

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

FORM 10-K

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

For the fiscal year ended December 31, 2019  
OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_  
Commission File Number 001-33497

**Amicus Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or Other Jurisdiction of  
Incorporation or Organization)  
**1 Cedar Brook Drive, Cranbury, NJ**  
(Address of Principal Executive Offices)

**71-0869350**  
(IRS Employer  
Identification Number)  
**08512**  
(Zip Code)

**(609) 662-2000**

(Registrant's Telephone Number, Including Area Code)

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

<u>Title of each class</u>	<u>Trading Symbols(s)</u>	<u>Name of each exchange on which registered</u>
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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 if the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes  No

The aggregate market value of the 252,198,093 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, 2019) was \$3,147,432,201. 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.

As of February 19, 2020, there were 257,244,659 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2020 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.

	<b>PART I</b>	
Item 1.	BUSINESS	3
Item 1A.	RISK FACTORS	23
Item 1B.	UNRESOLVED STAFF COMMENTS	66
Item 2.	PROPERTIES	66
Item 3.	LEGAL PROCEEDINGS	66
Item 4.	MINE SAFETY DISCLOSURES	66
	<b>PART II</b>	
Item 5.	MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES	67
Item 6.	SELECTED FINANCIAL DATA	69
Item 7.	MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS	70
Item 7A.	QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK	81
Item 8.	FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA	82
Item 9.	CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE	121
Item 9A.	CONTROLS AND PROCEDURES	121
Item 9B.	OTHER INFORMATION	121
	<b>PART III</b>	
Item 10.	DIRECTORS, EXECUTIVE OFFICERS, AND CORPORATE GOVERNANCE	122
Item 11.	EXECUTIVE COMPENSATION	122
Item 12.	SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS	122
Item 13.	CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE	122
Item 14.	PRINCIPAL ACCOUNTING FEES AND SERVICES	122
	<b>PART IV</b>	
Item 15.	EXHIBITS, FINANCIAL STATEMENT SCHEDULES	123
Item 16.	FORM 10-K SUMMARY	127
	SIGNATURES	128

## 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," "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 progress and results of our preclinical and clinical trials of our drug candidates and gene therapy candidates, including but not limited to AT-GAA, CLN6 and CLN3;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200") and gene therapies;
- the scope, progress, results, and costs of preclinical development, laboratory testing, and clinical trials for our product candidates including those testing the use of a pharmacological chaperone co-administered with ERT for the treatment of Pompe disease ("AT-GAA") and gene therapies for the treatment of rare genetic metabolic diseases;
- the future results of on-going preclinical research and subsequent clinical trials for cyclin-dependent kinase-like 5 ("CDKL5") deficiency, Pompe gene therapy, Fabry gene therapy, Niemann-Pick Type C ("NPC"), Mucopolysaccharidosis Type IIIB ("MPSIIIB") and next generation Mucopolysaccharidosis Type IIIA ("MPSIIIA"), including our ability to obtain regulatory approvals and commercialize these gene therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates;
- any changes in regulatory standards relating to the review of our product candidates;
- 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;
- our ability to successfully commercialize Galafold® ("migalastat HCl");
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold®, AT-GAA and our gene therapy candidates;
- our ability to obtain reimbursement for Galafold®;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®;
- our ability to obtain market acceptance of Galafold®;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- 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, 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 collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;
- our ability to adjust to changes in the European and United Kingdom markets in the wake of the United Kingdom leaving the European Union;

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. FABRAZYME, MYOZYME, LUMIZYME, and REPLAGAL are the property of their respective owners.

- the extent to which our business could be adversely impacted by the effects of the COVID-19 “coronavirus” outbreak or by other health epidemics or pandemics;
- 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”, 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 acquisitions, mergers, dispositions, joint ventures, collaborations or 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.

## 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 of product opportunities led by our novel medicine for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease in the clinic, and an industry leading rare disease gene therapy portfolio.

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.”), United Kingdom (“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), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the U.S. Food and Drug Administration (“FDA”) granted Breakthrough Therapy designation to AT-GAA for the treatment of late onset Pompe disease.

We have established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children’s Hospital (“NCH”) and an expanded collaboration with the University of Pennsylvania (“Penn”). Our pipeline includes gene therapy programs in rare, neurologic lysosomal disorders (“LDs”), specifically: CLN6, CLN3, CLN8, and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder (“CDD”), Niemann-Pick Type C (“NPC”), Mucopolysaccharidosis Type IIIB (“MPSIIIB”), as well as a next generation program in Mucopolysaccharidosis Type IIIA (“MPSIIIA”). Our expanded collaboration with Penn also provides us with exclusive disease-specific access and the option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies.

#### Our Strategy

Our strategy is to create, manufacture, test, and deliver the highest quality medicines for people living with rare metabolic diseases through internally 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. In addition to our programs in Fabry and Pompe, we have begun to leverage our global capabilities to develop and expand our robust pipeline through our recent entry into genomic medicine. We have made significant progress toward fulfilling our vision to build a leading global biotechnology company focused on rare metabolic diseases.

Highlights of our progress include:

- *Commercial and regulatory success in Fabry disease.* For the year ended December 31, 2019, Galafold® revenue totaled \$182.2 million, an increase of \$91.0 million compared to the prior year. We continue to see strong commercial momentum and continue to expand into additional geographies. In the countries we have been operating the longest, such as Germany and the United Kingdom, we see an increasing proportion of previously untreated patients come onto Galafold®. 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 clinical program milestones.* We completed enrollment in a global pivotal study of AT-GAA (ATB200-03, also known as PROPEL) and enrolled 123 participants with late-onset Pompe disease at 59 global sites. We reported positive data from a Phase 1/2 clinical study to evaluate Pompe disease patients treated with our novel treatment paradigm AT-GAA. The U.S. FDA also granted Breakthrough Therapy designation for AT-GAA for the treatment of late-onset Pompe disease. In the first quarter of 2020, the British Medicines and Healthcare Products Regulatory Agency issued a Promising Innovative Medicine designation for AT-GAA for the treatment of late-onset Pompe disease.

- *Pipeline advancement and growth.* We have established an industry leading gene therapy portfolio of medicines for people living with rare metabolic diseases through a license with NCH and an expanded collaboration with Penn. In 2019, we reported positive interim clinical data from the first eight patients in the CLN6 study. Additionally, in 2019, four programs were added to the pipeline through ongoing collaborations with Penn to pursue research and development of novel gene therapies for Pompe disease, Fabry disease, CDD, NPC, MPSIIIB, as well as a next generation program in MPSIIIA.
- *Manufacturing.* We continue to manufacture our Pompe biologic at commercial scale (1,000L) for our pivotal PROPEL study and commercial supply. Our supply agreement with WuXi Biologics and current capacity are expected to produce sufficient quantities to support commercial needs as quickly as possible after receipt of applicable regulatory approvals if obtained. For gene therapy, we have recently entered into strategic partnerships with two best-in-class contract development and manufacturing organizations: Catalent Biologics and Thermo Fisher Scientific. Catalent Biologics will support our clinical manufacturing capabilities and capacity for multiple active preclinical lysosomal disorder programs that are currently in development in collaboration with Penn. Thermo Fisher will assist with late-stage clinical and commercial-scale capabilities and provides us with immediate clinical and commercial manufacturing capabilities and capacity for the Amicus intrathecal AAV Batten disease gene therapy programs.
- *Financial strength.* Total cash, cash equivalents, and marketable securities of \$452.7 million at December 31, 2019 compared to \$504.2 million at December 31, 2018. The current cash position, including expected Galafold® revenues, is sufficient to fund ongoing Fabry, Pompe, and gene therapy program operations into the first half of 2022. Potential future 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 approved Galafold® for 348 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 367 Fabry-causing mutations, which represent up to half of all patients with Fabry disease. Approvals have also been granted in over 40 countries around the world, including the U.S., E.U., U.K., Japan, and others. We plan to continue to launch Galafold® in additional countries during 2020.

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 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.

### Gene Therapy for Fabry Disease

We are committed to continued innovation for all people living with Fabry disease. For people living with Fabry disease who have non-amenable variants, which are not suitable for Galafold® as a monotherapy, our strategy is to develop a Fabry gene therapy. In October 2018, we further expanded our gene therapy portfolio through a collaboration agreement with Penn to pursue research and development of novel gene therapies for Fabry disease and other indications. In October 2019, we disclosed preliminary data from a Fabry AAV gene therapy using an Amicus-engineered transgene that demonstrated high levels of GLA activity and robust GL-3 reduction in a mouse model of 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, and the U.S., which collectively screened more than 500,000 newborns, found the incidence of Fabry disease mutations to be between 1:2,400 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).

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.

### 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, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with a pharmacological chaperone, AT2221, to improve activity and stability. We initiated a global Phase 3 clinical study ("ATB200-03" or "PROPEL") of AT-GAA in adult patients with late onset Pompe disease in December 2018.

The pharmacological chaperone, AT2221 is not an active ingredient that contributes directly to GAA substrate reduction but instead acts to stabilize ATB200. The small molecule pharmacological chaperone AT2221 binds and stabilizes ATB200 in circulation to improve the uptake of active enzyme in key disease-relevant tissues, resulting in increased clearance of accumulated substrate, glycogen.

Our strategy is to enhance the body of clinical data for AT-GAA in ongoing clinical studies. Based on regulatory feedback from both the U.S. FDA and the European Medicines Agency ("EMA"), the Phase 3 PROPEL study is expected to support approval for a broad indication, including ERT-switch and treatment-naïve patients, if the results are favorable.

In October 2019, we reported additional interim data from our clinical study ATB200-02 at the 24th International Annual Congress of the World Muscle Society. Highlights included muscle function, safety, and tolerability data in patients as well as pharmacodynamic data (muscle damage biomarker, creatine kinase, disease substrate biomarker, and urine hexose tetrasaccharide). Muscle function improved in 16 out of 18 patients at 24 months. Mean six-minute walk test ("6MWT") improved in both ERT-naïve and ERT-switch patients with continued benefit observed out to month 24. All 5 ERT-naïve patients showed increases from baseline in 6MWT distance at all time points out to month 24. To date, adverse events have been generally mild and transient. AT-GAA has resulted in a low rate of infusion-associated reactions ("IARs") following over 1,500+ infusions (28 events of IARs in eight patients). The clinical pharmacokinetic profile has been consistent with previously reported preclinical data. Treatment with AT-GAA resulted in persistent and durable reductions in creatine kinase and urine hexose tetrasaccharide across all patient cohorts up to month 24.

### ***Gene Therapy for Pompe Disease***

As part of our long-term commitment to provide multiple solutions to address the significant unmet needs of the Pompe community, we are also advancing a next-generation gene therapy treatment for Pompe disease. In October 2018, we further expanded our gene therapy portfolio through a collaboration agreement with Penn to pursue research and development of novel gene therapies for Pompe disease and other indications.

In April 2019, we presented initial preclinical data from our investigational adeno-associated viral ("AAV") gene therapy program for Pompe disease. This initial preclinical study in Pompe knockout mice administered a single high dose of AAV gene therapy with either unmodified wild-type hGAA ("unmodified hGAA") or an Amicus/Penn engineered hGAA transgene with a Lysosomal-Targeting Cell receptor binding motif ("engineered hGAA"). The Amicus/Penn engineered hGAA AAV gene therapy demonstrated more robust and consistent glycogen reduction compared to unmodified hGAA AAV gene therapy, in all key tissues assessed in a Pompe mouse model. In the central nervous system, the engineered hGAA AAV gene therapy also showed robust glycogen reduction in neuronal cells, suggesting this may be an effective way to address neuronal aspects of Pompe disease. Unmodified hGAA AAV gene therapy showed minimal glycogen reduction in neuronal cells. This preclinical study provides initial validation for combining Amicus-engineered transgenes with Penn's AAV gene therapy technologies.

### ***Pompe Disease Background***

Like Fabry disease, Pompe disease is an 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, one product, an ERT, is approved for the treatment of Pompe disease: alglucosidase alfa by Sanofi Aventis.

### ***Gene Therapy for Various Types of Batten Disease***

We are researching potential first-in-class gene therapies for multiple forms of Batten disease. Batten disease is the common name for a broad class of rare, fatal, inherited disorders of the nervous system also known as neuronal ceroid lipofuscinoses, or NCLs. In these diseases, a defect in a specific gene triggers a cascade of problems that interferes with a cell's ability to recycle certain molecules. Each gene is called CLN (ceroid lipofuscinosis, neuronal) and given a different number designation as its subtype. There are 13 known forms of Batten disease often referred to as CLN1-8; 10-14. The various types of Batten disease have similar features and symptoms but vary in severity and age of onset.

Most forms of Batten disease/NCLs usually begin during childhood. The clinical course often involves progressive loss of independent adaptive skills such as mobility, feeding, and communication. Patients may also experience vision loss, personality changes, behavioral problems, learning impairment, and seizures. Patients typically experience progressive loss of motor function and eventually those affected become wheelchair-bound, are then bedridden, and die prematurely.

We have two clinical programs in CLN6 and CLN3 Batten disease, and several preclinical programs including CLN8, CLN1 and other types of Batten disease. CLN6 Batten disease results from a mutation in the CLN6 gene which primarily affects the nervous system and results in a late-infantile form of Batten disease. CLN3 Batten disease, the most common form of Batten disease, results from a mutation in the CLN3 gene which primarily affects the nervous system and results in a juvenile form of Batten disease. CLN8 Batten disease results from a mutation in the CLN8 gene which primarily affects the nervous system and results in a late-infantile form of Batten disease. CLN1 Batten disease results from a mutation in the CLN1 gene which primarily affects the nervous system and results in an infantile form of Batten disease.

The CLN6 Batten disease Phase 1/2 study completed target enrollment, with thirteen patients receiving a single administration of adeno-associated virus serotype 9 AAV-CLN6 gene therapy. In August 2019, we reported positive interim clinical data from the first eight patients in the study. The AAV-CLN6 gene therapy demonstrated a positive impact on motor and language function. Seven out of eight patients maintained stable Hamburg Motor and Language scores or had an initial change (+1 to -1 points) followed by stabilization. In October 2019, we reported additional interim clinical data further supporting the impact of one-time intrathecal AAV gene therapy in children with CLN6 Batten disease. This interim data suggested stabilization of various components of the Hamburg Motor, Language, Seizure, and Vision scores in most patients from baseline to month 12 or 24, in particular those patients treated at a younger age, compared to the progression expected in matched untreated patients. The CLN6 Batten population is approximately 1,000 patients across our commercial landscape today and there are no approved therapies for this disorder.

In the fourth quarter of 2018, we announced the initiation of a Phase 1/2 study to evaluate the safety and efficacy of a single intrathecal administration of adeno-associated virus serotype 9 AAV-CLN3 gene therapy in children with CLN3 Batten disease. In the Phase 1/2 study, a total of three patients were dosed in the low dose group, and based on the safety profile to date, the data safety monitoring board cleared us to begin enrollment in the high dose cohort of up to three additional patients. One high dose patient has been dosed, with no serious adverse events to date following a single administration of AAV-CLN3 gene therapy. CLN3 impacts approximately 5,000 patients across our commercial landscape today and there are no approved therapies for this disorder.

### ***CDKL5 Deficiency Disorder***

We are researching a potential first-in-class protein replacement therapy approach for CDD. In addition, through our collaboration with Penn, we are researching a gene therapy for CDD. CDKL5 is a gene on the X-chromosome encoding the CDKL5 protein that regulates the expression of several essential proteins for normal brain development. Genetic mutations in the CDKL5 gene result in CDKL5 protein deficiency and CDD. This disorder manifests clinically as persistent seizures starting in infancy, followed by severe impairment in neurological development. Most children affected by CDD cannot walk or care for themselves and may also suffer from scoliosis, visual impairment, sensory issues, and gastrointestinal complications.

### ***Other Preclinical Gene Therapies***

We have a number of additional gene therapies in active preclinical development, including gene therapies for NPC, MPSIIIB, as well as a next generation program in MPSIIIA. Our strategy is to develop first or best in class AAV gene therapies for these rare devastating pediatric neurological lysosomal storage diseases.

### ***Strategic Alliances and Arrangements***

We will continue to evaluate business development opportunities as appropriate that 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 metabolic diseases. We are exploring potential collaborations, alliances, and other business development opportunities on a regular basis. These opportunities may include the acquisition of preclinical-stage, clinical-stage or marketed products so long as such transactions are consistent with our strategic plan to develop and provide therapies to patients living with rare and orphan diseases.

## Acquisitions

### *Celenex, Inc.*

In September 2018, we expanded our pipeline by acquiring the rights and related intellectual property of ten gene therapy programs through the acquisition of Celenex, Inc. ("Celenex"). Celenex is a private, clinical stage gene therapy company whose lead programs are ten gene therapy programs including CLN6 and CLN3, which are in clinical stage, and several programs in pre-clinical stage. Pursuant to the terms of the agreement, we acquired Celenex for cash consideration of \$100 million. We also agreed to pay up to an additional \$15 million in connection with the achievement of certain development milestones, \$262 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 NCH. Under this license agreement, NCH is eligible to receive development and sales-based milestones of up to \$7.8 million for each product.

### *MiaMed, Inc.*

In July 2016, we acquired MiaMed, Inc., ("MiaMed"), which is a pre-clinical biotechnology company focused on developing protein replacement therapy for CDD and related diseases. As part of the transaction, we may be obligated to pay up to an additional \$83.0 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 agreed to issue an aggregate of 7.2 million shares of our common stock to the former stockholders of Callidus. In addition, 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<sup>®</sup> and our ongoing clinical programs:

- We own issued U.S. patents that cover the use of migalastat, the active pharmaceutical ingredients in Galafold<sup>®</sup>, in the treatment of Fabry disease, which expire in 2027, 2029, 2037 or 2038 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 methods of treating a patient diagnosed with Fabry disease with migalastat and their foreign counterparts. Any patents issuing from these applications will expire in 2038, 2039, 2040, or 2041 and 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, most 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 in 2034, 2035 or 2037. We also have pending U.S. patent applications covering compositions, methods of treatment, methods of manufacture, and formulations with anticipated expiry in 2033, 2035, 2036, 2037, 2038, or 2040.
- 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.

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 and 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 effective 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 effective filing date.

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

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 NCH. Under this license agreement, NCH is eligible to receive development and sales-based milestones of up to \$7.8 million for each product.

##### *University of Pennsylvania*

In October 2018, we expanded our gene therapy portfolio through a collaboration agreement with Penn to pursue research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, CDD, and one additional undisclosed rare metabolic disorder. In May 2019, we further expanded the collaboration from three to six programs for rare genetic diseases and now includes specifically: NPC, MPSIIIB, as well as a next generation program in MPSIIIA. This expanded collaboration with Penn also provides us with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. Under the expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in 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. We will provide \$10.0 million each year during the five-year agreement to fund the discovery research program. In connection with the collaboration agreement, in 2018, we made an upfront payment of \$7 million in cash to Penn that was expensed to research and development expense in the Consolidated Statements of Operations.

##### *GlaxoSmithKline*

In November 2013, we entered into a Revised Agreement (the "Revised Agreement") with GlaxoSmithKline ("GSK"), pursuant to which, we obtained global rights to develop and commercialize Galafold<sup>®</sup> as a monotherapy and in combination with ERT for Fabry disease. The Revised Agreement amends and replaces in its entirety the earlier agreement entered into between us and GSK in July 2012. Under the terms of the Revised Agreement, for Galafold<sup>®</sup> monotherapy, GSK is eligible to receive post-approval and sales-based milestones, as well as tiered royalties in the mid-teens in eight major markets outside the U.S. There was no other consideration paid to GSK as part of the Revised Agreement.

#### **Manufacturing**

We continue to rely on contract manufacturers to supply the active biopharmaceutical ingredients and final drug product for Galafold<sup>®</sup>, other pharmacological chaperones, our next-generation ERT product candidates, and our gene therapy 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.

While our third-party manufacturers have met our current manufacturing requirements, we anticipate taking steps to increase our manufacturing capabilities for our gene therapy platform. Our current arrangement with third-party manufacturers provide sufficient quantities of our program materials to meet anticipated clinical trial 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 <sup>(1)</sup>	Indication	Product	Class of Product	Status	2019 Sales (in millions)
Sanofi Aventis	Fabry Disease	Fabrazyme <sup>®</sup>	ERT	Marketed	€813
	Pompe Disease	Myozyme <sup>®</sup> / Lumizyme <sup>®</sup>	ERT	Marketed	€918
	Fabry Disease	GZ402671	Oral GCS Inhibitor	Phase 2	N/A
	Pompe Disease	GZ402666 ("neo GAA")	ERT	Phase 3	N/A
Takeda	Fabry Disease	Replagal <sup>®</sup>	ERT	Marketed	N/A
Idorsia	Fabry Disease	Lucerastat	Oral Therapy	Phase 3	N/A
Protalix Biotherapeutics	Fabry Disease	PRX-102	ERT	Phase 2/3	N/A
Avrobio	Fabry Disease	AVR-RD-01	Gene Therapy	Phase 1/2	N/A
Freeline	Fabry Disease	FLT190	Gene Therapy	Phase 1/2	N/A
Sangamo	Fabry Disease	ST-920	Gene Therapy	Phase 1/2	N/A
AskBio	Pompe Disease	ACTUS-101	Gene Therapy	Phase 1/2	N/A
Audentes	Pompe Disease	AT845	Gene Therapy	Phase 1/2	N/A
Roche (Spark)	Pompe Disease	SPK3006	Gene Therapy	Phase 1/2	N/A

<sup>(1)</sup> Reflects commercial products and product candidates for which IND has been filed or are in clinical development.

## 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 biologic product license applications ("BLAs"), or to issue warning letters, 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 Good Laboratory Practice ("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. 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 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 BLA must submit a proposed REMS; the FDA will not approve the 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 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 Abbreviated New Drug Application ("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.

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 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. 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 21CFR314 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. 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.

### ***Patient Protection and Affordable Care Act of 2010***

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***

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes as well as regulations related to payments and transfers of value to healthcare providers, the protection of the security and privacy of protected health information, and other compliance efforts. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties, and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services, reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

### ***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. and U.K. regulatory systems, we are mandated to submit MAAs in 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. and U.K. It is compulsory for medicinal products manufactured using biotechnological processes, for orphan medicinal products and for human products containing a new active substance which was not authorized in the Community before 20 May 2004 (date of entry into force of Regulation (EC) No 726/2004) and which are intended for the treatment of AIDS, cancer, neurodegenerative disorder or diabetes. The centralized procedure is optional for any other products containing new active substances not authorized in the Community before 20 May 2004 or for products which constitute a significant therapeutic, scientific or technical innovation or for which a Community authorization is in the interests of patients at Community level. When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the European Medicines Agency, to be assessed by the Committee for Medicinal Products for Human Use ("CHMP"). The procedure results in a Commission decision, which is valid in all E.U. Member States and the U.K. Centrally-authorized products may be marketed in all Member States. Centralized procedure: Full copies of the MA application are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's 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 MA has been granted.

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, which is compulsory for medicines produced by certain biotechnological processes and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all E.U. member states and U.K. 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. and U.K. 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. and U.K. 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 U.K. and that without incentives it is unlikely that sales of the drug in the E.U. and U.K. 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. and U.K. 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 for protocol assistance and access to the centralized regulatory procedures before and during the first year after marketing approval, which 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 drug exclusivity, which means the EMA may not approve any other application to market the same 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 provide a significant benefit over the existing orphan product. This demonstration of significant benefit may be done at the time of initial approval or in post-approval studies, depending on the type of marketing authorization granted.

We have obtained a positive opinion for our pediatric investigation plan ("PIP") in the E.U. and U.K. for Galafold® for the treatment of Fabry disease as well. In May 2016, we announced that we had received full European Commission approval for migalastat HCl, under the product name Galafold®, 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. 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. and U.K. Medicines authorized across the E.U. and U.K. 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.

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 rest of 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. 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.

In a referendum held in U.K. on June 23, 2016, a majority of those voting voted for the U.K. to leave the E.U., commonly referred to as "Brexit". On March 29, 2017, the U.K. government delivered to the European Council notice of its intention to leave the E.U. The negotiation period (under Article 50 of the Treaty on European Union) had been extended repeatedly; however, on January 24, 2020, the U.K. and the E.U. entered into a withdrawal agreement pursuant to which the U.K. formally left the E.U. on January 31, 2020, but will, for a transition period ending on December 31, 2020, maintain access to the E.U. single market and to the global trade deals negotiated by the E.U. on behalf of its members and remain subject to E.U. law. The ultimate impact of Brexit will depend on the terms that are negotiated in relation to the U.K.'s future relationship with the E.U. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the U.K. determines which E.U. laws to replicate or replace.

### ***U.S. Foreign Corrupt Practices Act***

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business abroad or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

### ***Pharmaceutical Pricing and Reimbursement***

In the U.S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers, and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare product candidates, and efforts are underway by the current U.S. administration and states to reduce the cost of prescription drugs overall. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the U.S. government enacted legislation providing a partial prescription drug benefit for Medicare recipients that began in 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through managed care organizations and other health care delivery systems operating pursuant to this legislation. These organizations would negotiate prices for our products, which are likely to be lower than we might otherwise obtain. Federal, state, and local governments in the U.S. continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for biopharmaceuticals such as the drug candidates that we are developing.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals. With the current administration and Congress, there have been efforts to make additional legislative changes, including repeal and replacement of certain provisions of the PPACA. It is unclear what impact such legislative changes will have on the availability of healthcare and/or containing or lowering the costs of healthcare.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the U.S. has increased and will continue to increase the pressure on pharmaceutical pricing.

### **Employees**

As of December 31, 2019, we had 584 full-time employees. None of our employees were represented by a labor union. We have not experienced any work stoppages and consider our employee relations to be good.

## Our Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our global headquarters are located at 1 Cedar Brook Drive, Cranbury, NJ 08512 and our telephone number is (609) 662-2000. Our website address is [www.amicusrx.com](http://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, 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 on our website at [www.amicusrx.com](http://www.amicusrx.com) under the "Investors — Corporate Governance" caption and in print to any stockholder upon request. Any waivers or material amendments to the Code will be posted promptly on our website.

## ITEM 1A. RISK FACTORS

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations, and future growth prospects could be materially and adversely affected.

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

***We depend heavily on sales of our first product, Galafold<sup>®</sup>, in Europe, the U.S. and Japan. Moreover, if we are unable to commercialize Galafold<sup>®</sup> 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<sup>®</sup> for the treatment of Fabry disease and rely upon sales of Galafold<sup>®</sup> primarily in Europe and growing sales in the U.S. and Japan. Our ability to generate material product revenues will depend heavily on the successful development, regulatory approval, and commercialization of Galafold<sup>®</sup>. We began the commercial launch of Galafold<sup>®</sup> in the E.U. and U.K. in May 2016, in Japan in June 2018 and in the U.S. in August 2018 and continue to seek commercial approval in additional foreign jurisdictions. Approvals have been granted in over 40 countries around the world. We will continue to study Galafold<sup>®</sup> in a confirmatory Phase 4 program and other supportive Phase 4 studies. If the results of the Phase 4 studies negatively change the benefit/risk profile of Galafold<sup>®</sup>, the commercial success of Galafold<sup>®</sup> may be substantially diminished. Any adverse market event with respect to Galafold<sup>®</sup>, 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>, 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>;
- continuing to build and maintain an infrastructure capable of supporting product sales, marketing, and distribution of Galafold<sup>®</sup> 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<sup>®</sup>, where approved, whether alone or in collaboration with others;
- acceptance of Galafold<sup>®</sup>, where approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including potential generics and potential gene therapies;
- a continued acceptable safety profile of Galafold<sup>®</sup>;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;

- protecting and enforcing our rights in our intellectual property portfolio; and
- obtaining and maintaining a commercially viable price for our products.

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<sup>®</sup>, which would materially harm our business.

***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<sup>®</sup> 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 EMA, the PMDA, the 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.

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

Obtaining approval for all of our product candidates 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 approval of any of our product candidates for many reasons, including, but not limited to:

- our failure to demonstrate to the satisfaction of the applicable regulatory authorities that any of our product candidates are safe and effective for a particular indication;
- the results of clinical trials may not meet the level of statistical significance or other efficacy or safety parameters required by the applicable regulatory authorities for approval;
- the applicable regulatory authority may disagree with the number, design, size, conduct, or implementation of our clinical trials or conclude that the data fail to meet statistical or clinical significance;
- the applicable regulatory authority may not find the data from preclinical studies and clinical trials sufficient to demonstrate that the product candidate's clinical and other benefits outweigh its safety risks;
- the applicable regulatory authority may disagree with our interpretation of data from preclinical studies or clinical trials, and may reject conclusions from preclinical studies or clinical trials, or determine that primary or secondary endpoints from clinical trials were not met, or reject safety conclusions from such studies or trials;
- the applicable regulatory authority may not accept data generated at one or more of our clinical trial sites;
- the applicable regulatory authority may determine that we did not properly oversee our clinical trials or follow the regulatory authority's advice or recommendations in designing and conducting our clinical trials;
- an advisory committee, if convened by the applicable regulatory authority, may recommend against approval of our application or may recommend that the applicable regulatory authority require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, or even if an advisory committee, if convened, makes a favorable recommendation, the respective regulatory authority may still not approve the product candidate; 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, and this 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.

***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<sup>®</sup> or product candidates including AT-GAA, CLN6 and CLN3, 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 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, which in turn could delay or prevent us from generating significant revenues from its sale or adversely affect our reputation.

***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<sup>®</sup>, or any product candidate if and when they are approved.***

To achieve commercial success for any approved product, we must continue to develop and maintain a sales and marketing organization or outsource commercialization to third parties. We have established our own sales and marketing capabilities to promote Galafold<sup>®</sup> in Europe, Japan, the U.S. and other foreign jurisdictions with a targeted sales force. 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 any of our products or product candidates. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. 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<sup>®</sup>, or our product candidates, 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; 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 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;
- our distributors may experience financial difficulties;
- our distributors may experience compliance related issues and associated government investigations;
- 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, Batten 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, Batten 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 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 alternative treatments, including generics and gene therapies;
- the prevalence and severity of any side effects;
- the ability to offer our product and product candidates 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; 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 and product candidates 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® and Lumizyme® for the treatment of Pompe disease and has another product for Pompe in development, Neo-GAA. We are also aware of other enzyme replacement and substrate reduction therapies in development by third parties for 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 reaches commercialization.

We believe that many competitors, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies, are attempting to develop therapies for many of our target indications. 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 including our gene therapies. 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 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 tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign 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 the recent spread of COVID-19 “coronavirus”), 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.

***The impact of Brexit on our international operations is currently unknown but could have a material impact on our business.***

In a referendum held in the U.K. on June 23, 2016, a majority of those voting voted for the U.K. to leave E.U., commonly referred to as “Brexit”. On March 29, 2017, the U.K. government delivered to the European Council notice of its intention to leave the E.U. The negotiation period (under Article 50 of the Treaty on European Union) had been extended repeatedly; however, on January 24, 2020, the U.K. and the E.U. entered into a withdrawal agreement pursuant to which the U.K. formally left the E.U. on January 31, 2020, but will, for a transition period ending on December 31, 2020, maintain access to the E.U. single market and to the global trade deals negotiated by the E.U. on behalf of its members and remain subject to E.U. law. The ultimate impact of the “leave” vote will depend on the terms that are negotiated in relation to the U.K.’s future relationship with the E.U. Brexit could impair the Company’s ability to transact business in the U.K. and E.U. countries. Brexit has already and could continue to adversely affect European and/or worldwide economic and market conditions and could continue to contribute to instability in the global financial markets. The long-term effects of Brexit will depend in part on any new trade agreements the U.K. makes to retain access to E.U. markets following the U.K.’s withdrawal transition period from the E.U. Negotiations of a trade agreement may be unsuccessful, and the U.K. may not reach agreement with the E.U. on the future terms of the U.K.’s relationship with the E.U.

Without an agreement, there will be a period of considerable uncertainty particularly in relation to the financial and banking markets and the regulation of the pharmaceutical industry, including the regulatory approval process.

We expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the U.K. determines which E.U. laws to replicate or replace. If the U.K. were to significantly alter its regulations affecting the pharmaceutical industry, we could face significant new costs relating to the development, manufacture, and marketing of our current and future products. It may also be time-consuming and expensive for us to alter our internal operations in order to comply with any new regulations. Altered regulations could also add time and expense to the process by which our current product or product candidates receive or maintain regulatory approval in the U.K. and the E.U. Following Brexit, approval of medications approved through the E.U. centralized procedure, such as Galafold®, will remain in effect through grandfathering. Our international headquarters are in Marlow, U.K. Guidance from the EMA provides that the Company must transfer marketing authorization to a holder in the E.U. In compliance with such guidance, we have moved our regulatory portfolio to Ireland which is the marketing authorization holder in the E.U. We have also completed preparation for Brexit given what is currently known, which is subject to change after the transition period.

Among other outcomes, Brexit could disrupt the free movement of goods, services and people between the U.K. and the E.U., and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in the U.K. and the E.U. In addition, changes to U.K. immigration policy as a result of Brexit could adversely affect our ability to retain talent for our European operations. Given the lack of comparable precedent, it is unclear what financial, trade, regulatory, and legal implications the final withdrawal of the U.K. from the E.U. would have and how such withdrawal would affect us. Any of these effects, and others we cannot anticipate, could negatively affect our business and financial condition.

***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 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, the current administration and Congress in the U.S. will 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. For the last several years government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications.



In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, was enacted in the U.S. As discussed below, this legislation imposes cost-containment and other measures affecting the amount of reimbursement for our current and any future marketed products. The full effects of this legislation depend on a number of factors, many of which are beyond our control, including new regulations and guidance issued by Centers for Medicare & Medicaid Services ("CMS") and other federal and state agencies. A majority of states have passed legislation and other states are considering legislation intended to control the price and reimbursement of prescription drugs. State Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any prescription drug for which supplemental rebates are not being paid. It is likely that federal and state legislatures and health agencies will continue to focus on additional health care reform measures in the future that will impose additional constraints on prices and reimbursements for our marketed products.

Further, there have been numerous efforts at all levels of federal and state government to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the out-of-pocket cost of prescription drugs, and reform government program reimbursement methodologies for drugs. At the federal level, there are proposals for drug price control measures that could be enacted in future legislation. Additionally, on May 11, 2018, President Trump laid out his administration's "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services has solicited feedback on some of these measures and may implement others impacting our business under its existing authority. There have been several recent U.S. Congressional inquiries and proposed legislation designed to address these issues, including legislation recently signed by President Trump to ban clauses in commercial health insurance that restrict pharmacists from sharing pricing information. CMS has also proposed a series of policy changes designed to promote prescription drug affordability and transparency. At the state level, legislatures are becoming increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures. In some cases, these measures are designed to encourage importation from other countries and bulk purchasing.

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 medical products. We cannot be sure that coverage and reimbursement will continue to be available for Galafold® or any product 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.

***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 or biologic 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 the company 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 or untitled letters;
- 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 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.***

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of 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 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 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 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 and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of 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 and chiropractors) 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; 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<sup>®</sup>, 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.

***Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.***

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell Galafold<sup>®</sup> or any product candidates for which we obtain marketing approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

The pricing of pharmaceutical products, in general, and specialty drugs, in particular, has also been a topic of concern in the U.S. government, including by the current administration and Congress. There can be no assurance as to how this scrutiny on pricing of pharmaceutical products will impact future pricing of our products or orphan drugs or pharmaceutical products generally and government programs in particular.

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 pharmaceutical industry 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;
- 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.

In addition, 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 2025.

There have also been significant ongoing efforts to modify or eliminate the Affordable Care Act. For example, the Tax Cuts and Jobs Act ("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, beginning in 2019. The Joint Committee on Taxation estimates that the repeal will result in over 13 million fewer Americans maintaining their health insurance coverage over the next ten years and is likely to lead to increases in insurance premiums.

On January 20, 2017, the President signed an executive order directing federal agencies to exercise existing authorities to reduce burdens associated with the Affordable Care Act pending further action by Congress. In April 2018, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule and guidance documents which changed requirements for health plans sold through the Affordable Care Act marketplaces for 2019. These changes include, for example, (i) turning over responsibility for ensuring that marketplace plans have enough health care providers in their networks to the states that rely on the federal HealthCare.gov exchange; (ii) allowing states to alter aspects of the essential health benefits required of health plans sold through the federal and state insurance marketplaces; (iii) eliminating certain Small Business Health Options Program, or SHOP, regulatory requirements; and (iv) outlining criteria by which insurers may reduce the percentage of income allocated to patient care. The U.S. Department of Labor issued a final rule in June 2018 to expand the availability of association health plans available to small business owners and self-employed individuals, beginning on September 1, 2018. These association health plans will not be required to provide the essential health benefits mandated by the Affordable Care Act. These and other regulations may impact coverage of certain health care services.

We expect that further changes to the Affordable Care Act, as well as other healthcare reform measures that have been proposed and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenue. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may compromise our ability to generate revenue, attain profitability or commercialize our product candidates.

In August 2017, President Trump signed into law the Food & Drug Administration Reauthorization Act (FDARA). This legislation imposes significant new requirements for clinical trial sponsors which will affect, among other things, obtaining orphan drug designation, and the development of drugs and biological products for pediatric use. Galafold<sup>®</sup> and ATB200/AT2221 have obtained orphan drug designations from the FDA, but this legislation may result in new regulations which might materially impact

our business. Under the new legislation, an applicant for orphan drug designation must show that its product provides a significant therapeutic advantage over an already approved or licensed drug in terms of greater efficacy, greater safety, or by providing a major contribution to patient care.

In 2019, both the House and Senate passed comparable prescription drug price reduction legislation. While both bills would require pharmaceutical manufacturers to pay a rebate if drug prices outpace inflation, the House bill would empower the Secretary of Health and Human Services to negotiate prices directly with manufacturers. Both bills address the Medicare Part D coverage gap by capping out-of-pocket costs. Though the Congressional Budget Office estimates the House bill would result in a \$456 billion decrease in federal health care expenditures, it also predicts that the legislation would cause fewer drugs to be introduced to the U.S. market over the next decade.

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

In the E.U., similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the E.U. or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

***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. Further, any labeling approved by the FDA for Galafold® or any of our other product candidates may include restrictions on use, 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. 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 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.

***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;
- 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 and therefore to obtain a return on the investments we have made in our product or product candidates.

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. 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 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.

***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 are focusing a substantial effort in our research and development efforts on these gene therapy platforms, and our future success depends on the successful development of these therapeutic approaches. 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. The number of gene therapy products approved in the Western world is rapidly increasing. Approved products include Spark's gene therapy product, which received approval from the FDA in 2017, GlaxoSmithKline's Strimvelis, and Novartis's and Gilead's CAR-T therapies, which received approval from the FDA in 2017, Avexis's Zolgensma which received FDA approval in 2019, and Bluebird Bio's Zynteglo which received E.U. and U.K. approval in 2019. Given the few precedents of approved gene therapy products, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the U.S., the E.U., the U.K. or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval. Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In addition, the FDA can put an investigational new drug application, or IND, on clinical hold if the information in an IND is not sufficient to assess the risks in patients or a safety issue emerges in preclinical or clinical studies. Before a clinical study can begin at any institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval studies, limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

***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. 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.

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

In connection with seeking marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. This is particularly the case with AT-GAA, as there can be no assurance of the outcome of the Phase 3 PROPEL study or that the study results will meet regulatory standards for approval.

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, CLN6, CLN3 and other 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 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, CLN6 and CLN3 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, including the current CLN-3 study and other studies we may initiate. 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.

***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 of Galafold<sup>®</sup>, a small molecule for Fabry disease and in a next generation ERT treatment for Pompe disease, AT-GAA. In 2018 we also made a significant investment in potential gene therapies for Fabry, Pompe, CDD, Batten's disease 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 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.

***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, including AT-GAA, CLN6 and CLN3 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. For example, we have reported data from a Phase 1/2 clinical trial of AT-GAA in Pompe disease. The data is based on a small patient sample and therefore may not be predictive of future results in the Phase 3 PROPEL study. PROPEL study results may not support further development, or even if such results are favorable, we may not be able to successfully complete the development of, obtain accelerated, conditional or standard regulatory approval for, or successfully commercialize AT-GAA. Similarly, we recently reported preliminary results from initial patients in the CLN-6 trial. Results from these initial patients may not be predictive of results of the full data set, we may not be able to demonstrate safety and efficacy and the FDA, EMA and other regulatory authorities may not accept this data as sufficient for approval. 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 the existing CLN-6, CLN-3 or other 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 gene therapy technology. The product candidates in our gene therapy program are being developed for the treatment of diseases in which there is little clinical experience, which increases the difficulty in selecting appropriate endpoints and the risk that regulatory authorities may not consider the endpoints of clinical trials to provide clinically meaningful results. As a result, if the FDA requires 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, 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 and EMA. 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. Obtaining orphan drug exclusivity for our product candidates, in the E.U., U.K. and U.S., may be important to the product candidate's success. 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.

#### **Risks Related to Our Financial Position and Need for Additional Capital**

***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 multiple 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 and have incurred losses in each period since our inception. For the year ended December 31, 2019, we have a net loss of \$356.4 million, and we have an accumulated deficit of \$1.8 billion at December 31, 2019.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we:

- continue our development and commercialization of, and seek regulatory approvals for, product candidates in the U.S., the E.U., U.K., Japan and other foreign countries, as applicable;
- conduct additional clinical trials to support the full approval of Galafold® in the U.S. and post-approval commitments or trials;
- continue communicating with the EMA, as necessary, regarding post-marketing requirements and clinical trials for Galafold®;
- continue to or initiate the regulatory submission process for marketing approval of Galafold® 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;

- continue our preclinical studies and clinical trials on the use of AT-GAA for Pompe disease and our gene therapies for Fabry, Pompe, Batten's, Niemann Pick-C, MPS and other LDs; and
- continue our preclinical studies of and potentially conduct clinical studies of ERT and gene therapy for CDD.

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<sup>®</sup>, in May 2016, with the U.S. and Japan commercial launches in 2018 and are now approved in 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, 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 and operating expense 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<sup>®</sup>;
- develop and maintain a commercial organization capable of sales, marketing, and distribution for Galafold<sup>®</sup> and any product candidates we intend to market, 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<sup>®</sup> or any of our other product candidates that may receive regulatory approval, including pediatric trials and patient registries;
- successfully complete development activities, including the necessary preclinical studies and clinical trials, with respect to product candidates, including AT-GAA and our gene therapies;
- complete and submit regulatory submissions to the FDA and obtain regulatory approval for our product candidates including AT-GAA and our gene therapies; and
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities.

In addition, because of the numerous risks and uncertainties associated with product development, including that our product candidates may not advance through development or achieve the safety and efficacy endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. Furthermore, we anticipate incurring significant costs associated with commercializing these products.

Even if we are able to generate significant revenues from the sale of our products, we may not 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 Galafold<sup>®</sup> revenues, is sufficient to fund ongoing Fabry and Pompe, and gene therapy program operations into the first half of 2022. Potential future business development collaborations, restructurings, pipeline expansion, and investment in biologics or gene therapy 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<sup>®</sup> 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<sup>®</sup> and any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own;
- the scope, progress, results, and costs of preclinical development, laboratory testing, and clinical trials for our product candidates and any other product candidates that we may in-license or acquire;
- the cost of manufacturing drug supply for our preclinical studies and clinical trials, including the significant cost of manufacturing AT-GAA and our gene therapies;
- the cost of transferring manufacturing technologies for our gene therapies to CMOs;
- 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 require that we perform more studies than those that we currently anticipate for our product and product candidates;
- 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 emergence of competing technologies and other adverse market developments;
- 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. 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 remaining convertible note holders and Pharmakon Debt Financing 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® or our product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market our technologies that we would otherwise prefer to develop and market ourselves.

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

On December 21, 2016, we issued \$250 million aggregate principal amount of 3.00% unsecured Convertible Senior Notes due 2023 (the "Convertible Notes"), in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act. The Convertible Notes bear interest at a fixed rate of 3.00% per year, payable semiannually on June 15 and December 15 of each year, beginning on June 15, 2017. The Convertible Notes will mature on December 15, 2023, unless earlier repurchased, redeemed, or converted in accordance with their terms. The Convertible Notes are convertible at the option of the holders, under certain circumstances and during certain periods, into cash, shares of the Company's common stock, par value \$0.01 per share, or a combination thereof and may be settled.

In September 2018, we entered into a loan agreement with BioPharma Credit PLC, an investment fund managed by Pharmakon Advisors, L.P. (the "Pharmakon Debt Financing") as the lender, for a \$150.0 million non-dilutive senior secured term loan (the "Senior Secured Term Loan") with an interest rate equal to 3-month LIBOR plus 7.50% per annum, subject to a floor and ceiling on the rate, which matures in five years. We received net proceeds of \$146.6 million in September 2018, after deducting fees and estimated expenses payable by us. There are no warrants or any equity conversion features associated with the Senior Secured Term Loan.

During the first and second quarters of 2019, we entered into separate, privately negotiated exchange agreements (the "Exchange Agreements") with a limited number of holders (the "Holders") of the unsecured Convertible Senior Notes due in 2023 ("Convertible Notes"). Under the terms of the Exchange Agreements, the Holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of our common stock, par value \$0.01 per share. Additionally, we terminated the Capped Call Confirmations related to the exchange of the Convertible Notes for cash proceeds of \$19.9 million.

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 or obtain financing sufficient to satisfy our debt payment obligations 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.

***Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate may adversely affect our financial results.***

Certain of our outstanding debt is indexed to the London Interbank Offered Rate ("LIBOR"). On July 27, 2017, the Financial Conduct Authority ("FCA"), which regulates LIBOR, announced its intention to phase out LIBOR rates by the end of 2021. It is not possible to predict the further effect of the FCA's announcement, any changes in the methods by which LIBOR is determined, or any other reforms to LIBOR that may be enacted in the U.K., the E.U. or elsewhere. Such developments may cause LIBOR to perform differently than in the past or cease to exist. In addition, any other legal or regulatory changes made by the FCA, ICE Benchmark Administration Limited, the European Money Markets Institute (formerly Euribor-EBF), the European Commission or any other successor governance or oversight body, or future changes adopted by such body, in the method by which LIBOR is determined or the transition from LIBOR to a successor benchmark may result in, among other things, a sudden or prolonged increase or decrease in LIBOR, a delay in the publication of LIBOR, and changes in the rules or methodologies in LIBOR, which may discourage market participants from continuing to administer or to participate in LIBOR's determination, and, in certain situations, could result in LIBOR no longer being determined and published. If a published U.S. dollar LIBOR rate is unavailable after 2021, the interest rates on our debt which is indexed to LIBOR will be determined using alternative methods, which may result in interest obligations which are more than or do not otherwise correlate over time with the payments that would have been made on such debt if U.S. dollar LIBOR was available in its current form. Further, the same costs and risks that may lead to the unavailability of U.S. dollar LIBOR may make one or more of the alternative methods impossible or impracticable to determine. Any of these proposals or consequences could have a material adverse effect on our financing costs, and as a result, our financial condition, operating results and cash flows.

***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. 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.

In addition, the announcement of Brexit and the continued uncertainty around the full impact of it and the exact trade arrangements upon exit has adversely impacted global markets, including currencies, and resulted in a decline and volatility in the value of the British pound and the Euro, as compared to the U.S. dollar and other currencies. Volatility in exchange rates and global financial markets is expected to continue due to a number of factors, including uncertainty surrounding Brexit trade arrangements and continued political and economic uncertainty globally.

***We may acquire other 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 the research collaboration with Penn to develop gene therapies in 2018 and expanded in 2019. 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.

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

As of December 31, 2019, the Company had federal, state, and foreign net operating loss carry forwards ("NOLs") of approximately \$1,036 million, \$897.8 million, and \$30.6 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 2017 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 2019 will expire in 2029 through 2039. The foreign NOLs are subject to differing expirations beginning in 2026. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), 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 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 increase state taxes owed.

## **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. 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; or
- patent authorities will not identify deficiencies in our patent applications and refuse to grant our patents.

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 ATB200, Galafold<sup>®</sup>, 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.

The patents that we have licensed from Mt. Sinai School of Medicine relating to use of Galafold<sup>®</sup> to treat Fabry disease expired in 2018 in the U.S. and expired in 2019 in all other jurisdictions. 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 do not hold composition of matter patents covering Galafold<sup>®</sup> but we have several method of treatment patents issued. We do have composition of matter patents, method of manufacture and other patents issued for ATB200. We also have pending applications covering Galafold<sup>®</sup>, ATB200 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. 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. 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 may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.***

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

***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, 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.

***Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.***

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

***If 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.

***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 NCH and 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.

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

The U.S. Patent and Trademark Office and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents are required to be paid to the U.S. Patent and Trademark Office and foreign patent agencies in several stages over the lifetime of the patents. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

***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 NCH 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 our Dependence on Third Parties**

***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 do not currently own or operate manufacturing facilities for clinical or commercial production of our product or product candidates. We currently lack the resources and the capabilities to manufacture ourselves any of our product or product candidates 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 manufacture 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. Further, our gene therapies may require new or specialized manufacturing with limited third-party manufacturers available to provide these services. 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;
- 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; 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 regulations setting forth cGMP. 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<sup>®</sup>. Our 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 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 and clinical trials, and we rely, or will rely, on these other manufacturers for commercial distribution of our product and, if 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 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, 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 App Tec Biopharmaceuticals, 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, 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 recent out-breaks of SARS, COVID-19 "coronavirus" or other similar illnesses in PRC could impact operations at Wuxi. Although currently there has been no impact on operations 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.

***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, our collaborators may not 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.

**Risks Related to our Business, Employee Matters and Managing Growth**

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

We are highly dependent on John F. Crowley, our Chairman and Chief Executive Officer, Bradley L. Campbell, our President and Chief Operating Officer, and Daphne Quimi, our Chief Financial Officer. These executives each have significant pharmaceutical industry experience. The loss of the services of any of these executives 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 these executives 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. Crowley or on any of our other executive officers.

Recruiting and retaining qualified scientific, clinical and sales and marketing personnel will also be critical to our success, including our Research and Gene Therapy Center of Excellence 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, 2019, we had 584 full-time employees. As our development and commercialization strategies develop, we will need additional managerial, operational, sales, marketing, financial, technical operations and other resources. In particular, we are expanding our scientific and managerial support for gene therapy. 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.

***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, shareholders, government agencies and others through private actions, class actions, administrative proceedings, regulatory actions 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. 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 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.

***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, 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.



***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, 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.

***Our business and operations would suffer significant harm in the event of health epidemics and other outbreaks***

Our business could be adversely impacted by the effects of the COVID-19 “coronavirus” outbreak originating in the PRC, or by other health epidemics or pandemics. We currently rely on WuXi App Tec Biopharmaceuticals, a company based in 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 COVID-19 or other health epidemic.

In addition, our operations and sales channels are global and any travel bans or other restrictions that may be imposed in order to contain the spread of an outbreak may disrupt our and our other business partners’ ability to conduct business around the world, could adversely impact our supply chain and may hinder the ability of our patients to receive treatment from their caregivers or in our on-going clinical trials. This may also result in our inability to obtain raw materials needed for the manufacture of our products, reduce the sales of our products for patient treatment and interfere with the conduct of our clinical trials.

Although currently there has been no impact on operations and we, Wuxi and our other business partners have robust mitigation plans in place, there can be no assurance that operations would not be negatively impacted in the future, resulting in negative impacts on our financial condition and results of operations.

**Risks Related to our Common Stock**

***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 43% of our common stock as of December 31, 2019. 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.

***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.

***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;
- the impact of Brexit on our operations, supply chain, regulatory approvals and personnel;

- 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.

***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.

*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.

*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.

#### **Item 1B. UNRESOLVED STAFF COMMENTS**

None.

#### **Item 2. PROPERTIES**

The following table contains information about our current significant leased properties as of December 31, 2019.

Location	Approximate Square Feet	Use	Lease expiry date <sup>(1)</sup>
Cranbury, New Jersey, U.S.	90,000	Office and laboratory	March 2026
Marlow, United Kingdom	36,796	Office	August 2028
Philadelphia, Pennsylvania, U.S.	50,816	Office and laboratory	September 2044
Princeton, New Jersey, U.S.	21,922	Office	January 2022

<sup>(1)</sup>Includes renewal options on leases which the Company is 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**

We are not currently a party to any legal proceedings.

#### **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 19, 2020 was \$10.81 per share. As of February 19, 2020, there were 22 holders of record of our common stock.

#### **Dividends**

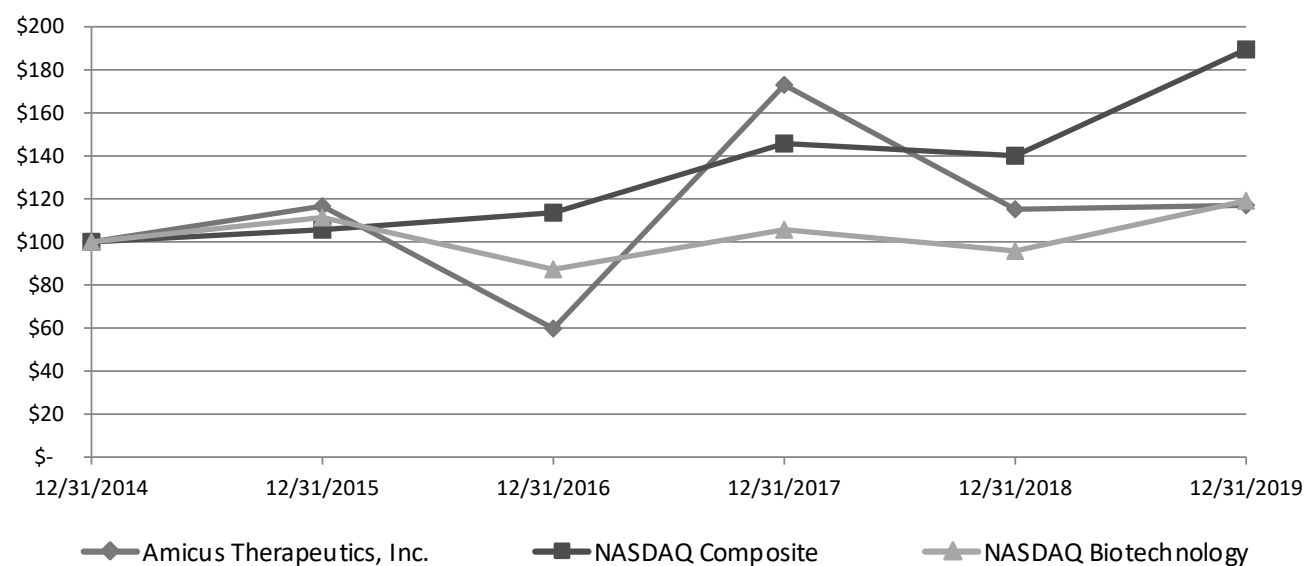
We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance the development and growth of our business. We do not intend to declare or pay cash dividends to our stockholders in the foreseeable future.

#### **Recent Sales of Unregistered Securities**

We did not sell any equity securities during the fiscal year ended December 31, 2019 in transactions that were not registered under the Securities Act.

## 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.



	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019
Amicus Therapeutics, Inc.	\$100	\$117	\$60	\$173	\$115	\$117
NASDAQ Composite	\$100	\$106	\$114	\$146	\$140	\$189
NASDAQ Biotechnology	\$100	\$111	\$87	\$106	\$96	\$119

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

## Issuer Purchases of Equity Securities

We did not repurchase any shares of our common stock during the year ended December 31, 2019. We have not announced any plans or programs for the repurchase of our common stock. However, employees surrendered 301,059 shares to the Company, during the year ended December 31, 2019 at a weighted average price of \$10.75 per share for the payment of the minimum tax liability withholding obligations upon the vesting of restricted stock units. We do not consider this a share buyback program.

## Item 6. SELECTED FINANCIAL DATA

### Statement of Operations Data (in thousands except share and per share data)

	2019	Years Ended December 31,			
		2018	2017	2016	2015
Net product sales	\$ 182,237	\$ 91,245	\$ 36,930	\$ 4,958	\$ —
Cost of goods sold	21,963	14,404	6,236	833	—
Gross profit	160,274	76,841	30,694	4,125	—
Operating expenses:					
Research and development	286,378	270,902	149,310	104,793	76,943
Selling, general, and administrative	169,861	127,200	88,671	71,151	47,269
Changes in fair value of contingent consideration payable	3,297	3,300	(234,322)	6,760	4,377
Loss on impairment of assets	—	—	465,427	—	—
Restructuring charges	—	—	—	69	15
Depreciation and amortization	4,775	4,216	3,593	3,242	1,833
Total operating expenses	464,311	405,618	472,679	186,015	130,437
Loss from operations	(304,037)	(328,777)	(441,985)	(181,890)	(130,437)
Other income (expense):					
Interest income	10,249	10,461	4,096	1,602	929
Interest expense	(18,872)	(22,402)	(17,240)	(5,398)	(1,578)
Loss on exchange of convertible notes	(40,624)	—	—	—	—
Change in fair value of derivatives	—	(2,739)	—	—	—
Loss on extinguishment of debt	—	—	—	(13,302)	(952)
Other (expense) income	(2,626)	(5,632)	6,008	(4,793)	(80)
Loss before income tax	(355,910)	(349,089)	(449,121)	(203,781)	(132,118)
Income tax (expense) benefit	(478)	94	165,119	3,739	—
<b>Net loss attributable to common stockholders</b>	<b>\$ (356,388)</b>	<b>\$ (348,995)</b>	<b>\$ (284,002)</b>	<b>\$ (200,042)</b>	<b>\$ (132,118)</b>
Net loss attributable to common stockholders per common share — basic and diluted	\$ (1.48)	\$ (1.88)	\$ (1.85)	\$ (1.49)	\$ (1.20)
Weighted-average common shares outstanding — basic and diluted	240,421,001	185,790,021	153,355,144	134,401,588	109,923,815

### Balance Sheet Data (in thousands)

	As of December 31,				
	2019	2018	2017	2016	2015
Cash, cash equivalents, and marketable securities	\$ 452,740	\$ 504,152	\$ 358,562	\$ 330,351	\$ 214,033
Working capital	391,261	464,971	321,925	229,105	142,985
Total assets	850,207	789,951	627,024	1,036,845	908,384
Total liabilities	373,782	447,039	274,174	676,694	560,550
Accumulated deficit	(1,768,610)	(1,412,222)	(1,063,610)	(779,608)	(579,566)
Total stockholders' equity	476,425	342,912	352,850	360,151	347,834

## 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 developing novel medicines for rare. We have a portfolio of product opportunities led by our novel medicine for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease in the clinic, and an industry leading rare disease gene therapy portfolio.

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."), United Kingdom ("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), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy designation to AT-GAA for the treatment of late onset Pompe disease.

We have established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children's Hospital ("NCH") and an expanded collaboration with the University of Pennsylvania ("Penn"). Our pipeline includes gene therapy programs in rare, neurologic lysosomal disorders ("LDs"), specifically: CLN6, CLN3, CLN8, and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Niemann-Pick Type C ("NPC"), Mucopolysaccharidosis Type IIIB ("MPSIIIB"), as well as a next generation program in Mucopolysaccharidosis Type IIIA ("MPSIIIA"). Our expanded collaboration with Penn also provides us with exclusive disease-specific access and the option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies.

During the second quarter of 2019, we completed an underwritten equity offering and issued 18.7 million shares of our common stock at \$10.75 per share, inclusive of the fully exercised option to purchase additional shares from the initial offering. This transaction resulted in net proceeds of \$189.0 million, after deducting underwriting discounts and commissions and offering expenses.

During the first and second quarters of 2019, we entered into separate, privately negotiated exchange agreements (the "Exchange Agreements") with a limited number of holders (the "Holders") of the unsecured Convertible Senior Notes due in 2023 ("Convertible Notes"). Under the terms of the Exchange Agreements, the Holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of our common stock, par value \$0.01 per share. Additionally, we terminated the Capped Call Confirmations related to the exchange of the Convertible Notes for cash proceeds of \$19.9 million.

### Consolidated Results of Operations

The following section generally discusses 2019 and 2018 items and year-to-year comparisons between 2019 and 2018. Discussions of 2017 items and year-to-year comparisons between 2018 and 2017 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, 2018.

#### Year Ended December 31, 2019 Compared to Year Ended December 31, 2018

The following table provides selected financial information for the Company:

(in thousands)	Years Ended December 31,		
	2019	2018	Change
Net product sales	\$ 182,237	\$ 91,245	\$ 90,992
Cost of goods sold	21,963	14,404	7,559
Cost of goods sold as a percentage of net product sales	12.1%	15.8%	(3.7)%
Operating expenses:			
Research and development	286,378	270,902	15,476
Selling, general, and administrative	169,861	127,200	42,661
Changes in fair value of contingent consideration payable	3,297	3,300	(3)
Depreciation and amortization	4,775	4,216	559
Other income (expense):			
Interest income	10,249	10,461	(212)
Interest expense	(18,872)	(22,402)	3,530
Loss on exchange of convertible notes	(40,624)	—	(40,624)
Change in fair value of derivatives	—	(2,739)	2,739
Other (expense) income	(2,626)	(5,632)	3,006
Income tax (expense) benefit	(478)	94	(572)
Net loss attributable to common stockholders	\$ (356,388)	\$ (348,995)	\$ (7,393)

*Net Product Sales.* Net product sales increased \$91.0 million during the year ended December 31, 2019 compared to the same period in the prior year. The increase was primarily due to Galafold® being approved for sale in the U.S. and Japan in the third and second quarters of 2018, respectively, as well as continued growth in the European market.

*Cost of Goods Sold.* Cost of goods sold includes manufacturing costs as well as royalties associated with sales of our product. Cost of goods sold as a percentage of net product sales was 12.1% during the year ended December 31, 2019 compared to 15.8% during the same period in the prior year primarily due to the proportion of sales in countries subject to a higher royalty burden.

*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,	
<b>Projects</b>	<b>2019</b>	<b>2018</b>
Third-party direct project expenses		
Galafold® (Fabry Disease)	\$ 20,347	\$ 12,665
AT-GAA (Pompe Disease)	103,884	55,919
Gene therapy programs	39,836	137
Pre-clinical and other programs	1,166	1,562
Total third-party direct project expenses	<u>165,233</u>	<u>70,283</u>
Other project costs		
Personnel costs	81,496	62,999
Other costs	39,649	30,620
Total other project costs	<u>121,145</u>	<u>93,619</u>
Business development transactions	—	107,000
Total research and development costs	<u>\$ 286,378</u>	<u>\$ 270,902</u>

The \$15.5 million increase in research and development costs was primarily due to increases in clinical research and manufacturing costs with the advancement and enrollment of clinical studies in the Pompe program, an increase in gene therapy programs driven by the pipeline growth, as well as support for ongoing regulatory requirements, approval in new geographies, and pediatric and other studies to support label expansion of Galafold®. There were also increases in personnel and other costs associated with the advancement and enrollment of clinical studies and investments in manufacturing. This was primarily offset by \$100 million in expenses associated with the acquisition of ten gene therapy assets with the Celenex transaction and the \$7 million license upfront payment related to the collaboration agreement with Penn in 2018.

*Selling, General, and Administrative Expense.* Selling, general, and administrative increased \$42.7 million primarily due to the expanded geographic scope of the ongoing commercial launch of Galafold® and related operational costs of our global business, including establishing commercial organizations and related teams in the U.S. and Japan.

*Loss on Exchange of Convertible Notes.* During the first and second quarters of 2019, the Company entered into separate, privately negotiated Exchange Agreements with a limited number of holders of the Convertible Notes. As a result of this exchange, the Company recognized a loss on exchange of debt of \$40.6 million in the Consolidated Statements of Operations, and \$215.0 million in additional paid-in-capital and common stock of \$0.4 million in the Consolidated Balance Sheets for the year ended December 31, 2019.

*Income Tax (Expense) Benefit.* The income tax expense for the year ended December 31, 2019 was \$0.5 million. We are subject to income taxes in various jurisdictions. Our tax liabilities are largely dependent on the distributions of pre-tax earnings among the many jurisdictions in which we operate. The income tax benefit for the year ended December 31, 2018 of \$0.1 million was primarily related to provision to return variances.

## Critical Accounting Policies and Significant Judgments and Estimates

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

### Revenue Recognition

Our net product sales consist of sales of Galafold® for the treatment of Fabry disease. We have recorded revenue on sales where Galafold® is available either on a commercial basis or through a reimbursed EAP. 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 third-party discounts and rebates. The identified variable consideration is recorded as a reduction of revenue at the time revenues from sales 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.

We elected the portfolio approach practical expedient in applying ASC Topic 606, *Revenue from Contracts with Customers*, to our identified revenue streams. Contracts within each revenue stream have similar characteristics and we believe the results of this approach would not differ materially than if we applied ASC Topic 606 to each individual contract.

### 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 include 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.

The information presented for the periods prior to January 1, 2019 has not been restated and is reported under the accounting standard in effect for those periods.

### ***Research and Development Expenses***

We expect to continue to incur substantial research and development expenses as we continue to develop our product candidates. Research and development expense consists of:

- internal costs associated with our research and clinical development activities;
- fees owed to third-party contract research organizations in connection with preclinical, toxicology studies and clinical trials;
- payments we make to contract manufacturers, investigative sites, and consultants in connection with clinical trials;
- technology license costs;
- manufacturing development costs;
- personnel-related expenses, including salaries, benefits, travel, and related costs for the personnel involved in drug discovery and development;
- activities relating to regulatory filings and the advancement of our product candidates through preclinical studies and clinical trials; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent, facility maintenance, as well as laboratory and other supplies.

We have multiple research and development projects ongoing at any one time. We utilize our internal resources, employees, and infrastructure across multiple projects. We record and maintain information regarding external, out-of-pocket research and development expenses on a project-specific basis.

We expense research and development costs as incurred, including payments made to date under our license agreements. We believe that significant investment in product development is a competitive necessity and plan to continue these investments in order to realize the potential of our product candidates.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the remainder of the development of our product candidates. As a result, we are not able to reasonably estimate the period, if any, in which material net cash inflows may commence from our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with the conduct, duration, and cost of clinical trials, which vary significantly over the life of a project as a result of evolving events during clinical development, including:

- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patients;
- the number of patients that ultimately participate in the trials;
- the results of our clinical trials; and
- any mandate by the FDA or other regulatory authority to conduct clinical trials beyond those currently anticipated.

Our expenditures are subject to additional uncertainties, including the terms and timing of regulatory approvals, and the expense of filing, prosecuting, defending, and enforcing any patent claims or other intellectual property rights. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay, or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of the foregoing variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development, regulatory approval, and commercialization of that product candidate. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those which we currently anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Drug development takes several years and millions of dollars in development costs.

### ***Share-based Compensation***

#### *Stock Option Grants*

In accordance with the applicable accounting guidance, we estimate the fair value of each equity award granted. 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 stock-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was based on our historical volatility since our initial public offering in May 2007. We determine the average expected life using our actual historical data versus a "simplified" method used in prior quarters. The "simplified" method of estimating the expected exercise term uses the mid-point between the vesting date and the end of the contractual term. 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 "RSU's")*

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.

### ***Business Combinations***

We assign fair value to the tangible and intangible assets acquired and liabilities assumed based upon their estimated fair values on the acquisition date of 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, we estimate the fair value of contingent acquisition consideration payments utilizing a probability-based income approach inclusive of an estimated discount rate.

Although we believe the assumptions and estimates made are reasonable, they are based in part on historical experience and information obtained from the management of the acquired businesses and are inherently uncertain. Examples of critical estimates in valuing any contingent acquisition consideration issued or which may be issued and the intangible assets we have acquired or may acquire in the future include but are not limited to:

- the feasibility and timing of achievement of development, regulatory, and commercial milestones;
- expected costs to develop the in-process research and development into commercially viable products; and
- future expected cash flows from product sales.

Unanticipated events and circumstances may occur which may affect the accuracy or validity of such assumptions, estimates, or actual results.

### ***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 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. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. No indicators of impairment were noted during the years ended December 31, 2019 and December 31, 2018.

### ***Valuation of 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. Each period we reassess the fair value of the contingent acquisition consideration payable associated with certain acquisitions and record changes in the fair value as contingent consideration expense. Increases or decreases in the fair value of the contingent acquisition 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 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<sup>®</sup>, 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, debt issuances, Galafold<sup>®</sup> revenues, collaborations, and other financing arrangements.

### **Sources of Liquidity**

During the first and second quarters of 2019, we entered into separate, privately negotiated Exchange Agreements with a limited number of holders of the Convertible Notes. Under the terms of the Exchange Agreements, the limited number of holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of our common stock, par value \$0.01 per share. Additionally, we terminated the Capped Call Confirmations related to the exchange of the Convertible Notes for cash proceeds of \$19.9 million.

During the second quarter of 2019, we completed an underwritten equity offering and issued 18.7 million shares of common stock at \$10.75 per share, inclusive of the fully exercised option to purchase additional shares from the initial offering. This transaction resulted in net proceeds of \$189.0 million, after deducting underwriting discounts, commissions, and offering expenses.

During the third quarter of 2018, we entered into a loan agreement with BioPharma Credit PLC, as the lender, for a \$150.0 million non-dilutive senior secured term loan (the "Senior Secured Term Loan") with an interest rate equal to 3-month LIBOR plus 7.50% per annum, subject to a floor and ceiling on the rate, which matures in five years. We received net proceeds of \$146.6 million in September 2018, after deducting fees and expenses. There are no warrants or any equity conversion features associated with the Senior Secured Term Loan. For additional information, see "—Note 12. Debt" in our Notes to Consolidated Financial Statements.

During the first quarter of 2018, we issued, through an underwritten offering, 20.2 million shares of our common stock resulting in net proceeds of \$294.6 million after deducting underwriting discounts and commissions and offering expenses.

### **Cash flow discussion**

As of December 31, 2019, we had cash, cash equivalents, and marketable securities of \$452.7 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 5. 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, 2019 was \$250.4 million. The components of net cash used in operations included the net loss for the year ended December 31, 2019 of \$356.4 million and the net change in operating assets and liabilities of \$11.6 million. The change in operating assets was primarily due to increases in accounts receivable by \$11.1 million due to increased commercial sales of Galafold<sup>®</sup>, an increase in prepaid and other current assets of \$3.3 million to support commercial activities for Galafold<sup>®</sup> launch, and an increase in inventory of \$5.1 million. The net cash used in operations was also impacted by an increase in accounts payable and accrued expenses of \$46.7 million, mainly related to program expenses and support for the commercial launch of Galafold<sup>®</sup>. This was partially offset by a decrease in deferred reimbursement of \$5.5 million.



Net cash used in operations for the year ended December 31, 2018 was \$300.0 million. The components of net cash used in operations included the net loss for the year ended December 31, 2018 of \$349.0 million, and the net increase in operating assets of \$16.1 million. The change in operating assets was primarily due to increases in accounts receivable by \$13.3 million and inventory of \$4.2 million due to commercial sales of Galafold<sup>®</sup>, partially offset by a decrease in prepaid and other current assets of \$2.5 million for spending to support commercial activities for Galafold<sup>®</sup> launch. The net cash used in operations was also impacted by an increase in accounts payable and accrued expenses of \$17.1 million, mainly related to program expenses and support for the commercial launch of Galafold<sup>®</sup>, and a decrease in deferred reimbursement of \$6.3 million due to payment of a milestone.

#### ***Net Cash Provided by (Used in) Investing Activities***

Net cash provided by investing activities for the year ended December 31, 2019 was \$95.2 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash provided by investing activities reflects \$499.0 million for the sale and redemption of marketable securities, partially offset by \$383.9 million for the purchase of marketable securities and \$20.0 million for the acquisition of property and equipment.

Net cash used in investing activities for the year ended December 31, 2018 was \$121.2 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash used in investing activities reflects \$578.4 million for the purchase of marketable securities, \$6.3 million for the acquisition of property and equipment, partially offset by \$463.5 million for the sale and redemption of marketable securities.

#### ***Net Cash Provided by Financing Activities***

Net cash provided by financing activities for the year ended December 31, 2019 was \$217.5 million. Net cash provided by financing activities primarily reflects \$189.0 million from the issuance of common stock, net of issuance costs paid, \$19.9 million from termination of capped call and \$12.3 million from the exercise of stock options and warrants, partially offset by \$3.2 million from the purchase of vested restricted stock units.

Net cash provided by financing activities for the year ended December 31, 2018 was \$450.8 million. Net cash provided by financing activities primarily reflects \$294.6 million from the issuance of common stock, net of issuance costs, \$146.6 million in proceeds from the Senior Secured Term Loan, net of issuance costs and estimated fees, \$9.1 million from the exercise of stock options, and \$3.6 million from the exercise of warrants, partially offset by \$2.8 million from the purchase of vested RSU's.

#### **Funding Requirements**

We expect to incur losses from operations for 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 progress and results of our preclinical and clinical trials of our drug candidates and gene therapy candidates, including but not limited to AT-GAA, CLN6 and CLN3;
- the cost of manufacturing drug and gene therapy supply for our clinical and preclinical studies, including the significant cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200") and gene therapies;
- the scope, progress, results, and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of a pharmacological chaperone co-administered with ERT for the treatment of AT-GAA and gene therapies for the treatment of rare genetic metabolic diseases;
- the future results of on-going preclinical research and subsequent clinical trials for CDD, Pompe gene therapy, Fabry gene therapy, NPC, MPSIIB and next generation MPSIIIA, including our ability to obtain regulatory approvals and commercialize these gene therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates;
- any changes in regulatory standards relating to the review of our product candidates;
- 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;
- our ability to successfully commercialize Galafold<sup>®</sup> ("migalastat HCl");
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold<sup>®</sup>, AT-GAA and our gene therapy candidates;
- our ability to obtain reimbursement for Galafold<sup>®</sup>;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold<sup>®</sup>;
- our ability to obtain market acceptance of Galafold<sup>®</sup>;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- 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, 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 collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;
- our ability to adjust to changes in the European and U.K. markets in the wake of the U.K. leaving the E.U.;
- the extent to which our business could be adversely impacted by the effects of the COVID-19 "coronavirus" outbreak or by other health epidemics or pandemics;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

While we continue to generate revenue from product sales, in the absence of additional funding, we expect our continuing operating losses to result in increases in our cash used in operations over the next several quarters and years. We may seek additional funding through public or private financings of debt or equity. We believe that our current cash position, including expected Galafold<sup>®</sup> revenues, is sufficient to fund ongoing Fabry, Pompe, and gene therapy program operations into the first half of 2022. Potential future business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

## Financial Uncertainties Related to Potential Future Payments

### Milestone Payments / Royalties

Celenex - With our acquisition of Celenex in 2018, we agreed to pay up to an additional \$15 million in connection with the achievement of certain development milestones, \$262 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to \$75 million in tiered sales milestone payments.

NCH - Celenex has an exclusive license agreement with NCH. Under this license agreement, NCH is eligible to receive development and sales-based milestones of up to \$7.8 million from us for each product.

Penn - Under our expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty, and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in 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. We will provide \$10.0 million each year during the five-year agreement to fund the discovery research program.

GlaxoSmithKline - In November 2013, we entered into the Revised Agreement (the "Revised Agreement") with GlaxoSmithKline ("GSK"), pursuant to which we have obtained global rights to develop and commercialize migalastat as a monotherapy and in combination with ERT for Fabry disease. The Revised Agreement amends and replaces in its entirety the earlier agreement entered into between us and GSK in July 2012 (the "Original Collaboration Agreement"). Under the terms of the Revised Agreement, there was no upfront payment from us to GSK. For migalastat monotherapy, 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. In addition, because we reacquired worldwide rights to migalastat, we are no longer eligible to receive any milestones or royalties we would have been eligible to receive under the Original Collaboration Agreement.

### Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2019 and the effects such obligations are expected to have on our liquidity and cash flows in future periods:

(in thousands)	Total	Less than 1 year	1-3 years	3-5 years	Over 5 years
Operating lease obligations <sup>(2)</sup>	\$ 215,641	\$ 9,738	\$ 21,246	\$ 21,391	\$ 163,266
Debt obligations, including interest <sup>(3)</sup>	206,715	14,708	38,594	153,413	—
Purchase obligations <sup>(4)</sup>	74,753	35,153	13,200	17,600	8,800
Other contractual obligations	\$ 16,500	\$ —	\$ 7,500	\$ 6,000	\$ 3,000
Total fixed contractual obligations <sup>(1)</sup>	<u>\$ 513,609</u>	<u>\$ 59,599</u>	<u>\$ 80,540</u>	<u>\$ 198,404</u>	<u>\$ 175,066</u>

<sup>(1)</sup> This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known, (b) any royalty payments to third parties as the amounts of such payments, timing, and/or the likelihood of such payments are not known, (c) amounts, if any, that may be committed in the future to construct additional facilities, (d) agreements with clinical research organizations and other outside contractors who are partially responsible for conducting and monitoring our clinical trials for our drug candidates including Galafold<sup>®</sup>. These contractual obligations are not reflected in the table above because we may terminate them without penalty, and (e) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

<sup>(2)</sup> Represents the future payments on operating leases for properties, equipment, and vehicles. For more details, refer to "— Note 13. Leases," in our Notes to Consolidated Financial Statements.

<sup>(3)</sup> Represents the future payments of principal and interest to be made on our \$2.8 million 3% unsecured Convertible Notes due 2023 (the "Convertible Notes") and our \$150 million Secured Senior Term Loan due 2023 ("Senior Secured Term Loan"). The Convertible Notes bear interest at a fixed rate of 3.00% per year, payable semiannually on June 15 and December 15 of each year, beginning on June 15, 2017 and will mature on December 15, 2023. The Senior Secured Term Loan bears interest at a rate equal to the 3-month LIBOR plus 7.5% per year, payable quarterly of each year, beginning on December 31, 2019 and will mature on September 28, 2023.

<sup>(4)</sup> Represents minimum purchase commitments due to third parties. 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. The purchase obligations included above are in addition to amounts included in total recorded on our December 31, 2019 Consolidated Balance Sheet.

We have no other lines of credit or other committed sources of capital. To the extent our capital resources are insufficient to meet future capital requirements, we will need to raise additional capital or incur indebtedness to fund our operations. We cannot assure you that additional debt or equity financing will be available on acceptable terms, if at all.

### Off-Balance Sheet Arrangements

We had no off-balance sheet arrangements as of December 31, 2019 and 2018.

### Recent Accounting Pronouncements

Please refer to "— Note 2. Summary of Significant Accounting Policies," in our Notes to 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 \$1.4 million as of December 31, 2019. 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, 2019, we had a \$150 million Senior Secured Term Loan that bears interest at a rate equal to the 3-month LIBOR plus 7.50% 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, 2019 was 9.95%. A hypothetical 100 basis point increase or decrease in the average interest rate on our variable rate debt would result in \$1.5 million change in the interest expense as of December 31, 2019.

The Financial Conduct Authority has announced the intent to phase out the use of LIBOR by the end of 2021. If LIBOR is discontinued, we may need to renegotiate the terms of the Senior Secured Term Loan in order to replace LIBOR with the new standard that is established. 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. There is currently no definitive information regarding the future utilization of LIBOR or of any particular replacement rate. As such, 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.

## Report of Independent Registered Public Accounting Firm

### 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, 2019. 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, 2019, 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, 2019 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report. This report appears on the following page.

Dated March 2, 2020

/s/ JOHN F. CROWLEY  
Chairman and Chief Executive Officer

/s/ DAPHNE QUIMI  
Chief Financial Officer

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, 2019, 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, 2019, 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, 2019 and 2018, 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, 2019, and the related notes and our report dated March 2, 2020 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 2, 2020

## 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, 2019 and 2018, 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, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, 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, 2019, 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 2, 2020 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 3 to the consolidated financial statements, the Company has a \$22.7 million contingent consideration liability recorded as of December 31, 2019 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 2, 2020

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

	December 31,	
	2019	2018
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 142,837	\$ 79,749
Investments in marketable securities	309,903	424,403
Accounts receivable	33,284	21,962
Inventories	14,041	8,390
Prepaid expenses and other current assets	20,008	16,592
Total current assets	520,073	551,096
Operating lease right-of-use assets, less accumulated amortization of \$5,342 and \$0 at December 31, 2019 and December 31, 2018, respectively	33,315	—
Property and equipment, less accumulated depreciation of \$17,604 and \$15,671 at December 31, 2019 and December 31, 2018, respectively	47,705	11,375
In-process research & development	23,000	23,000
Goodwill	197,797	197,797
Other non-current assets	28,317	6,683
<b>Total Assets</b>	<b>\$ 850,207</b>	<b>\$ 789,951</b>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable, accrued expenses, and other current liabilities	\$ 120,373	\$ 80,625
Deferred reimbursements	1,250	5,500
Operating lease liabilities	7,189	—
Total current liabilities	128,812	86,125
Deferred reimbursements	8,906	10,156
Convertible notes	2,131	175,006
Senior secured term loan	147,374	146,734
Contingent consideration payable	22,681	19,700
Deferred income taxes	5,051	6,465
Operating lease liabilities	53,531	—
Other non-current liabilities	5,296	2,853
Total Liabilities	373,782	447,039
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$.01 par value, 500,000,000 shares authorized, 255,417,869 and 189,383,924 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively	2,598	1,942
Additional paid-in capital	2,227,225	1,740,061
Accumulated other comprehensive loss:		
Foreign currency translation adjustment	2,785	495
Unrealized gain (loss) on available-for securities	40	(427)
Warrants	12,387	13,063
Accumulated deficit	(1,768,610)	(1,412,222)
Total stockholders' equity	476,425	342,912
<b>Total Liabilities and Stockholders' Equity</b>	<b>\$ 850,207</b>	<b>\$ 789,951</b>

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,		
	2019	2018	2017
Net product sales	\$ 182,237	\$ 91,245	\$ 36,930
Cost of goods sold	21,963	14,404	6,236
Gross profit	160,274	76,841	30,694
Operating expenses:			
Research and development	286,378	270,902	149,310
Selling, general, and administrative	169,861	127,200	88,671
Changes in fair value of contingent consideration payable	3,297	3,300	(234,322)
Loss on impairment of assets	—	—	465,427
Depreciation and amortization	4,775	4,216	3,593
Total operating expenses	464,311	405,618	472,679
Loss from operations	(304,037)	(328,777)	(441,985)
Other income (expenses):			
Interest income	10,249	10,461	4,096
Interest expense	(18,872)	(22,402)	(17,240)
Loss on exchange of convertible notes	(40,624)	—	—
Change in fair value of derivatives	—	(2,739)	—
Other (expense) income	(2,626)	(5,632)	6,008
Loss before income tax	(355,910)	(349,089)	(449,121)
Income tax (expense) benefit	(478)	94	165,119
<b>Net loss attributable to common stockholders</b>	<b>\$ (356,388)</b>	<b>\$ (348,995)</b>	<b>\$ (284,002)</b>
Net loss attributable to common stockholders per common share — basic and diluted	\$ (1.48)	\$ (1.88)	\$ (1.85)
Weighted-average common shares outstanding — basic and diluted	240,421,001	185,790,021	153,355,144

See accompanying Notes to Consolidated Financial Statements

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

	Years Ended December 31,		
	2019	2018	2017
Net loss	\$ (356,388)	\$ (348,995)	\$ (284,002)
Other comprehensive gain (loss):			
Foreign currency translation adjustment gain (loss), net of tax impact of \$889, \$0, and \$0, respectively	2,290	2,537	(3,604)
Unrealized gain (loss) on available-for-sale securities, net of tax impact of \$182, \$0, and \$0, respectively	467	9	(538)
Other comprehensive income (loss)	2,757	2,546	(4,142)
Comprehensive loss	\$ (353,631)	\$ (346,449)	\$ (288,144)

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, 2016	142,691,986	\$ 1,480	\$ 1,120,156	\$ 16,076	\$ 2,047	\$ (779,608)	\$ 360,151
Stock issued from exercise of stock options, net	2,878,681	29	16,272	—	—	—	16,301
Stock issued from equity financing	21,122,449	212	242,825	—	—	—	243,037
Restricted stock tax vesting	296,674	—	(1,596)	—	—	—	(1,596)
Stock-based compensation	—	—	23,101	—	—	—	23,101
Unrealized holding loss on available-for-sale securities	—	—	—	—	(538)	—	(538)
Foreign currency translation adjustment	—	—	—	—	(3,604)	—	(3,604)
Net loss	—	—	—	—	—	(284,002)	(284,002)
Balance at December 31, 2017	166,989,790	1,721	1,400,758	16,076	(2,095)	(1,063,610)	352,850
Stock issued from exercise of stock options, net	1,397,908	14	9,130	—	—	—	9,144
Stock issued from equity financing	20,239,839	202	294,381	—	—	—	294,583
Restricted stock tax vesting	303,173	—	(2,832)	—	—	—	(2,832)
Stock-based compensation	—	—	29,260	—	—	—	29,260
Reclassification upon ASU 2018-02 adoption	—	—	—	—	(383)	383	—
Warrants exercised	453,214	5	6,625	(3,013)	—	—	3,617
Change in fair value of derivatives	—	—	2,739	—	—	—	2,739
Unrealized holding gain on available-for-sale securities	—	—	—	—	9	—	9
Foreign currency translation adjustment	—	—	—	—	2,537	—	2,537
Net loss	—	—	—	—	—	(348,995)	(348,995)
Balance at December 31, 2018	189,383,924	1,942	1,740,061	13,063	68	(1,412,222)	342,912
Stock issued from exercise of stock options, net	1,967,087	20	11,456	—	—	—	11,476
Stock issued from equity financing	18,720,930	187	188,807	—	—	—	188,994
Restricted stock tax vesting	477,198	—	(3,235)	—	—	—	(3,235)
Stock issued for contingent consideration	771,804	8	9,308	—	—	—	9,316
Stock-based compensation	—	—	44,430	—	—	—	44,430
Warrants exercised	101,787	1	1,487	(676)	—	—	812
Equity component of the convertible notes	43,995,139	440	215,036	—	—	—	215,476
Termination of capped call confirmations	—	—	19,875	—	—	—	19,875
Unrealized holding gain on available-for-sale securities	—	—	—	—	467	—	467
Foreign currency translation adjustment	—	—	—	—	2,290	—	2,290
Net loss	—	—	—	—	—	(356,388)	(356,388)
Balance at December 31, 2019	255,417,869	\$ 2,598	\$ 2,227,225	\$ 12,387	\$ 2,825	\$ (1,768,610)	\$ 476,425

See accompanying Notes to Consolidated Financial Statements

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

	Years Ended December 31,		
	2019	2018	2017
<b>Operating activities</b>			
Net loss	\$ (356,388)	\$ (348,995)	\$ (284,002)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of debt discount and deferred financing	2,546	10,976	9,703
Depreciation and amortization	4,775	4,216	3,593
Stock-based compensation	44,430	29,260	23,101
Loss on exchange of convertible debt	40,624	—	—
Change in fair value of derivatives	—	2,739	(265)
Non-cash changes in the fair value of contingent consideration payable	3,297	3,300	(234,322)
Foreign currency remeasurement (gain) loss	254	3,217	(5,620)
Non-cash deferred taxes	(1,415)	—	(167,305)
Loss on impairment	—	—	465,427
Other	(149)	59	(8)
Changes in operating assets and liabilities:			
Accounts receivable	(11,114)	(13,294)	(7,725)
Inventories	(5,114)	(4,205)	(897)
Prepaid expenses and other current assets	(3,287)	2,488	(15,329)
Accounts payable, accrued expenses, and other current liabilities	46,742	17,115	12,563
Other non-current assets and liabilities	(10,117)	(581)	(9)
Deferred reimbursements	(5,500)	(6,250)	(12,600)
Net cash used in operating activities	\$ (250,416)	\$ (299,955)	\$ (213,695)
<b>Investing activities</b>			
Sale and redemption of marketable securities	499,047	463,502	323,753
Purchases of marketable securities	(383,882)	(578,394)	(490,468)
Capital expenditures	(20,012)	(6,308)	(4,526)
Net cash provided by (used in) investing activities	\$ 95,153	\$ (121,200)	\$ (171,241)
<b>Financing activities</b>			
Proceeds from issuance of common stock and warrants, net of issuance costs	188,994	294,584	243,037
Payment of finance leases	(420)	(334)	(308)
Purchase of vested restricted stock units	(3,235)	(2,832)	(1,596)
Proceeds from termination of capped call confirmations	19,875	—	—
Proceeds from exercise of stock options	11,476	9,144	16,301
Proceeds from exercise of warrants	812	3,617	—
Payment of contingent consideration	—	—	(10,000)
Proceeds from loan agreements, net of issuance costs	—	146,596	—
Net cash provided by financing activities	\$ 217,502	\$ 450,775	\$ 247,434
Effect of exchange rate changes on cash, cash equivalents, and restricted cash	\$ 1,729	\$ 1,518	\$ 1,326
<b>Net increase (decrease) in cash, cash equivalents, and restricted cash</b>	<b>63,968</b>	<b>31,138</b>	<b>(136,176)</b>
Cash, cash equivalents, and restricted cash at the beginning of the year	82,375	51,237	187,413
<b>Cash, cash equivalents, and restricted cash at the end of the year</b>	<b>\$ 146,343</b>	<b>\$ 82,375</b>	<b>\$ 51,237</b>

Years Ended December 31,  
2019      2018      2017

**Supplemental disclosures of cash flow information**

Tenant improvements paid through lease incentive	\$ 19,388	\$ —	\$ —
Cash paid during the period for interest	\$ 16,966	\$ 7,500	\$ 7,424
Contingent consideration paid in shares	\$ 9,316	\$ —	\$ —
Capital expenditures unpaid at the end of period	\$ 1,865	\$ 106	\$ —

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 of product opportunities led by the novel medicine for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease in the clinic, and an industry leading rare disease gene therapy portfolio.

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."), United Kingdom ("U.K."), and Japan, with multiple additional approvals granted and applications pending in several other geographies around the world.

The lead biologics program of the Company's pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy designation to AT-GAA for the treatment of late onset Pompe disease. In the first quarter of 2020, the British Medicines and Healthcare Products Regulatory Agency issued a Promising Innovative Medicine designation for AT-GAA for the treatment of late-onset Pompe disease.

The Company has established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children's Hospital ("NCH") and an expanded collaboration with the University of Pennsylvania ("Penn"). The Company's pipeline includes gene therapy programs in rare, neurologic lysosomal disorders ("LDs"), specifically: CLN6, CLN3, CLN8 and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Niemann-Pick Type C ("NPC"), Mucopolysaccharidosis Type IIIB ("MPSIIIB"), as well as a next generation program in Mucopolysaccharidosis Type IIIA ("MPSIIIA"). This expanded collaboration with Penn also provides the Company with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. For additional information, see "— Note 16. Collaboration Agreement."

During the second quarter of 2019, the Company completed an underwritten equity offering and issued 18.7 million shares of its common stock at \$10.75 per share, inclusive of the fully exercised option to purchase additional shares from the initial offering. This transaction resulted in net proceeds of \$189.0 million, after deducting underwriting discounts and commissions and offering expenses.

During the first and second quarters of 2019, the Company entered into separate, privately negotiated exchange agreements (the "Exchange Agreements") with a limited number of holders (the "Holders") of the unsecured Convertible Senior Notes due in 2023 ("Convertible Notes"). Under the terms of the Exchange Agreements, the Holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of the Company's common stock, par value \$0.01 per share. For additional information, see "— Note 12. Debt."

The Company had an accumulated deficit of approximately \$1.8 billion as of December 31, 2019 and anticipates incurring losses through the fiscal year ending December 31, 2020 and beyond. The Company has historically funded its operations through stock offerings, debt issuances, Galafold® revenues, collaborations, and other financing arrangements.

The current cash position, including expected Galafold® revenues, is sufficient to fund ongoing Fabry, Pompe, and gene therapy program operations into the first half of 2022. Potential future 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.

***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 comprehensive income (loss) in the 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 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, 2019 have arisen from product sales primarily in Europe and the U.S. 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, 2019, the Company recorded an allowance for doubtful accounts of \$0.1 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.

**Revenue Recognition**

The Company's net product sales consist of sales of Galafold® for the treatment of Fabry disease. The Company has recorded revenue on sales where Galafold® is available either on a commercial basis or through a reimbursed early access program ("EAP"). Orders for Galafold® are generally received from distributors and pharmacies, with the ultimate payor often a government authority. In 2019, one customer accounted for 22% of net product sales and 11% 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 revenues from sales of Galafold® are 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 from Galafold® disaggregated by geographic area:

(in thousands)	For the Year		
	2019	2018	2017
U.S.	\$ 52,478	\$ 7,223	\$ —
Ex-U.S.	129,759	84,022	36,930
Total net product sales	\$ 182,237	\$ 91,245	\$ 36,930

**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 product sales 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 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 participants 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.

***Other Comprehensive Income (Loss)***

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

The information presented for the periods prior to January 1, 2019 has not been restated and is reported under the accounting standard in effect for those periods. For additional information, see "-Note 13. Leases" and "-Note 2. Summary of Significant Accounting Policies, Recent Accounting Developments - Guidance Adopted in 2019."

***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 (the "Code"). All of the investments held in the Deferral Plan are classified as investments held-to-maturity 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, 2019, the Company had three equity-based employee compensation plans, which are described more fully in "— Note 9. 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 RSUs, and 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 17. 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. 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. Contingent acquisition consideration payable is shown as a non-current liability 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 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. No indicators of impairment were noted during the years ended December 31, 2019 and December 31, 2018.

**Recent Accounting Developments - Guidance Adopted in 2019**

ASU 2016-02 - In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). ASU 2016-02 requires the recognition of lease assets and lease liabilities on the balance sheet for all lease obligations and disclosing key information about leasing arrangements. ASU 2016-02 requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under previous generally accepted accounting principles. In August 2018, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements*, ("ASU 2018-11"). ASU 2018-11 provided entities with an additional transition method for adoption, whereby, an entity initially applies the new leases standard at the adoption date and recognizes a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. Effective January 1, 2019 the Company adopted ASU 2016-02, along with the amendments issued in 2017 and 2018, and elected the transition method in ASU 2018-11. The Company elected the package of transition provisions available for expired or existing contracts, which allowed the Company to carry forward its historical assessments of (i) whether contracts are or contain leases, (ii) lease classification and (iii) initial direct costs. In addition, the Company applied the short-term lease recognition exemption for leases with terms at inception not greater than 12 months and will apply the practical expedient not to separate lease and non-lease components for new and modified leases commencing after adoption. The information presented for the periods prior to January 1, 2019 has not been restated and is reported under the accounting standard in effect for those periods. Upon adoption, the Company recorded a lease liability with a corresponding right-of-use asset of \$17.6 million. The adoption did not have a material impact on the Consolidated Statements of Operations and the Consolidated Statements of Cash Flows.

**Recent Accounting Developments - Guidance Not Yet Adopted**

ASU 2019-12 - In December 2019, the FASB issued ASU 2019-15, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"). This new guidance removes specific exceptions to the general principles in Topic 740. It eliminates the need for an organization to analyze whether the following apply in a given period: (i) exception to the incremental approach for intraperiod tax allocation; (ii) exceptions to accounting for basis differences when there are ownership changes in foreign investments; and (iii) exception in interim period income tax accounting for year-to-date losses that exceed anticipated losses. ASU 2019-12 also improves financial statement preparers' application of income tax-related guidance and simplifies the following: (i) franchise taxes that are partially based on income; (ii) transactions with a government that result in a step up in the tax basis of goodwill; (iii) separate financial statements of legal entities that are not subject to tax; and (iv) enacted changes in tax laws in interim periods. ASU 2019 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. Early adoption is permitted for public business entities for periods for which financial statements have not yet been issued. An entity that elects early adoption in an interim period should reflect any adjustments as of the beginning of the annual period that includes that interim period. Additionally, an entity that elects early adoption should adopt all the amendments in the same period. The Company is currently assessing the impact that this standard will have on its Consolidated Financial Statements upon adoption.

ASU 2018-15 - In August 2018, the FASB issued ASU 2018-15, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40)*: ("ASU 2018-15"), relating to a customer's accounting for implementation, set-up, and other upfront costs incurred in a cloud computing arrangement that is hosted by a vendor. Under the new guidance, a customer will apply the same criteria for capitalizing implementation costs as it would for an arrangement that has a software license. The new guidance does not affect the accounting for the service element of a hosting arrangement that is a service contract. The new guidance also prescribes the balance sheet, income statement and cash flow classification of the capitalized software costs and related amortization expense and requires additional quantitative and qualitative disclosures. ASU 2018-15 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019 for public companies. The Company will adopt this guidance prospectively on January 1, 2020, and it believes the adoption of this guidance will not have a material impact on its Consolidated Financial Statements or related disclosures.

ASU 2018-13 - In August 2018, the FASB issued ASU 2018-03, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). The amendments modify the disclosure requirements in Topic 820. ASU 2018-13 is effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The amendments on (i) changes in unrealized gains and losses, (ii) the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and (iii) the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. The Company will adopt this guidance on January 1, 2020, and it believes the adoption of this guidance will not have a material impact on its Consolidated Financial Statements or related disclosures.

ASU 2017-04 - In January 2017, the FASB issued ASU 2017-04, *Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment* ("ASU 2017-04"). ASU 2017-04 simplifies the recognition and measurement of a goodwill impairment loss by eliminating Step 2 of the quantitative goodwill impairment test. The guidance requires a one-step impairment test in which an entity compares the fair value of a reporting unit with its carrying amount and recognizes an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value, if any. ASU 2017-04 is effective for fiscal years beginning after December 15, 2019 and should be applied on a prospective basis. The Company will adopt this guidance on January 1, 2020, and it believes the adoption of this guidance will not have a material impact on its Consolidated Financial Statements or related disclosures.

ASU 2016-13 - In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires financial assets measured at amortized cost basis to be presented at the net amount expected to be collected and amends guidance on the impairment of financial instruments. ASU 2016-13 is effective for public companies who are SEC filers for fiscal years beginning after December 15, 2019, including interim periods within those years. The Company will adopt this guidance on January 1, 2020, and it believes the adoption of this guidance will not have a material impact on its Consolidated Financial Statements or related disclosures.

**3. Acquisitions**

**Acquisition of Celenex**

In September 2018, the Company expanded its pipeline by acquiring the rights and related intellectual property of ten gene therapy programs through its acquisition of Celenex, Inc., ("Celenex"). Celenex is a private, clinical stage gene therapy company whose lead programs are ten gene therapy programs including CLN6 and CLN3, which are in clinical stage, and several programs in pre-clinical stage. Pursuant to the terms of the agreement, the Company acquired Celenex for cash consideration of \$100 million. The Company has also agreed to pay up to an additional \$15 million in connection with the achievement of certain development milestones, \$262 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 ("NCH"). Under this license agreement, NCH is eligible to receive development and sales-based milestones of up to \$7.8 million for each product.

The Company evaluated the Celenex transaction and concluded that the transaction did not meet the definition of a business and was an asset acquisition. Given the fact that the license has no alternative future use, the \$100.0 million upfront payment was expensed to research and development expense in the Consolidated Statements of Operations for the year ended December 31, 2018.

**Acquisition of MiaMed, Inc.**

In July 2016, the Company entered into an Agreement and Plan of Merger (the "MiaMed Agreement") with MiaMed, Inc., ("MiaMed"). MiaMed is a pre-clinical biotechnology company focused on developing protein replacement therapy for CDD and related diseases. Under the terms of the MiaMed Agreement, the former holders of MiaMed's capital stock received an aggregate of \$6.5 million, comprised of (i) approximately \$1.8 million in cash (plus MiaMed's cash and cash equivalents at closing and less any of MiaMed's unpaid third-party fees and expenses related to the transaction), and (ii) 825,603 shares of the Company's common stock. In addition, the Company also agreed to pay up to an additional \$83.0 million in connection with the achievement of certain clinical, regulatory, and commercial milestones, for a potential aggregate deal value of \$89.5 million. The Company evaluated the transaction and concluded that it only acquired inputs and did not acquire any processes. The Company will need to develop its own processes in order to produce an output. Therefore, the Company accounted for the transaction as an asset acquisition and accordingly \$6.5 million was expensed to research and development expense in the Consolidated Statements of Operation for the year ended December 31, 2016.

***Acquisition of Scioderm, Inc.***

In September 2015, the Company acquired Scioderm Inc., ("Scioderm"), a privately-held biopharmaceutical company focused on developing innovative therapies for treating the rare disease, Epidermolysis Bullosa ("EB"). The acquisition potentially leveraged the Scioderm development team's EB expertise with the Company's global clinical infrastructure to advance SD-101 toward regulatory approvals and the Company's commercial, patient advocacy, and medical affairs infrastructure to support a successful global launch. The acquisition of Scioderm was accounted for as a purchase of a business in accordance with ASC 805 *Business Combinations*.

At the end of the first quarter of 2017, the Company achieved 100% enrollment in the Phase 3 clinical study of SD-101 and the milestone payment of \$10 million due for this event, was paid in April 2017. On September 13, 2017, the Company reported that top-line data from the randomized, double-blind, placebo-controlled Phase 3 clinical study ("ESSENCE, SD-5") to assess the efficacy and safety of the novel topical wound-healing agent SD-101 did not meet the primary endpoints or secondary endpoints in participants with EB. Based on these top-line data, the Company has no current plans to invest in any additional clinical studies or commercial preparation activities for SD-101. This event led the Company to assess the carrying amount of the program's tangible and intangible assets against their respective fair values. Based on the assessment, the Company recognized a loss on impairment of intangible assets in the amount of \$463.7 million and \$1.7 million in fixed assets recorded within loss on impairment of assets within the Consolidated Statements of Operations. Since the study did not meet the primary and secondary endpoints, the Company concluded that they will not make the potential milestone payments indicated in the Asset Purchase Agreement to the former Scioderm holders. Accordingly, the Company recognized a gain of \$254.7 million in changes in fair value of contingent consideration payable in the third quarter of 2017, in order to decrease the liability to zero. The Company also recognized \$0.4 million in selling, general, and administrative costs and \$8.1 million in research and development expenses related to the wind-down of operations for the Phase 3 ESSENCE study and ongoing extension studies SD-004 and SD-006, as well as income tax benefit of \$164.7 million due to the reduction of the deferred tax liability related to Scioderm IPR&D, in the Consolidated Statements of Operations in the third quarter of 2017.

***Acquisition of Callidus Biopharma, Inc.***

In November 2013, the Company acquired Callidus Biopharma, Inc., ("Callidus"), a privately-held biologics company focused on developing best-in-class ERTs for LDs with its lead ERT ATB200 for Pompe disease in late preclinical development.

The fair value of the contingent acquisition consideration payments was estimated by applying a probability-based income approach utilizing an appropriate discount rate. Key assumptions include discount rate and various probability factors. This estimation was based on significant inputs that are not observable in the market, referred to as Level 3 inputs. Some of the more significant assumptions used in the valuation include (i) the probability and timing related to the achievement of certain developmental milestones and (ii) and the discount rate. See "— Note 11. Assets and Liabilities Measured at Fair Value", for additional discussion regarding fair value measurements of the contingent acquisition consideration payable. The Company determined the fair value of the contingent consideration to be \$22.7 million at December 31, 2019, which is payable beyond the next twelve months, resulting in an increase in the contingent consideration payable and related expense of \$3.3 million in the year ended December 31, 2019. The expense is recorded in the Consolidated Statement of Operations within the changes in fair value of contingent consideration line item.

During the fourth quarter of 2018, the Company reached a clinical milestone for Callidus, which was the dosing of the first patient in a Phase 3 study. The milestone payment for this event was \$9.0 million which was paid in the Company's stock during the first quarter of 2019.

For further information, see "— Note 4. Goodwill and Intangible Assets."

**4. Goodwill and Intangible Assets**

In connection with the acquisitions, the Company initially recognized IPR&D of \$486.7 million and goodwill of \$197.8 million. 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. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value.

As discussed in "— Note 3. Acquisitions", in September 2017, the Company reported that top-line data from the randomized, double-blind, placebo-controlled Phase 3 clinical study ("ESSENCE, SD-005") to assess the efficacy and safety of the novel topical wound-healing agent SD-101 did not meet the primary endpoints or secondary endpoints in participants with EB. This event led to an assessment to determine if an impairment had occurred for goodwill and IPR&D. Based on tests for impairment, the Company determined that IPR&D had been impaired, however goodwill was not impaired based on qualitative and market capitalization tests performed. The loss on impairment of IPR&D of \$463.7 million was recorded within loss on impairment of assets in the Consolidated Statements of Operations for the year ended December 31, 2017.

The following table represents the changes in IPR&D for the years ended December 31, 2019 and 2018, respectively:

	<b>(in millions)</b>
<b>Balance at December 31, 2017</b>	\$ 23.0
<b>Change in IPR&amp;D</b>	—
<b>Balance at December 31, 2018</b>	\$ 23.0
<b>Change in IPR&amp;D</b>	—
<b>Balance at December 31, 2019</b>	\$ 23.0

The following table represents the changes in Goodwill for the years ended December 31, 2019 and 2018, respectively:

	<b>(in millions)</b>
<b>Balance at December 31, 2017</b>	\$ 197.8
<b>Change in goodwill</b>	—
<b>Balance at December 31, 2018</b>	\$ 197.8
<b>Change in goodwill</b>	—
<b>Balance at December 31, 2019</b>	\$ 197.8

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

As of December 31, 2019, the Company held \$142.8 million in cash and cash equivalents and \$309.9 million of available-for-sale debt securities which are reported at fair value on the Company's Consolidated Balance Sheets. Unrealized holding gains and losses are reported within accumulated other comprehensive loss in the 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, such marketable 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.

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.

**Amicus Therapeutics, Inc.**  
**Notes To Consolidated Financial Statements — (Continued)**

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

(in thousands)	As of December 31, 2019			
	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Cash and cash equivalents	\$ 142,837	\$ —	\$ —	\$ 142,837
Corporate debt securities	145,875	121	(5)	145,991
Commercial paper	73,659	53	(2)	73,710
Asset-backed securities	77,731	79	—	77,810
U.S. government agency bonds	11,999	2	(10)	11,991
Money market	350	—	—	350
Certificates of deposit	51	—	—	51
	<u>\$ 452,502</u>	<u>\$ 255</u>	<u>\$ (17)</u>	<u>\$ 452,740</u>
Included in cash and cash equivalents	\$ 142,837	\$ —	\$ —	\$ 142,837
Included in marketable securities <sup>(1)</sup>	309,665	255	(17)	309,903
Total cash, cash equivalents, and marketable securities	<u>\$ 452,502</u>	<u>\$ 255</u>	<u>\$ (17)</u>	<u>\$ 452,740</u>

<sup>(1)</sup> As of December 31, 2019, \$9.5 million of marketable securities have maturity dates greater than 12 months and are available to convert into cash, if needed.

(in thousands)	As of December 31, 2018			
	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Cash and cash equivalents	\$ 79,749	\$ —	\$ —	\$ 79,749
Corporate debt securities	240,969	7	(250)	240,726
Commercial paper	115,245	—	(104)	115,141
Asset-backed securities	68,215	4	(84)	68,135
Money market	350	—	—	350
Certificates of deposit	51	—	—	51
	<u>\$ 504,579</u>	<u>\$ 11</u>	<u>\$ (438)</u>	<u>\$ 504,152</u>
Included in cash and cash equivalents	\$ 79,749	\$ —	\$ —	\$ 79,749
Included in marketable securities	424,830	11	(438)	424,403
Total cash, cash equivalents, and marketable securities	<u>\$ 504,579</u>	<u>\$ 11</u>	<u>\$ (438)</u>	<u>\$ 504,152</u>

For the year ended December 31, 2019 there were no realized gains or losses. For the fiscal year ended December 31, 2018, there were nominal realized gains. The cost of securities sold is based on the specific identification method.

Unrealized loss positions in the available-for-sale debt securities as of December 31, 2019 and 2018 reflect temporary impairments that have been in a loss position for less than twelve months and as such are recognized in other comprehensive gain (loss). The fair value of these available-for-sale debt securities in unrealized loss positions was \$42.6 million and \$403.1 million as of December 31, 2019 and 2018, respectively.

**Amicus Therapeutics, Inc.**  
**Notes To Consolidated Financial Statements — (Continued)**

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, 2019	December 31, 2018	December 31, 2017
Cash and cash equivalents	\$ 142,837	\$ 79,749	\$ 49,060
Restricted cash	3,506	2,626	2,177
Cash, cash equivalents, and restricted cash shown in the Consolidated Statements of Cash Flows	<u>\$ 146,343</u>	<u>\$ 82,375</u>	<u>\$ 51,237</u>

**6. Inventories**

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

(in thousands)	December 31, 2019	December 31, 2018
Raw materials	\$ 6,544	\$ 1,291
Work-in-process	3,660	3,485
Finished goods	3,837	3,614
<b>Total inventories</b>	<u>\$ 14,041</u>	<u>\$ 8,390</u>

The Company recorded a reserve for inventory of \$0.2 million as of December 31, 2019 and 2018, respectively.

**7. Property and Equipment**

Property and equipment consist of the following:

(in thousands)	December 31,	
	2019	2018
Property and equipment consist of the following:		
Computer equipment	\$ 6,185	\$ 4,691
Computer software	1,607	1,298
Research equipment	14,568	8,445
Furniture and fixtures	5,157	4,876
Leasehold improvements	30,294	7,425
Vehicles	124	209
Land	3,190	—
Construction in progress	4,184	102
Gross property and equipment	<u>65,309</u>	<u>27,046</u>
Less accumulated depreciation	(17,604)	(15,671)
Net property and equipment	<u>\$ 47,705</u>	<u>\$ 11,375</u>

Depreciation expense was \$4.5 million and \$4.2 million for the years ended December 31, 2019 and 2018, respectively.

**8. Accounts Payable, Accrued Expenses, and Other Current Liabilities**

Accounts payable, accrued expenses, and other current liabilities consist of the following:

(in thousands)	December 31,	
	2019	2018
Accounts payable	\$ 21,722	\$ 6,606
Accrued professional fees	7,832	2,276
Accrued contract manufacturing & contract research costs	17,800	5,890
Accrued compensation and benefits	27,156	21,731
Accrued program fees	17,016	16,674
Accrued royalties	5,196	4,463
Accrued interest	3,679	4,189
Accrued milestones	4,000	9,000
Accrued sales rebates and discounts	5,900	3,636
Accrued taxes	7,300	1,330
Other	2,772	4,830
	\$ 120,373	\$ 80,625

**9. Stockholders' Equity**

***Common Stock and Warrants***

As of December 31, 2019, 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 March 2019, 101,787 warrants were exercised at \$7.98 per share of common stock resulting in gross cash proceeds of \$0.8 million.

As discussed in "— Note 1. Business" during the second quarter of 2019, the Company completed an underwritten equity offering and issued 18.7 million shares of its common stock at \$10.75 per share, inclusive of the fully exercised option to purchase additional shares from the initial offering. This transaction resulted in net proceeds of \$189.0 million, after deducting underwriting discounts and commissions and offering expenses.

As discussed in "— Note 11. Assets and Liabilities Measured at Fair Value", the Company reached a clinical milestone, which was the dosing of the first patient in a Phase 3 study, related to the contingent consideration from the acquisition of Callidus. The milestone for this event was \$9.0 million, which was paid in Company common stock in the first quarter of 2019 and resulted in a \$9.3 million impact on stockholder's equity.

As discussed in "— Note 12. Debt", during the first and second quarters of 2019, the Company entered into separate, privately negotiated Exchange Agreements with the Holders of the Convertible Notes. Under the terms of the Exchange Agreements, the Holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of Company's common stock, par value \$0.01 per share.

In February 2018, the Company completed an underwritten offering of 20.2 million shares of its common stock at \$15.50 per share, inclusive of the fully exercised option to purchase additional shares from the initial offering. This transaction resulted in net proceeds of \$294.6 million, after deducting underwriting discounts and commissions and offering expenses.

In April 2018, 453,214 warrants were exercised at \$7.98 per share of common stock resulting in gross cash proceeds of \$3.6 million.

In June 2018, the Company's stockholders approved an amendment to the Company's Restated Certificate of Incorporation to increase the number of shares of common stock, par value \$0.01 per share, that the Company is authorized to issue from 250 million shares to 500 million shares.

In July 2017, the Company completed an underwriting offering of 21.1 million shares of its common stock at \$12.25 per share. This transaction resulted in net proceeds of \$243.0 million, after deducting underwriting discounts and commissions and offering expenses.

***Nonqualified Cash Plan***

The Company's Deferral Plan, (the "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 \$4.4 million and \$2.7 million as of December 31, 2019 and 2018, respectively, with corresponding approximate amounts of liability.

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

***Equity Incentive Plans***

The Company's Equity Incentive Plans consist of the Amended and Restated 2007 Equity Incentive Plan (the "Plan") and the 2007 Director Option Plan (the "2007 Director Plan"). The Plan provides for the granting of restricted stock 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 2007 Director Plan is intended to promote the recruiting and retention of highly qualified eligible directors and strengthen the commonality of interest between directors and stockholders by encouraging ownership of common stock of the Company. Under the provisions of each 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. Options under the 2007 Director Plan may be granted to new directors upon joining the Board of Directors and vest in the same manner as options under the Plan. In addition, options are granted to independent directors at each annual meeting of stockholders and vest on the date of the annual meeting of stockholders of the Company in the year following the year during which the options were granted. As of December 31, 2019, the Company has reserved up to 10,667,216 shares for issuance under the Plan and the 2007 Director Plan.

**10. Share based Compensation**

The Company's Equity Incentive Plans consist of the Plan and the 2007 Director 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. The 2007 Director Plan is intended to promote the recruiting and retention of highly qualified eligible directors and strengthen the commonality of interest between directors and stockholders by encouraging ownership of common stock of the Company. 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.

On December 21, 2018, the Board of Directors of the Company approved an amendment (the "Amendment") to the Plan. The Amendment 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 ("Options") 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 PRSU.

**Stock Option Grants**

The Company uses the fair value method of measuring stock-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 stock-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was based on our historical volatility since our initial public offering in May 2007. Beginning in the third quarter of 2017, the average expected life is determined using our actual historical data versus a "simplified" method used in prior quarters. The "simplified" method of estimating the Company did not have sufficient reliable exercise data to justify a change from the use of the "simplified" method of estimating the expected exercise term of employee stock option grants. The impact from this change was not material. 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 is estimated on the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions:

	Years Ended December 31,		
	2019	2018	2017
Expected stock price volatility	74.1%	78.6%	82.8%
Risk free interest rate	2.4%	2.4%	2.0%
Expected life of options (years) <sup>(1)</sup>	5.68	5.62	6.18
Expected annual dividend per share	\$ 0.00	\$ 0.00	\$ 0.00

<sup>(1)</sup>The average expected life is determined using actual historical data.

The weighted average grant-date fair value per share of options granted during 2019, 2018, and 2017 were \$6.67, \$10.19, and \$5.09, respectively.

A summary of the Company's stock options for the year ended December 31, 2019 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, 2016	15,497.5	\$ 7.37		
Granted	3,695.3	\$ 7.17		
Exercised	(2,878.7)	\$ 5.67		
Forfeited	<u>(1,133.0)</u>	\$ 9.55		
Options outstanding, December 31, 2017	15,181.1	\$ 7.48		
Granted	2,348.0	\$ 14.96		
Exercised	(1,398.0)	\$ 6.54		
Forfeited	(313.1)	\$ 9.55		
Expired	<u>(8.0)</u>	\$ 10.76		
Options outstanding, December 31, 2018	15,810.0	\$ 8.63		
Granted	4,091.0	\$ 10.29		
Exercised	(1,967.0)	\$ 5.83		
Forfeited	(879.0)	\$ 11.07		
Expired	<u>(331.0)</u>	\$ 13.38		
Options outstanding, December 31, 2019	16,724.0	\$ 9.15	6.4	\$ 30.8
Vested and unvested expected to vest, December 31, 2019	16,111.2	\$ 9.08	6.3	\$ 30.6
Exercisable at December 31, 2019	10,646.5	\$ 8.33	5.1	\$ 27.0

The aggregate intrinsic value of options exercised during the years ended December 31, 2019, 2018 and 2017 was \$11.8 million, \$11.9 million, and \$20.8 million respectively. Cash proceeds from stock options exercised during the years ended December 31, 2019, 2018, and 2017 were \$11.5 million, \$9.1 million, and \$16.3 million, respectively. As of December 31, 2019, the total unrecognized compensation cost related to non-vested stock options granted was \$32.4 million and is expected to be recognized over a weighted average period of 2.5 years.

**Amicus Therapeutics, Inc.**  
**Notes To Consolidated Financial Statements — (Continued)**

*Restricted Stock Units and Performance-Based Restricted Stock Units (collectively "RSU's")*

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, 2019 is as follows:

	Number of Share	Weighted Average Grant Date Fair Value	Weighted Average Remaining Years	Aggregate Intrinsic Value
	(in thousands)			(in millions)
Non-vested units as of December 31, 2017	2,575.1	\$ 5.85		
Granted	1,811.9	\$ 16.11		
Vested	(530.0)	\$ 6.01		
Forfeited	(145.0)	\$ 9.65		
Non-vested units as of December 31, 2018	3,712.0	\$ 10.59		
Granted	3,526.0	\$ 10.92		
Vested	(921.0)	\$ 8.49		
Forfeited	(525.0)	\$ 10.52		
Non-vested units as of December 31, 2019	5,792.0	\$ 11.18	2.4	\$ 56.4

For the year ended December 31, 2019, 920,782 RSUs have vested and all non-vested units are expected to vest over their normal term. As of December 31, 2019, there was \$39.8 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 2.4 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:

(in thousands)	Years Ended December 31,		
	2019	2018	2017
Equity compensation expense recognized in:			
Research and development expense	\$ 17,575	\$ 11,740	\$ 10,328
Selling, general, and administrative expense	26,855	17,520	12,773
Total equity compensation expense	\$ 44,430	\$ 29,260	\$ 23,101

**11. 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.

**Amicus Therapeutics, Inc.**  
**Notes To Consolidated Financial Statements — (Continued)**

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, 2019 are identified in the following table:

(in thousands)	Level 2	Total
<b>Assets:</b>		
Commercial paper	\$ 73,710	\$ 73,710
Asset-back securities	77,810	77,810
Corporate debt securities	145,991	145,991
U.S. Government Agency Bonds	11,991	11,991
Money market funds	4,768	4,768
	<u>\$ 314,270</u>	<u>\$ 314,270</u>

(in thousands)	Level 2	Level 3	Total
<b>Liabilities:</b>			
Contingent consideration payable	\$ —	\$ 22,681	\$ 22,681
Deferred compensation plan liability	4,419	—	4,419
	<u>\$ 4,419</u>	<u>\$ 22,681</u>	<u>\$ 27,100</u>

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, 2018 are identified in the following table:

(in thousands)	Level 2	Total
<b>Assets:</b>		
Commercial paper	\$ 115,141	\$ 115,141
Asset-back securities	68,135	68,135
Corporate debt securities	240,726	240,726
Money market funds	3,082	3,082
	<u>\$ 427,084</u>	<u>\$ 427,084</u>

(in thousands)	Level 2	Level 3	Total
<b>Liabilities:</b>			
Contingent consideration payable	\$ —	\$ 19,700	\$ 19,700
Deferred compensation plan liability	2,732	—	2,732
	<u>\$ 2,732</u>	<u>\$ 19,700</u>	<u>\$ 22,432</u>

The Company's Convertible Notes falls into the Level 2 category within the fair value level hierarchy. The fair value was determined using broker quotes in a non-active market for valuation. The fair value of the Convertible Notes at December 31, 2019 was approximately \$5.0 million.

The Company's Senior Secured Term Loan fall 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 approximates the fair value.

The Company did not have any Level 3 assets as of December 31, 2019 or December 31, 2018.



***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, 2019. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2019.

***Contingent Consideration Payable***

The contingent consideration payable resulted from the acquisition of Callidus, as discussed in "— Note 3. Acquisitions." The most recent valuation was determined using a probability weighted discounted cash flow valuation approach. Using this approach, expected future cash flows are calculated over the expected life of the agreement, are discounted, and then exercise scenario probabilities are applied. The valuation is performed quarterly. 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 Company may be required to record losses in future periods.

The following significant unobservable inputs were used in the valuation of the contingent consideration payable of Callidus for the ATB-200 Pompe program:

<u>Contingent Consideration Liability</u>	<u>Fair value as of December 31, 2019</u> (in thousands)	<u>Valuation Technique</u>	<u>Unobservable Input</u>	<u>Range</u>
Clinical and regulatory milestones	\$ 22,390	Probability weighted discounted cash flow	Discount rate	9.6%
			Probability of achievement of milestones	75% - 78%
			Projected year of payments	2021 - 2022

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 clinical milestone, which was the dosing of the first patient in a Phase 3 study, related to the contingent consideration from the acquisition of Callidus. The milestone for this event was \$9.0 million, which was paid in Company common stock in the first quarter of 2019, resulting in \$9.3 million impact on stockholder's equity.

The following table shows the change in the balance of contingent consideration payable for the year ended December 31, 2019 and 2018, respectively:

<u>(in thousands)</u>	<u>Year ended December 31,</u>	
	<u>2019</u>	<u>2018</u>
Balance, beginning of the period	\$ 19,700	\$ 25,400
Milestones payable, included in accrued expenses	—	(9,000)
Changes in fair value during the period, included in the Consolidated Statements of Operations	3,297	3,300
Adjustment for contingent consideration paid in stock	(316)	—
Balance, end of the period	<u>\$ 22,681</u>	<u>\$ 19,700</u>

***Deferred Compensation Plan - Investment and Liability***

The Deferred Compensation Plan (the "Deferral Plan") provides certain key employees and members of the Board of Directors with an opportunity to defer the receipt of such participant's base salary, bonus and director's fees, as applicable. Deferral Plan assets are classified as trading securities and recorded at fair value with changes in the investment's fair value recognized in the period they occur. The asset investments consist of market exchanged mutual funds. The Company considers its investments in marketable securities as available-for-sale and classifies these assets and related liability within the fair value hierarchy as Level 2, primarily utilizing broker quotes in a non-active market for valuation of these securities.

**12. Debt**

***Senior Secured Term Loan due 2023***

In September 2018, the Company entered into a loan agreement with BioPharma Credit PLC as the lender. The loan agreement provides for a \$150 million senior secured term loan ("Senior Secured Term Loan") with an interest rate equal to the 3-month LIBOR plus 7.50% per annum and matures in 5 years from the maturity date. The Senior Secured Term Loan will be repaid in four quarterly payments equal to 12.50% thereof starting on the forty-eight month anniversary of the date of the first credit extension with the balance due on the Maturity Date. Interest is payable quarterly in arrears. The Senior Secured Term Loan contains certain customary representations and warranties, affirmative and negative covenants, and events of default applicable to the Company and certain of its subsidiaries but does not include any financial covenants relating to the achievement or maintenance of revenue or cash flow. If an event of default occurs and is continuing, the lender may declare all amounts outstanding under the Senior Secured Term Loan to be immediately due and payable. The Company received net proceeds of \$146.6 million in September 2018, after deducting fees and estimated expenses.

***Convertible Notes due 2023***

In December 2016, the Company issued at par value \$250 million aggregate principal amount of Convertible Notes, which included the exercise in full of the \$25 million over-allotment option granted to the initial purchasers of the Convertible Notes in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act (the "Note Offering"). Interest is payable semiannually on June 15 and December 15 of each year, beginning on June 15, 2017. The Convertible Notes will mature on December 15, 2023, unless earlier repurchased, redeemed, or converted in accordance with their terms. The Convertible Notes are convertible at the option of the Holders, under certain circumstances and during certain periods, into cash, shares of the Company's common stock or a combination thereof. The net proceeds from the Note Offering were \$243.0 million, after deducting fees and estimated expenses. In addition, the Company used approximately \$13.5 million of the net proceeds from the issuance of the Convertible Notes to pay the cost of the capped call transactions ("Capped Call Confirmations") that the Company entered into in connection with the issuance of the Convertible Notes. In accounting for the issuance of the Convertible Notes, the Company separated the Convertible Notes into liability and equity components based on their relative values. The Convertible Notes were initially convertible into approximately 40.8 million shares of the Company's common stock under certain circumstances prior to maturity at a conversion rate of 163.3987 shares per \$1,000 principal amount of Convertible Notes, which represents a conversion price of approximately \$6.12 per share of common stock, subject to adjustment under certain conditions. Holders may convert their Convertible Notes at their option at specified times prior to the maturity date of December 15, 2023, only if:

- during any fiscal quarter commencing after March 31, 2017, if the last reported sale price of the Company's common stock for at least 20 trading days in the period of 30 consecutive trading days ending on the last trading day of the immediately preceding fiscal quarter is equal to or more than 130% of the conversion price of the Convertible Notes on the last day of such preceding fiscal quarter;
- a holder submits its Convertible Notes for conversion during the five business day period following any five consecutive trading day period in which the trading price for the Convertible Notes, per \$1,000 principal amount of the Convertible Notes, for each such trading day was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate of the Convertible Notes on such date;
- the Company issues to all or substantially all of the holders of common stock rights options or warrants entitling them for a period of not more than 60 calendar days after the date of such issuance to subscribe for or purchase shares of the common stock, at a price per share less than the average of the Last Reported Sale Prices of the common stock for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of such issuance or distributes to all or substantially all holders of the common stock the Company's assets, debt securities or rights to purchase the Company's securities which distribution has a per share value of exceeding 10% of the Last Reported Sale Price of the common stock on the Trading Day immediately preceding the date of announcement of such distribution;
- the Company enters into specified corporate transactions; or
- the Company has had a call for redemption, the holder can convert up until the second trading day immediately preceding the redemption date.

The Convertible Notes will be convertible, at the option of the note holders, regardless of whether any of the foregoing conditions have been satisfied, on or after September 15, 2023 at any time prior to the close of business on the second scheduled trading day immediately preceding the stated maturity date of December 15, 2023.

On February 15, 2018, the Company entered into an underwriting agreement relating to an underwritten public offering of 19.4 million shares of the Company's common stock. Under the terms of the underwriting agreement, the Company granted the underwriters an option, exercisable for 30 days after February 16, 2018, to purchase up to an additional 2.9 million shares of the Company's common stock, which was exercised with respect to 885,000 shares of the Company's common stock.

Subsequent to the underwritten public offering on February 15, 2018, the Company did not have sufficient unissued authorized shares to cover a conversion of the Convertible Notes. As a result, the Company accounted for the portion of the bifurcated conversion feature and of the Capped Call Confirmations that would not be able to be net share settled as a current derivative liability and as a derivative asset, respectively. The fair value of the derivative liability for the conversion feature and derivative asset for the Capped Call Confirmations at February 15, 2018 was determined to be \$507.4 million and \$13.6 million, respectively, of which the portion that was determined to not be able to be net share settled was recorded with a corresponding impact to additional-paid-in-capital. Subsequent changes to fair value of the derivatives were recorded in the second quarter of 2018 through earnings on the Company's Consolidated Statements of Operations resulting in a change in fair value of derivatives for the year ended December 31, 2018 of \$2.7 million.

Following the approval by the stockholders of the Company on June 7, 2018, to increase the authorized shares of common stock to 500,000,000, the Company has sufficient unissued authorized shares to cover a conversion of the Convertible Notes. As a result, the derivative liability and derivative asset were reclassified into additional-paid-in-capital. The fair value of the derivative liability for the conversion feature and derivative asset for the Capped Call Confirmations at June 7, 2018 was determined to be \$88.3 million and \$2.4 million, respectively.

The Capped Call Confirmations were expected generally to reduce the potential dilution to the common stock upon any conversion of the Convertible Notes and/or offset the cash payments the Company is required to make in excess of the principal amount upon conversion of the Convertible Notes in the event that the market price of the common stock was greater than the strike price of the Capped Call Confirmations (which initially corresponded to the initial conversion price of the Convertible Notes and is subject to certain adjustments under the terms of the Capped Call Confirmations), with such reduction and/or offset subject to a cap based on the cap price of the Capped Call Confirmations. The Capped Call Confirmations had an initial cap price of \$7.20 per share, which represented a premium of approximately 50% over the closing price of the Company's common stock on The NASDAQ Global Market on December 15, 2016 and was subject to certain adjustments under the terms of the Capped Call Confirmations. The Capped Call Confirmations covered, subject to anti-dilution adjustments substantially similar to those applicable to the Convertible Notes, the number of shares of common stock that underlay the Convertible Notes. The Capped Call Confirmations did not meet the criteria for separate accounting as a derivative as they were indexed to the Company's common stock. The premiums paid for the Capped Call Confirmations were included as a net reduction to additional paid-in capital.

During the first and second quarters of 2019, the Company entered into separate, privately negotiated Exchange Agreements with the Holders of the Convertible Notes. Under the terms of the Exchange Agreements, the Holders agreed to exchange an aggregate principal amount of \$247.2 million of Convertible Notes held by them in exchange for an aggregate of approximately 44.0 million shares of Company common stock, par value \$0.01 per share. In addition, pursuant to the Exchange Agreements, the Company made aggregate cash payments of \$1.3 million to the Holders to satisfy accrued and unpaid interest to the closing date of the transactions, along with cash in lieu of fractional shares. These transactions resulted in \$215.0 million in additional paid-in-capital and common stock of \$0.4 million on the Consolidated Balance Sheets as of December 31, 2019. Additionally, the Company recognized a net loss on the exchange of debt of \$40.6 million on the Consolidated Statements of Operations during the year ended December 31, 2019. During the second half of the year there were no additional debt conversion transactions.

During the first and second quarter of 2019, the Company terminated the Capped Call Confirmations related to the exchange of the Convertible Notes for proceeds of approximately \$19.9 million.

The last reported sale price of the Company's common stock was equal to or more than 130% of the conversion price of the Convertible Notes for at least 20 trading days of the 30 consecutive trading days ending on the last day of the year. As a result, the Convertible Notes are currently convertible into the Company's common stock.

The Convertible Notes and Senior Secured Term Loan consist of the following:

<u>(in thousands)</u>	<u>As of December 31,</u>	
	<u>2019</u>	<u>2018</u>
Principal	\$ 152,825	\$ 400,000
Less: debt discount <sup>(1)</sup>	(2,974)	(74,145)
Less: deferred financing <sup>(1)</sup>	(346)	(4,115)
Net carrying value of the debt	<u>\$ 149,505</u>	<u>\$ 321,740</u>

<sup>(1)</sup> Included in the Consolidated Balance Sheets within Convertible Notes and Senior Secured Term Loan and amortized to interest expense over the remaining life of the Convertible Notes and Senior Secured Term Loan using the effective interest rate method.

The following table sets forth interest expense recognized related to the Convertible Notes and Senior Secured Term Loan for the years ended December 31, 2019 and 2018 respectively:

<u>(in thousands)</u>	<u>2019</u>	<u>2018</u>
Contractual interest expense	\$ 16,483	\$ 11,426
Amortization of debt discount	\$ 2,381	\$ 10,421
Amortization of deferred financing	\$ 165	\$ 555
Effective interest rate of the liability component, Convertible debt	10.63%	10.85%
Effective interest rate of the liability component, Senior Secured Term Loan	10.16%	10.48%

**13. 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 year ended December 31, 2019, operating lease expense was \$10.8 million. For the year ended December 31, 2018, the Company paid \$4.9 million for amounts included in the measurement of operating lease liabilities and recorded \$21.8 million of right-of-use assets and \$19.4 million of tenant improvements paid through lease incentives in exchange for new operating lease liabilities.

Commitments under finance leases are not significant.

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

<b>(in thousands, except year and discount rate amounts)</b>	<b>December 31, 2019</b>
Operating lease ROU asset	\$ 33,315
Current portion of the operating lease liabilities	\$ 7,189
Non-current portion of the operating lease liabilities	53,531
Total operating lease liability	<u>\$ 60,720</u>
Weighted-average remaining lease terms (years)	18.2
Weighted-average discount rate	13.1%

At December 31, 2019, the future minimum operating lease payments were as follows:

<b>(in thousands)</b>	<b>Operating Lease</b>
2020	\$ 9,738
2021	10,787
2022	10,459
2023	10,809
2024	10,582
Thereafter	163,266
Total lease payments	215,641
Less lease incentives	(28,939)
Less imputed interest	(125,982)
Total operating lease liability	<u>\$ 60,720</u>

At December 31, 2018, the future minimum operating lease payments were as follows:

<b>(in thousands)</b>	<b>Operating Lease</b>
2019	\$ 6,244
2020	4,063
2021	3,560
2022	3,371
2023	3,611
Thereafter	10,038
Total lease payments	<u>\$ 30,887</u>

Rent expense, including fees for utilities and common area maintenances under ASC 840 for the years ended December 31, 2018 and 2017 were \$5.7 million and \$3.9 million, respectively.

**14. Income Taxes**

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

<b>(in thousands)</b>	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
United States	\$ (393,955)	\$ (309,183)	\$ (440,696)
Foreign	38,045	(39,906)	(8,425)
Total	<u>\$ (355,910)</u>	<u>\$ (349,089)</u>	<u>\$ (449,121)</u>

Following were the components of income tax expense (benefit) for the years ended December 31, 2019, 2018, and 2017:

<b>(in thousands)</b>	<b>2019</b>	<b>2018</b>	<b>2017</b>
Current			
Federal	\$ —	\$ —	\$ —
State	—	6	9
Foreign	2,877	(100)	2,276
Deferred			
Federal	(984)	—	(150,015)
State	(1,415)	—	(17,389)
Foreign	—	—	—
Total	<u>\$ 478</u>	<u>\$ (94)</u>	<u>\$ (165,119)</u>

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2019, 2018 and 2017 are as follows:

	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
Statutory rate	(21)%	(21)%	(34)%
State taxes, net of federal benefit	—	(4)	(5)
Nondeductible IPR&D	—	6	(1)
Contingent consideration	—	1	(18)
Tax credits	(16)	(10)	(2)
Foreign income tax rate differential	9	2	5
Impact of 2017 Act	—	—	27
Nondeductible debt conversion	(1)	—	—
Other	—	—	5
Valuation allowance	29	26	(14)
Net	<u>— %</u>	<u>— %</u>	<u>(37)%</u>

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.

ASC 740, *Income Taxes*, requires the effects of changes in tax laws to be recognized in the period in which the legislation is enacted. However, due to the complexity and significance of the Tax Act's provisions, the SEC staff issued SAB 118, which allows companies to record the tax effects of the Tax Act on a provisional basis based on a reasonable estimate, and then, if necessary, subsequently adjust such amounts during a limited measurement period as more information becomes available. The measurement period ends when a company has obtained, prepared, and analyzed the information necessary to finalize its accounting, but cannot extend beyond one year from enactment. The Tax Act did not have a material impact on the Company's financial statements because its deferred temporary differences are fully offset by a valuation allowance. The Company did not have any significant offshore earnings from which to record the mandatory transition tax. During 2018 the Company operated in a consolidated loss position in its foreign operations and did not have a one-time tax on accumulated earnings of foreign subsidiaries.

As of December 31, 2017, the Company provisionally recorded certain impacts of the Tax Act including the adjustment to our net deferred tax liability arising from the reduction in the federal tax rate as well as the impact of mandatory deemed repatriation. Adjustments to these provisional amounts that we recorded in 2018 did not have a significant impact on the Company's Consolidated Financial Statements. The Company's accounting for the effects of the enactment of the Tax Act are now complete.

The Company recorded an income tax expense of \$2.9 million in 2019 for taxes in foreign jurisdictions and a \$2.4 million tax benefit in 2019 for taxes in U.S. federal and state jurisdictions.

The Company did not recognize interest or penalties related to income tax during the period ended December 31, 2019 and did not accrue for interest or penalties as of December 31, 2019. The Company does not have an accrual for uncertain tax positions as of December 31, 2019. Tax returns for years 2015 through 2018 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:

<b>(in thousands)</b>	<b>For Years Ended December 31,</b>	
	<b>2019</b>	<b>2018</b>
Deferred tax assets		
Intellectual property	\$ 46,521	\$ 48,339
Amortization/depreciation	2,329	3,732
Research tax credit	141,669	96,509
Net operating loss carry forwards	286,850	248,398
Deferred reimbursement	2,230	4,401
Non-cash stock issue	19,058	16,850
Interest carry forward limitation	2,224	1,032
Other	15,986	10,852
Gross deferred tax assets	516,867	430,113
Deferred tax liabilities		
Business acquisition	(5,051)	(6,465)
Royalty payable	(46,521)	(48,339)
Convertible notes	(653)	(16,666)
Advanced R&D payments	(2,611)	(2,103)
Other	(725)	—
Total net deferred tax assets	461,306	356,540
Less: valuation allowance	(466,357)	(363,005)
Net deferred tax liability	\$ (5,051)	\$ (6,465)

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, 2019 and 2018, the Company recorded valuation allowances of \$466.4 million and \$363.0 million, respectively, representing an increase in the valuation allowance of \$103.4 million in 2019, 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, 2019, the Company had federal, state, and foreign net operating loss carry forwards ("NOLs") of approximately \$1,036 million, \$897.8 million, and \$30.6 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 2017 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 2019 will expire in 2029 through 2039. The foreign NOLs are subject to differing expirations beginning in 2026. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended (the "Code") 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 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 increase state taxes owed.

The Company also has research and experimentation and orphan drug credit carryforwards of approximately \$27.6 million and \$114.0 million, respectively, which will expire in the years 2021 through 2039. Deferred tax assets for these carryforwards are subject to a full valuation allowance.

**15. Collaborative Agreements**

*Penn*

In October 2018, the Company expanded its gene therapy portfolio through a collaboration agreement with Penn to pursue research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, CDD and one additional undisclosed rare metabolic disorder.

In May 2019, the Company further expanded the collaboration from three to six programs for rare genetic diseases and now includes specifically: NPC, MPS IIIB, as well as a next generation program in MPS IIIA. This expanded collaboration with Penn also provides the Company with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. Under the expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in 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. The Company will provide \$10.0 million each year during the five-year agreement to fund the discovery research program. In connection with the collaboration agreement, the Company made an upfront payment of \$7 million in cash to Penn that was expensed to research and development expense in the Consolidated Statements of Operations.

*GlaxoSmithKline*

In November 2013, Amicus entered into the Revised Agreement with GlaxoSmithKline ("GSK"), pursuant to which Amicus has obtained global rights to develop and commercialize Galafold<sup>®</sup> as a monotherapy and in combination with ERT for Fabry disease. The Revised Agreement amends and replaces in its entirety the earlier agreement entered into between Amicus and GSK in July 2012 ("Expanded Collaboration Agreement"). Under the terms of the Revised Agreement, there was no upfront payment from Amicus to GSK. For Galafold<sup>®</sup> monotherapy, 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. For the year ended December 31, 2019, the Company incurred approximately \$15.5 million of royalty expenses under the revised agreement with GSK.

Under the terms of the Revised Agreement, GSK will no longer jointly fund development costs for all formulations of Galafold<sup>®</sup>.

In evaluating the impact of both the Expanded Collaboration Agreement and the Revised Agreement, the Company applied the accounting guidance regarding the impact of potential future payments it may make in its role as a vendor (i.e., Amicus) to its customer (i.e., GSK) and evaluated if these potential future payments could be a reduction of revenue from GSK. If the potential future payments to GSK are as follows:

- a payment for an identifiable benefit, and
- the identifiable benefit is separable from the existing relationship between the Company and GSK, and
- the identifiable benefit can be obtained from a party other than GSK, and
- the Company can reasonably estimate the fair value of the identifiable benefit,

then the potential future payments would be treated separately from the collaboration and research revenue. However, if all these criteria are not satisfied, then the potential future payments are treated as a reduction of revenue.

Accordingly, the Company did not believe that, for accounting purposes, the new U.S. licensing rights to Galafold<sup>®</sup> obtained from GSK under the Expanded Collaboration Agreement, nor the ex U.S. licensing rights to Galafold<sup>®</sup> obtained from GSK under the Revised Agreement, represented a separate, identifiable benefit from the licenses in the Original Collaboration Agreement entered into between Amicus and GSK in 2010. The contingent amounts payable to GSK were not sufficiently separable from GSK's original license and the research and development reimbursements such that Amicus could not have entered into a similar exchange transaction with another party. Additionally, the Company cannot reasonably estimate the fair value of the worldwide licensing rights to Galafold<sup>®</sup>.

The Company determined that the potential future payments to GSK would be treated as a reduction of revenue and that the total amount of revenue to be received under the arrangement is no longer fixed or determinable as the contingent milestone payments are subject to significant uncertainty.

As a result, the Company no longer recognized any of the upfront license fees and premiums on the equity purchase from GSK until such time as the arrangement consideration becomes fixed or determinable, because an indeterminable amount may ultimately be payable back to GSK. These amounts (the balance of the unrecognized upfront license fee and the premium on the equity purchases) are classified as deferred reimbursements on the balance sheet.

For the year ended December 31, 2019, under the GSK collaboration agreements, we paid \$1.5 million in sales-based milestones. As of December 31, 2019, the Company recognized another \$4.0 million for sales-based milestones that were met, invoiced and recorded in accounts payable, accrued expenses and other current liabilities and \$10.2 million was recorded as deferred reimbursements in the Consolidated Balance Sheets. Additionally, the Company recognized a liability of \$5.2 million related to royalties payable to GSK in accounts payable and accrued expenses in the Consolidated Balance Sheets.

The recognition of Research Revenue was also affected by the determination that the overall total arrangement consideration was no longer fixed and determinable, despite the fact that the research activities continued and that the research expense reimbursements by GSK to Amicus were received as the research activities related to the reimbursement had been completed. Therefore, the research reimbursements from GSK were recorded as deferred reimbursements on the balance sheet and would not be recognized until the total arrangement consideration becomes fixed and determinable.

As a result, all revenue recognition was suspended until the total arrangement consideration would become fixed and determinable. In addition, future milestone payments made by the Company will be applied against the balance of this deferred reimbursements account. Revenue recognition for research expense reimbursements, the original upfront license fee, and the equity premiums will resume once the total arrangement consideration becomes fixed and determinable which will occur when the balance of the deferred reimbursements account is sufficient to cover all the remaining contingent milestone payments.

**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,		
	2019	2018	2017
Numerator:			
Net loss attributable to common stockholders	\$ (356,388)	\$ (348,995)	\$ (284,002)
Denominator:			
Weighted average common shares outstanding — basic and diluted	240,421,001	185,790,021	153,355,144

Dilutive common stock equivalents would include the dilutive effect of common stock options, convertible debt units, RSUs and warrants for common stock equivalents. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect. For the year ended December 31, 2019 there were 462 thousand potential common shares outstanding as a result of the Convertible Debt that were excluded from the diluted net loss per share calculation because their effect would have been anti-dilutive.

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)	Year ended December 31,		
	2019	2018	2017
Options to purchase common stock	16,724	15,810	15,181
Convertible debt	462	40,850	40,850
Outstanding warrants, convertible to common stock	2,555	2,657	3,110
Unvested restricted stock units	5,792	3,712	2,575
Vested restricted stock units, unissued	186	91	50
Total number of potentially issuable shares	25,719	63,120	61,766

**17. Selected Quarterly Financial Data (Unaudited)**

(in thousands except per share data)	Quarters Ended			
	March 31	June 30	September 30	December 31
<b>2019</b>				
Net product sales	\$ 34,046	\$ 44,130	\$ 48,768	\$ 55,293
Net loss	\$ (120,299)	\$ (84,551)	\$ (61,809)	\$ (89,729)
Basic and diluted net loss per common share <sup>(1)</sup>	\$ (0.56)	\$ (0.36)	\$ (0.24)	\$ (0.35)
<b>2018</b>				
Net product sales	\$ 16,696	\$ 21,309	\$ 20,596	\$ 32,644
Net loss	\$ (49,916)	\$ (61,833)	\$ (159,163)	\$ (78,083)
Basic and diluted net loss per common share <sup>(1)</sup>	\$ (0.28)	\$ (0.33)	\$ (0.84)	\$ (0.43)

<sup>(1)</sup> Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amounts because of differences on the weighted-average common shares outstanding during each period principally due to the effect of the Company issuing shares of its common stock during the year.

**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, 2019. 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, 2019, 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, 2019 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.

PART IV

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 2020 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 "Management," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Proposal No. 1 — Election of Directors"

We have adopted a Code of Business Ethics and Conduct for Employees, Executive Officers and Directors that applies to our employees, officers and directors and incorporate 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 at [www.amicusrx.com](http://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."

**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 "Equity Compensation Plan Information."

**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 "Certain Relationships and Related Transactions," "Director Independence," "Committee Compensation and Meetings of the Board of Directors," and "Compensation Committee Interlock and Insider Participation."

**Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.**

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

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

*1. Consolidated Financial Statements*

The Consolidated Financial Statements are filed as part of this report.

*2. Consolidated Financial Statement Schedules*

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

*3. Exhibits*

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
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	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1 (333-141700)	3/30/2007	4.1	
4.2	Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended	S-1 (333-141700)	3/30/2007	4.2	
4.3	Form of Warrant, issued on October 1, 2015	Form 8-K	10/1/2015	4.1	
4.4	Form of Warrant to Purchase Common Stock	Form 8-K	2/22/2016	4.1	
4.5	Form of Warrant to Purchase Common Stock	Form 8-K	7/1/2016	4.1	
4.6	Indenture, dated December 21, 2016, by and between the Registrant and Wilmington Trust, National Association	Form 8-K	12/21/2016	4.1	
4.7	Form of Indenture	Form S-3ASR	4/24/2016	4.7	
4.8	Description of the Registrant's securities				X

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
*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	Amended and Restated License Agreement, dated October, 31, 2008, by and between the Registrant and Mount Sinai School of Medicine of New York University	Form 10-K	2/6/2009	10.3	
+10.3	Exclusive License Agreement, dated as of June 8, 2005, by and between the Registrant and Novo Nordisk, A/S	S-1 (333-141700)	3/30/2007	10.5	
10.4	Form of Director and Officer Indemnification Agreement	S-1 (333-141700)	3/30/2007	10.17	
*10.5	Amended and Restated 2007 Director Option Plan and form of option agreement	Form 8-K	6/18/2010	10.2	
*10.6	2007 Employee Stock Purchase Plan	S-1/A (333-141700)	5/17/2007	10.24	
*10.7	Management Bonus Program Summary	Form 8-K	6/9/2016	10.1	
10.8	Lease Agreement dated August 16, 2011 between the Registrant and Cedar Brook 3 Corporate Center, L.P.	Form 8-K	8/16/2011	10.1	
10.9	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	
10.10	Credit and Security Agreement, by and between MidCap Funding III, LLC, as administrative agent, the Lenders listed in the Credit Facility Schedule thereto, the Registrant, and Callidus Biopharma, Inc., dated as of December 27, 2013	Form 8-K	12/30/2013	10.1	
+10.11	Second Restated Agreement, dated November 19, 2013 by and between the Registrant and Glaxo Group Limited	Form 10-K	3/3/2014	10.46	
*10.12	Amicus Therapeutics, Inc. Restricted Stock Unit Deferral Plan	Form 8-K	4/10/2014	10.1	
*10.13	Employment Agreement dated April 23, 2014, between the Registrant and John F. Crowley	Form 8-K	4/25/2014	10.1	
*10.14	Amended and Restated 2007 Equity Incentive Plan	Form 8-K	6/13/2016	10.1	
*10.15	Amicus Therapeutics, Inc. Cash Deferral Plan	Form 8-K	10/28/2016	10.1	
10.16	First Amendment to Credit and Security Agreement by and between MidCap Funding III, LLC, as administrative agent, the Lenders listed in the Credit Facility Schedule thereto, the Registrant, and Callidus Biopharma, Inc., dated as of April 27, 2015.	Form 8-K	4/28/2015	10.1	
10.17	Note and Warrant Purchase Agreement by and among the Registrant and the purchasers identified on the signature pages thereto, dated October 1, 2015	Form 8-K	10/1/2015	10.1	
10.18	First Amendment to Lease, dated September 9, 2015, by and between Cedar Brook 3 Corporate Center, L.P. and the Registrant	Form 8-K	9/14/2015	10.1	
*10.19	Retention Bonus Letter, dated March 10, 2016, by and between the Registrant and Jay Barth, M.D.	Form 8-K	3/15/2016	10.1	
10.20	Note and Warrant Purchase Agreement by and among the Registrant and the purchasers identified on the signature pages thereto, dated February 19, 2016.	Form 8-K	2/22/2016	10.1	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
10.21	Joinder to and Amendment of Note and Warrant Purchase Agreement by and among Amicus Therapeutics, Inc., Amicus Therapeutics UK Limited, Amicus Therapeutics International Holding LTD and the purchasers identified on the signature pages thereto, dated as of June 30, 2016	Form 8-K	7/1/2016	10.2	
*10.22	Amendment No. 1 to the Amended and Restated Amicus Therapeutics, Inc. 2007 Equity Incentive Plan	Form 8-K	7/29/2016	10.1	
*10.23	Secondment Letter, dated August 22, 2016 by and between the Registrant and Bradley Campbell	Form 8-K	8/23/2016	10.1	
10.24	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and P Redmile Ltd.	Form 8-K	12/21/2016	10.7	
10.25	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund, Ltd.	Form 8-K	12/21/2016	10.8	
10.26	Note Purchase Agreement, dated December 15, 2016, by among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund II, Ltd.	Form 8-K	12/21/2016	10.9	
10.27	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Special Opportunities Fund, Ltd.	Form 8-K	12/21/2016	10.10	
10.28	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Fund, LP	Form 8-K	12/21/2016	10.11	
10.29	Note Purchase Agreement, dated December 15, 2016, by and between Amicus Therapeutics International Holding LTD and GCM Grosvenor Special Opportunities Master Fund, Ltd.	Form 8-K	12/21/2016	10.12	
10.30	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	
10.31	Loan Agreement, dated as of September 19, 2018, by and among Amicus Therapeutics, Inc., as Borrower, certain subsidiaries of the Borrower, as Guarantors, and Biopharma Credit PLC, as Lender	Form 8-K	9/25/2018	10.1	
10.32	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	1/24/2019	10.1	
10.33	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	2/8/2019	10.1	
10.34	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	3/13/2019	10.1	



Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
10.35	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	5/22/2019	10.1	
10.36	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	6/19/2019	10.1	
10.37	Amendment #1 to the Amended and Restated Amicus Therapeutics, Inc. 2007 Equity Incentive Plan	Form 8-K	12/26/2018	10.1	
++10.38	Research, Collaboration and License Agreement with The Trustees of the University of Pennsylvania dated October 8, 2018	Form 10-K	2/28/2019	10.48	
10.39	Separation Agreement with William D. Baird III dated as of February 8, 2019	Form 10-K	2/28/2019	10.49	
10.40	Form of Call Option Partial Termination	Form 10-Q	5/9/2019	10.1	
10.41	Form of Capped Call Transaction Termination Agreement	Form 10-Q	8/8/2019	10.1	
**10.42	Amended and Restated Research, Collaboration & License Agreement, dated May 28, 2019, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania	Form 10-Q	8/8/2019	10.2	
10.43	Amendment #2 to the Amicus Therapeutics, Inc. Cash Deferral Plan.	Form 8-K	12/19/2019	10.1	
*10.44	Amendment No. 1 to Employment Agreement dated April 23, 2014 between the Registrant and John F. Crowley				X
*10.45	Employment Agreement dated February 18, 2020, between the Registrant and Ellen S. Rosenberg				X
*10.46	Employment Agreement dated February 18, 2020, between the Registrant and Bradley L. Campbell				X
*10.47	Employment Agreement dated February 18, 2020, between the Registrant and Jay Barth, M.D.				X
*10.48	Employment Agreement dated February 18, 2020, between the Registrant and Daphne Quimi				X
*10.49	Employment Agreement dated February 18, 2020 between the Registrant and Hung Do				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

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
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
101	The following financial information from this Annual Report on Form 10-K for the year ended December 31, 2019, 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, 2019, 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 2, 2020.

AMICUS THERAPEUTICS, INC.  
 (Registrant)  
 By: /s/ John F. Crowley  
 John F. Crowley  
 Chief Executive Officer

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Craig Wheeler</u> (Craig Wheeler)	Director	March 2, 2020
<u>/s/ Lynn Bleil</u> (Lynn Bleil)	Director	March 2, 2020
<u>/s/ Burke Whitman</u> (Burke Whitman)	Director	March 2, 2020

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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ John F. Crowley</u> (John F. Crowley)	Chairman and Chief Executive Officer (Principal Executive Officer)	March 2, 2020
<u>/s/ Daphne Quimi</u> (Daphne Quimi)	Chief Financial Officer (Principal Financial Officer)	March 2, 2020
<u>/s/ Samantha Prout</u> (Samantha Prout)	Global Controller (Principal Accounting Officer)	March 2, 2020
<u>/s/ Robert Essner</u> (Robert Essner)	Director	March 2, 2020
<u>/s/ Ted W. Love, M.D.</u> (Ted W. Love, M.D.)	Director	March 2, 2020
<u>/s/ Margaret G. McGlynn, R.Ph.</u> (Margaret G. McGlynn, R.Ph.)	Director	March 2, 2020
<u>/s/ Michael G. Raab</u> (Michael G. Raab)	Director	March 2, 2020
<u>/s/ Glenn Sblendorio</u> (Glenn Sblendorio)	Director	March 2, 2020

