ANY EXPRESS OR IMPLIED REPRESENTATION OR WARRANTY WHATSOEVER, EITHER ORAL OR WRITTEN, WHETHER ARISING BY LAW, COURSE OF DEALING, COURSE OF PERFORMANCE, USAGE OF TRADE OR OTHERWISE, ALL OF WHICH ARE EXPRESSLY DISCLAIMED, AND (B) EACH PARTY HERETO ACKNOWLEDGES THAT, IN ENTERING INTO THIS TERMINATION AGREEMENT, IT HAS NOT RELIED UPON ANY REPRESENTATION OR WARRANTY MADE BY THE OTHER PARTY, OR ANY OTHER PERSON ON SUCH OTHER PARTY'S BEHALF, EXCEPT AS SPECIFICALLY PROVIDED IN SECTION 2.4 AND THIS ARTICLE 4.

**4.3** **LIMITATION OF LIABILITY**. IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER OR ANY OF ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES, INCLUDING LOSS OF PROFITS OR OPPORTUNITY, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE ARISING OUT OF OR RELATING TO THIS TERMINATION AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREIN OR ANY BREACH HEREOF; PROVIDED THAT NOTHING IN THIS SECTION 4.3 SHALL BE DEEMED TO LIMIT (A) THE INDEMNIFICATION OBLIGATIONS UNDER SECTION 11.1 OF LICENSEE UNDER THE LICENSE AGREEMENT; OR (B) THE INDEMNIFICATION OR OTHER OBLIGATIONS OF PENN (IF ANY) OR ANY (SUB)LICENSEE OF PENN IF PENN AND A (SUB)LICENSEE EXECUTE AN AGREEMENT(S) PURSUANT TO WHICH PENN OBTAINS RIGHTS TO THE CDKL5 TECHNOLOGY AND/OR THE MPS IIIA TECHNOLOGY.

## ARTICLE 5
## TERM AND TERMINATION

**5.1 Term**. The term of this Termination Agreement shall commence on the Termination Effective Date and, unless terminated sooner as provided below, shall continue unless terminated in accordance with Section 5.2 below. Notwithstanding the foregoing, Penn's option and rights to any CDKL5 Technology or MPS IIIA Technology shall expire within the time periods specified in Section 2.3.1 or 2.3.2, as applicable, if [***]; provided that the restrictions on Licensee shall survive for those periods set forth in Sections 2.3.1 in the event that Penn terminates this Agreement pursuant to Section 5.2 below.

**5.2 Termination for Cause**. If either Party materially breaches any of its material obligations under this Termination Agreement, the non-breaching Party may give the breaching Party a written notice specifying the nature of the default, requiring it to cure such breach, and stating its intention to terminate this Termination Agreement. If such breach is not cured within [***] following such a notice for non-payment and [***] following such a notice for all other material breaches, such termination shall become effective upon a notice of termination by the other Party thereafter; provided that if there is a good faith dispute as to the existence of such material breach, such [***] or [***] period, as applicable, may be extended by mutual agreement of the Parties to allow the Parties additional time to continue good faith discussions to resolve the dispute.

**5.3 Effects of Termination**.

**5.3.1** Notwithstanding the termination or expiration of this Termination Agreement, the following provisions shall survive (to the extent applicable, for the period of time specified): [***]. Without limiting the foregoing, termination of the Termination Agreement by a Party shall not affect the rights and licenses granted to such Party by the other Party under this Termination Agreement.

**5.3.2** Termination of this Termination Agreement shall not relieve the Parties of any obligation or liability that, at the time of termination, has already accrued hereunder, or which is attributable to a period prior to the effective date of such termination. Termination of this Termination Agreement shall not preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Termination Agreement nor prejudice either Party's right to obtain performance of any obligation.

## ARTICLE 6
## MISCELLANEOUS

**6.1 Confidentiality**. Article 9 of the Collaboration Agreement is hereby incorporated herein by reference (and references to "this Agreement" in Article 9 of the Collaboration Agreement and the Confidential Information definition in Section 1.14 of the Collaboration Agreement will be deemed to include this Termination Agreement and the License Agreement, as if this Termination Agreement and the License Agreement were expressly referenced therein) and shall govern the existence and terms of this Termination Agreement, each of which is hereby deemed Confidential Information thereunder and hereunder.

**6.2 Relationship of the Parties**. Nothing in this Termination Agreement is intended or shall be deemed, for financial, tax, legal or other purposes, to constitute a partnership, agency, joint venture, fiduciary or employer-employee relationship between the Parties. The Parties are independent contractors and at no time will either Party make commitments or incur any charges or expenses for or on behalf of the other Party.

**6.3 Expenses**. Except as otherwise provided in this Termination Agreement, each Party shall pay its own expenses and costs incidental to the preparation of this Termination Agreement and to the consummation of the transactions contemplated hereby.

**6.4 Successors and Assignment**. The terms and provisions hereof shall inure to the benefit of, and be binding upon, the Parties and their respective successors and permitted assigns. Neither Party may assign or transfer this Termination Agreement or any of its rights or obligations created hereunder, by operation of law or otherwise, without the prior written consent of the other Party. Notwithstanding the foregoing, without Penn's consent, Licensee shall have the right to assign any of its rights or obligations under this Termination Agreement, or to transfer this Termination Agreement, to: (a) any of its Affiliates, [***]; or (b) a third party in connection with a merger, acquisition of all or substantially all of the business or assets of Licensee (whether by sale of stock or assets), consolidation, change of control or other similar transaction; provided that, in each case (b), such third party is bound by the terms of this Termination Agreement, by operation of law or otherwise. Any assignment not in accordance with this Section 6.4 shall be null and void.

**6.5 Further Actions**. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Termination Agreement.

**6.6 Entire Agreement of the Parties; Amendments**. This Termination Agreement, together with the Collaboration Agreement but only to the extent so incorporated or referenced herein and the License Agreement, contains the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersede any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter, including the Collaboration Agreement (except as expressly set forth herein). No waiver, modification or amendment of any provision of this Termination Agreement shall be valid or effective unless made in a writing referencing this Termination Agreement and signed by a duly authorized officer of each Party. In the event of any conflict between the terms of this Termination Agreement and the terms of the License Agreement, then this Agreement shall control with respect to subject matter expressly addressed herein, except that the terms of the License Agreement shall control solely to the extent pertaining to Licensee's and Penn's rights, licenses and obligations with respect to patent rights and other intellectual property controlled by Penn and licensed to Licensee pursuant to the License Agreement for Fabry Disease and/or Pompe Disease.

**6.7 Governing Law**. This Termination Agreement shall be governed by and interpreted in accordance with the laws of the Commonwealth of Pennsylvania, excluding application of any conflict of laws principles that would require application of the law of a jurisdiction outside of the Commonwealth of Pennsylvania.

**6.8 Dispute Resolution**. If a dispute arises between the Parties concerning this Termination Agreement, then the Parties will confer, as soon as practicable, in an attempt to resolve the dispute. Prior to initiation of outside dispute resolution or termination of this Termination Agreement for a material breach, each Party shall escalate such issue to [***] and such parties will engage in good faith discussions with regard to the applicable dispute within [***]. If the Parties are unable to resolve such dispute amicably through good faith discussion and such escalation within [***], then either Party may submit to the exclusive jurisdiction of, and venue in, the state and federal courts located in the Eastern District of Pennsylvania.

**6.9 Notice and Deliveries**. Any notice, request, approval or consent required or permitted to be given under this Termination Agreement shall be in writing and directed to a Party at its address or email address shown below or, in the case of Penn providing notice, such other address or email address as such Party shall have last given by notice to the other Party. A notice will be deemed received: if delivered personally, on the date of delivery; if mailed, [***] after deposit in the United States mail; if sent via courier, [***] after deposit with the courier service; or, in the case of Penn providing notice, if sent via email, upon receipt of confirmation of transmission (i.e., a read receipt e-mail is received by the sender) provided that a confirming copy of such notice is sent by certified mail, postage prepaid, return receipt requested.

***For Penn***

Penn Center for Innovation University of Pennsylvania
3600 Civic Center Blvd.
9th Floor Philadelphia, PA 19104
Attention: Managing Director

***with a copy to***:

University of Pennsylvania Office of General Counsel
2929 Walnut St., Suite 400
Philadelphia, PA 19104
Attention: General Counsel

***For Licensee***:

Amicus Therapeutics, Inc.
3675 Market Street
Philadelphia PA 19104
Attention: Chief Legal Officer
Email: GCOffice@amicusrx.com

***with a copy to***:

Wilson Sonsini Goodrich & Rosati
12235 El Camino Real
San Diego CA 92130
Attention: Miranda Biven
Email: mbiven@wsgr.com

**6.10 Waiver**. A waiver by either Party of any of the terms and conditions of this Termination Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any other term or condition hereof. All rights, remedies, undertakings, obligations and agreements contained in this Termination Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either Party.

**6.11 Severability**. When possible, each provision of this Termination Agreement will be interpreted in such manner as to be effective and valid under law, but if any provision of this Termination Agreement is held to be prohibited by or invalid under law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Termination Agreement. The Parties shall make a good faith effort to replace the invalid or unenforceable provision with a valid one which in its economic effect is most consistent with the invalid or unenforceable provision.

**6.12 Counterparts**. This Termination Agreement may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A facsimile or a portable document format (PDF) copy of this Termination Agreement, including the signature pages, will be deemed an original.

[*Signature page follows*]

**IN WITNESS WHEREOF**, the Parties have caused this Termination Agreement to be executed by their duly authorized representatives as of the Termination Effective Date.

**THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA**

By: /s/ John Swartley
Name: John Swartley
Title: AVP and Managing Director, PCI

**AMICUS THERAPEUTICS, INC.**

By: /s/ Bradley Campbell
Name: Bradley Campbell
Title: President & CEO

**Read and Acknowledged:**

By: /s/ Jim Wilson
Name: Jim Wilson
Title: Professor

**Schedule 1.3**
[***]

**Schedule 2.3.3(a)**
[***]

**Schedule 2.3.3(c)**
[***]

**Schedule 2.3.3(g)**
[***]

**Schedule 2.4.5**
[***]

**Schedule 3.2(a)**
[***]

**Schedule 3.2(b)**
[***]

**EXHIBIT 21**

**List of Subsidiaries of the Registrant**

1. Callidus Biopharma, Inc. (Delaware)
2. Celenex, Inc. (Delaware)
3. Scioderm, Inc. (Delaware)
4. MiaMed, Inc. (Delaware)
5. Amicus Therapeutics International Holding Limited (UK)
6. Amicus Therapeutics UK Limited (UK)
7. Amicus Therapeutics UK Operations Limited (UK)
8. Amicus Therapeutics SAS (France)
9. Amicus Therapeutics B.V. (Netherlands)
10. Amicus Therapeutics GmbH (Germany)
11. Amicus Therapeutics S.L.U. (Spain)
12. Amicus Therapeutics S.r.l. (Italy)
13. Amicus Therapeutics K.K. (Japan)
14. Amicus Therapeutics Canada Inc. (Canada)
15. Amicus Therapeutics PTY LTD (Australia)
16. Amicus Therapeutics US, LLC. (Delaware)
17. Amicus Biologics, Inc. (Florida)
18. Amicus Therapeutics ApS (Denmark)
19. Amicus Therapeutics Europe Limited (Ireland)
20. Amicus Therapeutics Switzerland GmbH (Switzerland)
21. Amicus GT Holdings, LLC (Delaware)
22. Caritas Therapeutics, LLC (Delaware)
23. Amicus Therapeutics France Services SAS (France)

**EXHIBIT 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-265531) pertaining to the Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan,
2. Registration Statement (Form S-3ASR No. 333-262987) pertaining to the Amicus Therapeutics, Inc., Automatic shelf registration statement of securities of well-known seasoned issuers,
3. Registration Statement (Form S-3 No. 333-260924) pertaining to the issuance of common stock and warrants in 2021,
4. Registration Statement (Form S-8 No. 333-257289) pertaining to the Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan,
5. Registration Statement (Form S-3ASR No. 333-252646) pertaining to the issuance of warrants in 2016,
6. Registration Statement (Form S-8 No. 333-243779) pertaining to the: 1) Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan and 2) Amicus Therapeutics, Inc. Amended and Restated 2007 Director Option Plan,
7. Registration Statement (Form S-8 No. 333-233153) pertaining to the Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan,
8. Registration Statement (Form S-3ASR No. 333-212414), pertaining to the acquisition of MiaMed, Inc.,
9. Registration Statement (Form S-3ASR No. 333-207210), pertaining to the acquisition of Scioderm, Inc.,
10. Registration Statement (Form S-8 No. 333-197202) pertaining to the Amicus Therapeutics, Inc. Cash Deferral Plan,
11. Registration Statement (Form S-8 No. 333-195194) pertaining to the Amicus Therapeutics, Inc. Restricted Stock Unit Deferral Plan,
12. Registration Statement (Form S-3 No. 333-192876), pertaining to the issuance of warrants,
13. Registration Statement (Form S-3 No. 333-192747), pertaining to the acquisition of Callidus Biopharma, Inc.,
14. Registration Statement (Form S-8 No. 333-174900) pertaining to the: 1) Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan and 2) Amicus Therapeutics, Inc. Amended and Restated 2007 Director Option Plan,
15. Registration Statement (Form S-8 No. 333-157219) pertaining to the: 1) Amicus Therapeutics, Inc. Amended and Restated 2007 Equity Incentive Plan and 2) Amicus Therapeutics, Inc. 2007 Director Option Plan, and
16. Registration Statement (Form S-8 No. 333-145305) pertaining to the: 1) Amicus Therapeutics, Inc. 2002 Equity Incentive Plan, as Amended, 2) Amicus Therapeutics, Inc. 2007 Equity Incentive Plan, 3) Amicus Therapeutics, Inc. 2007 Director Option Plan, 4) Amicus Therapeutics, Inc. 2007 Employee Stock Purchase Plan

of our reports dated March 1, 2023 with respect to the consolidated financial statements of Amicus Therapeutics, Inc., and the effectiveness of internal control over financial reporting of Amicus Therapeutics, Inc. included in this Annual Report (Form 10-K) of Amicus Therapeutics, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Iselin, New Jersey
March 1, 2023

**EXHIBIT 31.1**

**CERTIFICATIONS PURSUANT TO SECTION 302 OF**
**THE SARBANES-OXLEY ACT OF 2002**
**CERTIFICATION BY PRINCIPAL EXECUTIVE OFFICER**

I, Bradley L. Campbell, certify that:

1. I have reviewed this annual report on Form 10-K of Amicus Therapeutics, Inc.;

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

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

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

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2023

/s/ Bradley L. Campbell
Bradley L. Campbell
President and Chief Executive Officer

**EXHIBIT 31.2**

**CERTIFICATIONS PURSUANT TO SECTION 302 OF**
**THE SARBANES-OXLEY ACT OF 2002**
**CERTIFICATION BY PRINCIPAL FINANCIAL OFFICER**

I, Daphne Quimi, certify that:

1. I have reviewed this annual report on Form 10-K of Amicus Therapeutics, Inc.;

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

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

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

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2023

/s/ Daphne Quimi
Daphne Quimi
Chief Financial Officer

**EXHIBIT 32.1**

**Certification by the Principal Executive Officer Pursuant to 18 U. S. C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

Pursuant to 18 U. S. C. Section 1350, I, Bradley L. Campbell, hereby certify that, to the best of my knowledge, Amicus Therapeutics Inc., (the "Company") Annual Report on Form 10-K for the year ended December 31, 2022 (the "Report"), as filed with the Securities and Exchange Commission on March 1, 2023, fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended, and that the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Bradley L. Campbell

Bradley L. Campbell
President and Chief Executive Officer
March 1, 2023

**EXHIBIT 32.2**

**Certification by the Principal Financial Officer Pursuant to 18 U. S. C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

Pursuant to 18 U. S. C. Section 1350, I, Daphne Quimi, hereby certify that, to the best of my knowledge, the Amicus Therapeutics Inc. (the "Company") Annual Report on Form 10-K for the year ended December 31, 2022 (the "Report"), as filed with the Securities and Exchange Commission on March 1, 2023, fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended, and that the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Daphne Quimi

Daphne Quimi
Chief Financial Officer
March 1, 2023