

AMICUS THERAPEUTICS, INC.  
Form 10-K  
February 28, 2019

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

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FORM 10-K

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ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2018

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

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Amicus Therapeutics, Inc.  
(Exact name of registrant as specified in its charter)

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Delaware	71-0869350
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification Number)
1 Cedar Brook Drive, Cranbury, NJ	08512
(Address of Principal Executive Offices)	(Zip Code)
(609) 662-2000	

(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Name of each exchange on which registered
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Common Stock, par value \$0.01 per share	The NASDAQ Stock Market LLC
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Securities registered pursuant to Section 12(g) of the Act: None

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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

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such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§22.405) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer  Accelerated filer

Non-accelerated filer  Smaller reporting company

Emerging growth company

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

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

The aggregate market value of the 148,893,826 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, 2018) was \$2,325,721,562. 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 15, 2019, there were 223,708,827 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2019 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.

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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.

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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,” “like,” “may,” “might,” “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;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy (“ERT”) 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 pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of lysosomal storage disorders 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, including our ability to obtain regulatory approvals and commercialize CDKL5 therapies and obtain market acceptance for such therapies;
- the costs, timing and outcome of regulatory 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;
- 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 and obtain milestone, royalty or other payments from any such collaborators;
- our ability to adjust to changes in European and United Kingdom markets as the United Kingdom leaves the European Union; and
- fluctuations in foreign currency exchange rates; and changes in accounting standards.

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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.

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PART I

Item 1. BUSINESS

Overview

We are a global patient-dedicated biotechnology company engaged in the discovery, development and commercialization of a diverse set of novel treatments for patients living with rare metabolic diseases. With one medicine for Fabry disease achieving global approval, a differentiated biologic for Pompe disease in late-stage clinical development and fourteen gene therapy programs in the pipeline, including two clinical stage gene therapies for Batten disease, we have a leading portfolio of therapies for lysosomal storage disorders (“LSDs”).

The cornerstone of our portfolio is Galafold<sup>®</sup>, (also referred to as “migalastat HCl” or “migalastat”), the first and only approved oral precision medicine for people living with Fabry disease who have amenable genetic variants, or mutations. Galafold<sup>®</sup> is currently approved in the United States (“U.S.”), European Union (“EU”) and Japan, with additional approvals granted and applications pending in several geographies. During the third quarter of 2018, we initiated the commercial launch of Galafold<sup>®</sup> in the U.S. for the treatment of adult patients with a confirmed diagnosis of Fabry disease and an amenable genetic variant.

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. Our Chaperone-Advanced Replacement Therapy (“CHARP<sup>®</sup>”) platform technology is leveraged to combine our novel Pompe biologic ATB200 with a pharmacological chaperone AT2221.

During the second half of 2018, we expanded our portfolio to include fourteen new gene therapy programs. During the third quarter of 2018, we acquired worldwide development and commercial rights for ten gene therapy programs for neurologic LSDs developed at The Center for Gene Therapy at The Research Institute at Nationwide Children’s Hospital (“NCH”) and The Ohio State University through the acquisition of Celenex, Inc. (“Celenex”), a private, clinical stage gene therapy company, for cash consideration of \$100.0 million and additional consideration payable upon the achievement of certain development and approval milestones. The acquisition establishes Amicus as a leading company in neurologic LSDs. The lead programs in CLN6, CLN3, and CLN8 Batten disease are potential first-to-market curative therapies for these rare, devastating diseases.

In October 2018, we further expanded our gene therapy portfolio through a collaboration agreement with the Gene Therapy Program in the Perelman School of Medicine at the University of Pennsylvania (“Penn”) to pursue the research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, CDKL5 deficiency disorder (“CDD”) and one additional undisclosed rare metabolic disorder. This relationship will combine our protein engineering and glycobiology expertise with Penn’s adeno associated virus (“AAV”) gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability.

In February 2019, we announced that the U.S. Food and Drug Administration (“FDA”) granted Breakthrough Therapy Designation (“BTD”) to AT-GAA in late onset Pompe disease. AT-GAA is the first ever investigational product for Pompe disease to receive BTD. The BTD will facilitate multidisciplinary, comprehensive discussions of the AT-GAA development program with the FDA, including planned clinical trials and plans for expediting manufacturing development strategy. The BTD for AT-GAA is based on clinical efficacy results from the ongoing ATB200-02 Phase 1/2 clinical study, including improvements in six-minute walk distance in late onset Pompe patients and comparison to natural history of treated patients.

We believe that our platform technologies and our product pipeline uniquely position us and drive our commitment to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases.



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### 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 lead 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. Since the beginning of 2017, 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 in 2018 include:

Commercial and regulatory success in Fabry disease. During the year ended December 31, 2018, Galafold® revenue totaled approximately \$91.2 million. Revenue has been generated primarily in the EU since May of 2016. In 2018, we received approvals for Galafold® in the U.S. and Japan.

Pompe clinical program milestones. We reported a series of positive data from a Phase 1/2 clinical study to evaluate Pompe disease patients treated with our novel treatment paradigm AT-GAA for up to 18 months. We also initiated a global pivotal study of AT-GAA (ATB200-03, also known as PROPEL) which is expected to enroll approximately 100 participants with late-onset Pompe disease at up to 90 global sites.

Pipeline Growth: With 14 new gene therapy programs for LSDs, we have established a leading portfolio of medicines for people living with rare metabolic disorders. Through our license with NCH, we acquired worldwide development and commercial rights for ten gene therapy programs in rare, neurologic LSDs with lead programs in CLN6, CLN3, and CLN8 Batten disease. An additional four programs were added to the pipeline through the collaboration with Penn to pursue research and development of novel gene therapies for Pompe disease, Fabry disease, CDKL5 deficiency disorder (“CDD”) and one additional undisclosed rare metabolic disorder.

Manufacturing. We successfully scaled up manufacturing of our Pompe biologic to 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 serve the entire Pompe population as quickly as possible after receipt of applicable regulatory approvals. Through our collaborations with NCH and Penn, we also gain access to their preclinical manufacturing capabilities, clinical supply and CMO relationships for those gene therapy programs.

Financial strength. Total cash, cash equivalents and marketable securities of \$504.2 million at December 31, 2018 compared to \$358.6 million at December 31, 2017. The current cash position, including expected Galafold® revenues, is sufficient to fund ongoing Fabry, Pompe and gene therapy program operations into at least mid-2021. 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 EU 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 variant. The approved EU label includes 367 Fabry-causing variants, which represent up to half of all patients with Fabry disease. Approvals have also been granted in Australia, Canada, Israel, Japan, South Korea, and Switzerland, with additional applications pending in other geographies. We have been granted pricing and reimbursement in 22 countries. We plan to continue to launch Galafold® in additional countries during 2019.



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.

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### 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 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). Recent newborn screening studies in Italy, Taiwan, Austria and the U.S., which screened more than 526,000 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).

Based on this, 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 and agalsidase alfa. The net product sales of agalsidase beta and agalsidase alfa for 2018 were approximately \$742.5 million as publicly reported by Sanofi Aventis, and \$498.1 million as publicly reported by Takeda, respectively. 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. For additional information, see above “-Overview.”

### Novel ERT for Pompe Disease

We are leveraging our biologics capabilities and CHART® platform 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 2018, with the first patient dosed in December 2018.

Our strategy is to enhance the body of clinical data for AT-GAA in ongoing clinical studies, including the pivotal study (PROPEL) to deliver this potential new therapy to as many people living with Pompe disease as soon as possible. Based on regulatory feedback from both the U.S. FDA and the European Medicines Agency ("EMA"), the PROPEL study is expected to support approval for a broad indication, including ERT-switch and treatment-naïve patients.

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 to improve the uptake of active enzyme in key disease-relevant tissues, resulting in increased clearance of accumulated substrate, glycogen.

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In preclinical studies, AT-GAA demonstrated greater tissue enzyme levels and further substrate reduction compared to the currently approved ERT for Pompe disease (alglucosidase alfa).

On February 5, 2019 we reported additional interim data from our clinical study ATB200-02 at the 15th Annual WORLDSymposium™. Highlights included safety and tolerability data in patients as well as pharmacodynamic "PD" data (muscle damage biomarker and disease substrate biomarker). To date, adverse events have been generally mild and transient. AT-GAA has resulted in a low rate of infusion-associated reactions ("IARs") following 1,110+ infusions (16 events of IARs in six 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.

With regard to efficacy, muscle function improved in 16 out of 17 patients who have available data for up to 21 or 24 months. Mean 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 in 6MWT distance at all time points out to month 21. The ERT-naïve patients showed mean increases of 42 meters at month 6 (n=5), 63 meters at month 12 (n=5), and 55 meters at month 21 (n=5). 6MWT increased in 7/10, 9/10, and 8/8 ERT-switch patients at Months 6, 12, and 24 respectively. The ERT-switch patients showed mean increases of 24 meters at month 6 (n=10), 42 meters at month 12 (n=10), and 54 meters at month 24 (n=8). Other motor function tests generally showed mean improvements consistent with 6MWT distance out to month 21 or 24 in both ambulatory cohorts. Non-ambulatory ERT-switch patients showed improvements in upper extremity strength (which includes elbow and shoulder) from baseline to month 24, as measured by quantitative muscle testing and manual muscle testing. Pulmonary function improved in ERT-naïve patients and was generally stable in ERT-switch patients. In ERT-naïve patients, mean absolute change in forced vital capacity (FVC), one of the main measures of pulmonary function in Pompe disease, was +4.2% at month 6 (n=5), +4.5% at month 12 (n=5), and +6.1% at month 21 (n=5). In ERT-switch patients mean absolute change in FVC was -1.2% at month 6 (n=9), -3.0% at month 12 (n=9), and -0.6% at month 24 (n=7). Overall, other pulmonary tests of maximal inspiratory pressure (MIP), a measure of inhalation, and maximal expiratory pressure (MEP), a measure of exhalation, were stable or increased in both ERT-naïve and ERT-switch patients.

## Pompe Disease Background

Like Fabry disease, Pompe disease is an LSD 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 other product, an ERT, is approved for the treatment of Pompe disease: alglucosidase alfa. The net product sales of alglucosidase alfa for 2018 were approximately \$827.5 million as publicly reported by Sanofi Aventis.

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 as a potential cure 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, among other indications, Pompe disease. For additional information, see above “-Overview.”

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### CDKL5 Deficiency Disorder (“CDD”)

We are also researching a potential first-in-class protein replacement therapy approach. Through our collaboration with Penn, we are also 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.

### Batten Disease Product Candidates

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.

The two clinical stage gene therapies are in CLN3 and CLN6 Batten disease. The CLN6 Batten disease Phase 1/2 study completed target enrollment, with 12 patients receiving a single administration of adeno-associated virus serotype 9 AAV9-CLN6 gene therapy. We expect to report additional two-year data from CLN6 Batten disease Phase 1/2 study in 2019.

CLN6 Batten disease results from a mutation in the CLN6 gene which primarily affects the nervous system. The CLN6 population is approximately 1,000 patients across our commercial landscape today.

In the fourth quarter of 2018, the Company announced the initiation of a Phase 1/2 clinical study to evaluate the safety and efficacy of a single intrathecal administration of adeno-associated virus serotype 9 AAV9-CLN3 gene therapy in children with CLN3 Batten disease. CLN3 Batten disease, the most common form of NCL results from a mutation in the CLN3 gene which primarily affects the nervous system. Children with this condition develop vision impairment, intellectual disability, progressive loss of motor function, speech difficulties, and seizures which worsen over time. CLN3 impacts approximately 5,000 patients across our commercial landscape today and there are no approved therapies for this disorder.

### Strategic Alliances and Arrangements

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 four additional indications, including Pompe disease, Fabry disease, CDD and one additional undisclosed rare metabolic disorder. For additional information, see above “—Overview.” See also “—Collaboration and License Agreements” below for additional information on 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.

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### Our Technology Platforms

#### Pharmacological Chaperone Technology

Our pharmacological chaperone technology has allowed us to develop our personalized medicine Galafold® (a monotherapy), our Chaperone-Advanced Replacement Therapy (“CHART®”) technology platform (pharmacological chaperones in combination with ERT), and has advanced our protein engineering expertise in enzyme targeting and gene therapy. Pharmacological chaperones are small molecules designed to selectively bind to a target protein, increase its stability, and help keep it folded in the correct three-dimensional shape. For LSDs, pharmacological chaperones are designed to bind to, stabilize, and facilitate trafficking of both endogenous and exogenous enzymes to the lysosome.

#### Pharmacological Chaperone Monotherapy

As monotherapy agents for LSDs, pharmacological chaperones are designed to bind to and stabilize endogenous lysosomal enzymes for proper trafficking to the lysosome, which may also alleviate the buildup of mutant proteins in the endoplasmic reticulum. Once in the lysosome, the pharmacological chaperone disassociates and the enzyme is free to break down substrate. Based on this mechanism, individuals with certain genetic variants (amenable variants) that result in some residual biological activity are potentially eligible for pharmacological chaperone monotherapy. This is the technology basis of our Galafold® treatment.

#### CHART® Technology Platform

ERT is the standard of care for several LSDs, based on the intravenous infusion of recombinant or gene-activated human enzyme. The enzyme is delivered into the blood in order to be taken up by cells and then transported to the lysosome. Upon entering the lysosome, this enzyme is intended to perform the function of the absent or deficient endogenous enzyme. However, the pH in blood is higher than the enzyme's natural acidic environment in the lysosome. As a result, the infused enzyme may unfold and lose activity and may be misdirected to non-target tissues or rapidly cleared from the body. Exposure to high concentrations of infused enzymes can impact efficacy or cause adverse effects.

We are applying our CHART® technology for our current Pompe treatment paradigm AT-GAA, where our chaperone AT2221 is designed to bind to and stabilize our recombinant rhGAA enzyme ATB200. The pharmacokinetic data from our Phase 1/2 ATB200-02 clinical study in Pompe patients, in addition to other studies of pharmacological chaperones in combination with currently marketed ERTs, have established initial human proof of concept that a pharmacological chaperone can stabilize enzyme activity. This technology may improve the stability, uptake, and activity of the enzyme.

#### Our Protein Engineering Expertise for Enzyme Targeting and Gene Therapy

The uptake of ERTs into a patient's cells is mediated by a particular carbohydrate called mannose 6-phosphate (“M6P”). M6P enables binding and delivery of therapeutic drug to lysosomes via M6P receptors on cell surfaces. Many currently approved ERTs have limited amounts of M6P, thereby limiting the uptake of therapeutic drug into a patient's cells.

Our novel Pompe treatment paradigm AT-GAA includes our ERT ATB200 that is engineered with significantly higher amounts of M6P for improved lysosomal targeting and incorporates our chaperone AT2221 to improve enzyme stability.

In the case of gene therapy, limited amounts of M6P on the construct DNA may also limit uptake and require very high doses of protein in order to be taken up into a patient's cells. Through our relationship with Penn, we will combine Amicus' protein engineering and glycobiology expertise with Penn's AAV gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability. Our indications of focus include Fabry, Pompe, CDD and on additional undisclosed rare metabolic disorder.



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Acquisitions

Celenex, Inc.

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. 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 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.

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. Upon closing of the transaction we paid the former holders of MiaMed's capital stock 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 our Company's common stock. In addition, we 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. We accounted for this transaction as an acquisition of an asset as we did not acquire any employees from MiaMed; nor did we acquire any significant processes that we did not previously perform or manage.

Scioderm, Inc.

In September 2015, we 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 our global clinical infrastructure to advance SD-101 toward regulatory approvals and our 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. On September 13, 2017, we 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. Based on these top-line data, we have no current plans to invest in any additional clinical studies or commercial preparation activities for SD-101. The associated impairment of Scioderm IPR&D is discussed in "— Note 4. Goodwill and Intangible Assets" in our Notes to Consolidated Financial Statements.

Callidus Biopharma, Inc.

In November 2013, we entered into a merger agreement with Callidus Biopharma, Inc. ("Callidus"), a privately held biotechnology company that was engaged in developing a next-generation Pompe ERT. Callidus did not have complementary technologies but their technology was complementary to our own pharmacological chaperone technology.

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In connection with our acquisition of 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 will 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. We may, at our election, satisfy certain milestone payments identified in the merger agreement aggregating \$40 million in shares of our common stock. The milestone payments not permitted to be satisfied in common stock (as well as any payments that we are permitted to, but choose not to, satisfy in common stock), as a result of the terms of the merger agreement, will be paid in cash. During the fourth quarter of 2018, we 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 our common stock during the first quarter of 2019.

### 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 license rights to several issued patents in the U.S., current member states of the European Patent Convention and numerous pending and issued foreign applications, which are foreign counterparts of many of our U.S. patents. We also own or license rights to several pending U.S. applications. Our patent portfolio includes patents and patent applications with claims relating to methods of increasing and/or stabilizing deficient enzyme activity to treat genetic diseases. The patent positions for Galafold<sup>®</sup>, and ATB200/AT2221 pharmacological chaperone/ERT combination therapy are described below and include both patents and patent applications we own or exclusively license:

• We have an exclusive license to a number of issued U.S. patents that cover the use of Galafold<sup>®</sup> to treat Fabry disease, as well as corresponding European, Japanese, and Canadian patents. These exclusively licensed U.S. patents relating to Galafold<sup>®</sup> expired in 2018, while the European, Japanese, and Canadian patents will expire in 2019. The patents include claims covering methods of increasing the activity of and preventing the degradation of alpha-Gal A, and methods for the treatment of Fabry disease using Galafold<sup>®</sup>. In addition, we own two issued U.S. patents directed to dosing regimens with Galafold<sup>®</sup> that expire in 2027 (not including any extensions), as well as a pending application which, if granted, may result in a patent that also expires in 2027 (not including any extensions). Foreign counterpart patents are issued in Australia, Europe, Hong Kong, Mexico, and Japan, and foreign applications are pending in Australia, Canada, Europe, Hong Kong, Japan, and Mexico. Further, we own an issued U.S. patent directed to synthetic steps related to the commercial process for preparing Galafold<sup>®</sup>, which expires in 2026, as well as issued patents in China, Europe, Hong Kong, India, Israel, and Japan. We jointly own issued U.S., European, Hong Kong, and Mexican patents covering a method of determining whether male Fabry disease patients are likely to respond to treatment with Galafold<sup>®</sup> which expires in 2027. We have two issued U.S. patents covering a method of treating a

patient diagnosed with Fabry disease with Galafold<sup>®</sup> wherein the Fabry patient has one of several alpha-Gal A variants. These patents will expire in 2029. We also have a pending U.S. application covering a method of determining which alpha-Gal A variants are likely to be amenable to therapy with Galafold<sup>®</sup> which, if granted, will expire in 2029. Foreign counterpart patents have also been issued in Europe, Japan, Canada, Mexico, and Australia; all of which will also expire in 2029. We also have filed a patent application covering a method of treating renal symptoms in a Fabry patient in relevant jurisdictions. As of February 2019, we have allowance of the U.S. counterpart and when granted, the patent would expired in 2038.

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We have an exclusive license to pending patent applications covering the co-administration of Galafold® with ERT (recombinant alpha-Gal A). Patents covering specific combinations have issued in the U.S., Europe, Canada, China, India, Israel, Hong Kong, Japan, and Mexico. These issued patents will expire in 2024. We also own a U.S. patent application covering specific doses and dosing regimens of Galafold® to treat Fabry disease in combination with ERT (recombinant alpha-Gal A) in the U.S. and foreign counterpart applications in Australia, Canada, Europe, Hong Kong, Japan, and issued patents in Australia, Canada, and China. Any patents issuing from these applications will expire in 2032.

We have patents covering a co-formulation of recombinant acid alpha-glucosidase and Galafold® in the U.S. and Australia, as well as pending patent applications in the U.S., Australia, Canada, China, Europe, and Hong Kong. If patents issue from these applications, expiration will be in 2033 or 2034.

As part of the Callidus acquisition, we acquired a portfolio of patent applications including an application series covering reagents and methods for coupling targeting peptides to recombinant lysosomal enzymes, including recombinant acid alpha-glucosidase. Patents in this series are issued in the U.S., Canada, China and Europe, and applications are pending in the U.S., Europe, Japan, Brazil, Canada, China, and South Korea. If patents issue from these applications, expiration will be in 2032 to 2034 depending on the specific application.

Another patent application portfolio related to a modified lysosomal enzyme (acid alpha-glucosidase) that binds more effectively to the receptor and more potent than conventional recombinant enzymes. These applications pending in the U.S., Australia, Brazil, Canada, China, Eurasia, Europe, Israel, India, Japan, South Korea, Mexico, Singapore, Taiwan, South Africa, and other countries. If patents issue from this series, they will expire in 2035 to 2038.

As part of the acquisition of MiaMed, we acquired an exclusive worldwide license to certain patent rights held by the Università di Bologna. These patent rights include two issued U.S. patent and a pending U.S. patent application directed to novel CDD fusion proteins, as well as pending counterpart patent applications in several foreign countries. The issued U.S. patent and the patent applications, if issued, will expire in 2035.

From NCH through the acquisition of Celenex, we have an exclusive license to pending patent applications covering ten AAV program in neurodegenerative disorders, including CLN6, CLN3, and CLN8 Batten diseases. These patent rights include one issued European patent and several pending U.S. patent applications pertaining to various aspects of the gene therapy programs, as well as pending counterpart patent applications in several foreign countries. The issued European patent and the patent applications, if issued, will expire in 2033 or 2040.

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:

• The longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent application was filed prior to June 8, 1995; and

• 20 years from the earliest effective filing date, if the patent application was filed on or after June 8, 1995.

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 United States 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.

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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 further 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. This relationship will combine our protein engineering expertise with Penn's AAV gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability. In connection with the collaboration agreement, we made an upfront payment of \$7 million in cash to Penn in October 2018 that was expensed to research and development expense in the Consolidated Statements of Operations and agreed to certain milestone payments following the achievement of certain developmental and commercial milestone events by a licensed product in each

indication up to an aggregate of \$86.5 million per indication.

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### 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® 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® 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. For the year ended December 31, 2018, we recognized approximately \$6.9 million of royalty expense under the Revised Agreement.

### Mt. Sinai School of Medicine

We have acquired exclusive worldwide patent rights to develop and commercialize Galafold® and other pharmacological chaperones for the prevention or treatment of human diseases or clinical conditions by increasing the activity of wild-type and mutant enzymes pursuant to a license agreement with Mt. Sinai School of Medicine ("MSSM") of New York University. Under this agreement, to date, we have paid no upfront or annual license fees and we have no milestone or future payments other than royalties on net sales. This agreement expires upon expiration of the last of the licensed patent rights, which will be in 2019, or 2024 if we develop a product for combination therapy (pharmacological chaperone plus/ERT) and a patent issues from the pending application covering the combination therapy, subject to any patent term extension that may be granted.

Under our license agreements, if we owe royalties on net sales for one of our products to more than one of the above licensors, then we have the right to reduce the royalties owed to one licensor for royalties paid to another. The amount of royalties to be offset is generally limited in each license and can vary under each agreement. For Galafold® in 2018, we incurred \$0.8 million of royalty expense under the agreement with MSSM. Our rights with respect to these agreements to develop and commercialize Galafold® may terminate, in whole or in part, if we fail to meet certain development or commercialization requirements or if we do not meet our obligations to make royalty payments.

### Manufacturing

We continue to rely on contract manufacturers to supply the active biopharmaceutical ingredients and final drug product for Galafold®, 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. 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.

### 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, both through organic growth and 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.





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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 LSDs. 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 is 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	Indication	Product	Class of Product	Status	2018 Sales (in millions)
Sanofi Aventis	Fabry Disease	Fabrazyme®	ERT	Marketed	\$ 742.5
	Pompe Disease	Myozyme®/ Lumizyme®	ERT	Marketed	\$ 827.5
	Fabry Disease	GZ402671	Oral GCS Inhibitor	Phase 2	N/A
	Pompe Disease	GZ402666 ("neo GAA")	ERT	Phase 3	N/A
Takeda	Fabry Disease	Replagal®	ERT	Marketed	\$ 498.1
Protalix Biotherapeutics	Fabry Disease	PRX-102	ERT	Phase 2/3	N/A
Audentes	Pompe Disease	AT845	Gene Therapy	Preclinical	N/A
Sangamo	Fabry Disease	ST-920	Gene Therapy	Preclinical	N/A
Avrobio	Fabry Disease	AVR-RD-01	Gene Therapy	Phase 1/2	N/A
	Pompe Disease	AVR-RD-03	Gene Therapy	Preclinical	N/A
Spark	Pompe Disease	SPK-3006	Gene Therapy	Preclinical	N/A
Abeona	CLN3 Batten	ABO-201	Gene Therapy	Preclinical	N/A

**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.

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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 child bearing 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.

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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.

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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 a 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.



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### 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.





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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 a 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.

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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.

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### 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 EU 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 EU. 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 EU Member States. 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 EU. 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 EU member states. The Decentralized Procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states.

The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

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We have obtained an orphan medicinal product designation in the EU from the EMA for Galafold® for the treatment of Fabry disease ("FD"). The combination product, ATB200/AT2221, for the treatment of Pompe disease has currently received orphan drug designation in the U.S. with a pending review in the EU. 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 EU 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 EU and that without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the EU 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 EU 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 variant. 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 EU. Medicines authorized across the EU 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. 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 the United Kingdom ("UK") on June 23, 2016, a majority of those voting voted for the UK to leave the EU, commonly referred to as "Brexit". On March 29, 2017, the UK government delivered to the European

Council notice of its intention to leave the EU and, in the absence of an executed withdrawal agreement with the EU, the effective date of the UK's withdrawal from the EU will be March 29, 2019. The ultimate impact of the "leave" vote will depend on the terms that are negotiated in relation to the UK's future relationship with the EU. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which EU laws to replicate or replace.

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### 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, 2018, we had 508 full-time employees, 268 of whom were primarily engaged in research and development activities and 240 of whom provided selling and administrative services. 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.

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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.

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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 the EU, 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 the EU 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 EU 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. We will continue to study Galafold<sup>®</sup> in a confirmatory Phase 4 program. If the results of the Phase 4 program 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 EU, U.S., 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



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obtaining 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 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 United States and by comparable authorities in other countries. As of December 31, 2018, we have obtained regulatory approval to market Galafold<sup>®</sup> in the EU, Switzerland, Israel, Iceland, Liechtenstein, South Korea, Canada, Australia, the U.S. and Japan. 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 recently 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



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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 or product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA, EMA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our 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 these functions to third parties. We have established our own sales and marketing capabilities to promote Galafold<sup>®</sup> in the EU, 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 migalastat HCl, 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

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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 arrangements with third parties to perform sales and marketing services, 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, or Batten's disease in the study populations, particularly in these newer studies, accurately reflects the prevalence of these diseases in the broader world population. If our estimates of the prevalence of Fabry disease, Pompe disease, or Batten's disease 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;



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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 United States, the EU 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<sup>®</sup> 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<sup>®</sup> and Takeda's Replaga<sup>®</sup>, as well as other Fabry treatment products in development. In addition, Sanofi markets and sells Myozyme<sup>®</sup> and Lumizyme<sup>®</sup> for the treatment of Pompe disease. 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. 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 the recently acquired 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.

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A variety of risks associated with international operations could materially adversely affect our business. Galafold<sup>®</sup>, and any of our other product candidates that may be approved in the future for commercialization in the EU, 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, or natural disasters including earthquakes, typhoons, floods and fires.

In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the EU 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 UK on June 23, 2016, a majority of those voting voted for the UK to leave EU, commonly referred to as “Brexit”. On March 29, 2017, the UK government delivered to the European Council notice of its intention to leave the EU and, in the absence of an executed withdrawal agreement with the EU, the effective date of the United Kingdom’s withdrawal from the EU will be March 29, 2019. The ultimate impact of the “leave” vote will depend on the terms that are negotiated in relation to the UK’s future relationship with the EU. Brexit could impair the Company’s ability to transact business in the UK and EU 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 agreements the UK makes to retain access to EU markets following the UK’s withdrawal from the EU. Negotiation of the withdrawal agreement is ongoing and we have no certainty as to the future terms of the UK’s relationship with the EU until these negotiations have been completed. Alternatively, negotiations may be unsuccessful and the UK may not reach agreement with the EU on the future terms of the UK’s relationship with the EU. 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.

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We expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which EU laws to replicate or replace. If the UK 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 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 UK and the EU. Assuming there is no deal outlining the future relationship between the UK and the EU prior to March 29, 2019, the UK regulatory authority has provided some guidance on the continued availability of prescription drugs.

Following Brexit, approval of medications approved through the EU centralized procedure, such as Galafold<sup>®</sup>, will remain in effect through grandfathering. Our international headquarters are in Marlow, UK. Guidance from the EMA provides that the Company must transfer marketing authorization to a holder in the EU. The transfer must be fully completed and implemented before March 30, 2019. We are in the process of moving our regulatory portfolio to Ireland which will provide a marketing authorization holder in the EU.

Among other outcomes, the withdrawal could disrupt the free movement of goods, services and people between the UK and the EU, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in the UK and the EU. In addition, changes to UK 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 withdrawal of the UK from the EU 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. 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<sup>®</sup> 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 EU 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. 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.



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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. Some states are also considering legislation that would control the prices and reimbursement of prescription drugs, and 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, the current administration’s budget proposal for fiscal year 2019 contains drug price control measures that could be enacted during the 2019 budget process or in other 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 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.



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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.

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Non-compliance with EU 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 EU'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 United Kingdom, 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. There is also a separate false claims provision imposing criminal penalties. Applicable regulations of both the EMA and EU 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;

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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. Similarly, the collection and use of personal health data in the EU is governed by the EU 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 EU 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 EU 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 EU member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU 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 EU. 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



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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.

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In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. A significant number of provisions are not yet, or have only recently become, effective, but the Affordable Care Act is likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. We expect that the Affordable Care Act, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may compromise our ability to generate revenue, attain profitability or commercialize our products. Finally, there have been significant efforts to modify or eliminate the ACA. For example, the Tax Cuts and Jobs Act enacted on December 22, 2017 repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code, 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 Americans losing their health insurance coverage over the next ten years and is likely to lead to increases in insurance premiums. Further legislative changes to and regulatory changes under the ACA remain possible. It is unknown what form any such changes or any law proposed to replace the ACA would take, and how or whether it may affect our business in the future.

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.

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 EU, 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 EU 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. In particular, any labeling approved by the FDA for Galafold<sup>®</sup> or any of our other product candidates may include restrictions on use. 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.

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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<sup>®</sup> 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 United States, after an NDA is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA, or ANDA. The Federal Food, Drug, and Cosmetic Act, or the FD&C Act, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredients, dosage form, strength, route of administration, and conditions of use, or product labeling, as 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 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.



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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 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. and EU. We have recently acquired the rights to 14 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. Currently, only a few gene therapy products have been approved in the Western world, including 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. 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 EU 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 pediatric patients. 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.



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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. 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.

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.

For example, 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 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., EU 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 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;



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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 AT-GAA PROPEL study, the CLN-6 study and the 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.

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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 based our research and development efforts on our CHART® platform technologies to develop next-generation ERT products for Fabry, Pompe, and other LSDs, and have advanced our next generation ERT for Pompe to the clinic. In 2018 we also made a significant investment in potential gene therapies for Fabry, Pompe, CDD, Batten's disease and other LSDs. 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 these 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 results. A failure of one or more of our clinical trials may occur at any stage of testing.

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

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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 recently reported data from a Phase 1/2 clinical trial of AT-GAA (ATB200/AT2221) in Pompe disease. The data is based on a small patient sample and reported before completion of the study and therefore may not be predictive of future results. The results of additional preliminary data or data from the completed study or any future study may not yield results that are consistent with the data presented. Later study results may not support further development, or even if such later 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., EU, 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 EU 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 EU for Galafold® in May 2006. AT-GAA has also received this designation from the FDA. 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 applicable market exclusivity period for orphan drugs is ten years in the EU and seven years in the U.S. The EU 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 EU, 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. For a drug such as Galafold<sup>®</sup>, which is composed of small molecules, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use. Obtaining orphan drug exclusivity for our product candidates, both in the EU and in the U.S., may be important to the product candidate's and our CHART<sup>®</sup> program's success. If a competitor 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.

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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 ATB200/AT2221 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 the EU 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 recently acquired 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, 2018, we have a net loss of \$349.0 million, and we have an accumulated deficit of \$1.4 billion at December 31, 2018.

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 EU, 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 EU, as applicable;



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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 the EU, Japan and the U.S. or other territories in which we may receive regulatory approval;

• continue wind-down of our Phase 3 clinical trial of SD-101 for the treatment of EB;

• 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 and other LSDs; 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 currently generate limited revenue from the sale of products and may never become profitable.

We began the commercial launch of our first product, Galafold®, in May 2016, with the U.S. and Japan commercial launches in 2018. Accordingly, we have only generated limited revenue from product sales. 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 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 successfully commercialize, Galafold®;

• develop and maintain a commercial organization capable of sales, marketing, and distribution for Galafold® 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 migalastat HCl 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.



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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 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 proceeds from the recent Pharmakon Debt Financing (as defined below) and expected Galafold® revenues, is sufficient to fund ongoing Fabry and Pompe program operations into at least 2021. Potential future business development collaborations, 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® 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; or

- significantly curtail operations.

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

- the costs of commercialization activities, including maintaining sales, marketing, and distribution capabilities for Galafold® and any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own;

- 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.

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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, 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 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 quarter of 2019, we entered into separate, privately negotiated exchange agreements with a limited number of holders (the "Holders") of our Convertible Notes. Under the terms of the exchange agreements (the "Exchange Agreements"), the Holders agreed to exchange an aggregate principal amount of approximately \$184.6 million of Convertible Notes held by them in exchange for an aggregate of approximately 33.0 million shares of the our common stock, par value \$0.01 per share. In addition, pursuant to the Exchange Agreements, we made aggregate cash payments of approximately \$0.7 million to the Holders to satisfy accrued and unpaid interest to the closing date of the transaction, along with cash in lieu of fractional shares.

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.



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The conditional conversion feature of the Convertible Notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the Convertible Notes is triggered, holders of such notes will be entitled to convert the notes at any time during specified periods at their option, which are set forth in the applicable indenture. If one or more holders elect to convert their Convertible Notes, we have the option to settle conversions entirely in cash, in common stock or a combination thereof. In addition, even if holders do not elect to convert their Convertible Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced operations in February 2002. Our operations to date have been limited to organizing and staffing our company, acquiring and developing our technology, undertaking preclinical studies and clinical trials of our most advanced product candidates, including our first commercial product, Galafold<sup>®</sup>, and establishing our sales and marketing capabilities to promote Galafold<sup>®</sup> in the EU, Japan and the U.S. We have not yet generated material commercial sales for any of our product candidates. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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 recent acquisition of Celenex and the research collaboration with Penn to develop gene therapies. 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.



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

As of December 31, 2018, the Company had federal, state, and foreign net operating loss carry forwards ("NOLs") of approximately \$858.4 million, \$943.5 million, and \$35.0 million, respectively. The federal carry forward will expire in 2030 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the 2017 Tax Cut & Jobs Act. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2018 will expire in 2030 through 2038. The foreign NOLs have indefinite expiration. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of 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;

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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 and migalastat HCl. 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 will expire in 2019 in Europe, Japan, and Canada. In addition to patent protection outside of the U.S., we intend to seek orphan medicinal product designation 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> and we have method of manufacturing patent applications allowed for ATB200 as well as method of treatment patents allowed for migalastat HCl. There can be no assurance that the 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.

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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 EU 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 EU 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.

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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.

We are aware, for example, of U.S. patents, and corresponding international counterparts, owned by third parties that contain claims related to treating protein misfolding. 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 or that, if we choose or are required to seek a license with respect to such patents, such license would be available to us on acceptable terms or at all. 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.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other 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. Others may sue us for infringing their patent or other intellectual property rights or file nullity, opposition or interference proceedings against our patents, even if such claims are without merit, which would similarly harm our business.

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. 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.

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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 the Mount Sinai School of Medicine of New York University, NCH, and Penn pursuant to which we license key intellectual property relating to our lead 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.



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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.

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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, and demonstrating comparability of small batches to commercial scale batches. 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 demonstrate comparability to GMP commercial scale product for biologic products;
- inability to manufacture batches that meet specifications and quality standards;
- 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®. 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.

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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 EU. Failure to comply with such requirements, including with respect to clinical trials conducted outside the EU 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 store and distribute drug supplies for our preclinical development activities and clinical trials. Any performance failure on the part of our distributors could delay 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.

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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. 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.





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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 or, after regulatory approval has been obtained, our product candidates, the commercial launch of our product and product candidates would be delayed or there would be a shortage in supply, which would materially affect our ability to generate revenues from the sale of our product or product candidates.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization. As we scale up manufacturing of our product and product candidates and conduct required stability and comparability testing, we 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.

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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 the recent announcement of locating 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.



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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, 2018, we had 508 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 will be 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;
- improving our managerial, development, operational and financial systems and procedures;
- 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 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.

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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 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, 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.

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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.

### 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 22% of our common stock as of December 31, 2018. 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

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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 EU, 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;



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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.

The capped call transactions may affect the value of the Convertible Notes and our common stock.

In connection with the issuance of the Convertible Notes, we entered into capped call transactions with respect to the Convertible Notes with certain hedge counterparties. The capped call transactions will cover, subject to customary anti-dilution adjustments, the aggregate number of shares of common stock underlying the Convertible Notes and are expected generally to reduce potential dilution to the common stock upon conversion of the Convertible Notes in excess of the principal amount of such converted Convertible Notes. In connection with establishing their initial hedges of the capped call transactions, the hedge counterparties (or their affiliates) entered into various derivative transactions with respect to the common stock concurrently with, and/or purchased the common stock shortly after, the pricing of the Convertible Notes. The hedge counterparties (or their affiliates) are likely to modify their hedge positions by entering into or unwinding various derivative transactions with respect to the common stock and/or by purchasing or selling the common stock or other securities of ours in secondary market transactions prior to the maturity of the Convertible Notes (and are likely to do so during the settlement averaging period under the capped call transactions, which precedes the maturity date of the Convertible Notes, and on or around any earlier conversion date related to a conversion of the Convertible Notes). The effect, if any, of any of these transactions and activities on the market price of our common stock or the Convertible Notes will depend in part on market conditions and cannot be ascertained at this time, but any of these activities could adversely affect the value of our common stock, which could affect the value of the Convertible Notes and the value of our common stock, if any, that the convertible noteholders receive upon any conversion of the Convertible Notes.

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.



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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.

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If the common stock issued as consideration in our recent acquisition of MiaMed is sold, such sales could cause our common stock price to decline.

The issuance of our common stock in connection with the MiaMed acquisition could have the effect of depressing the market price for our common stock, through dilution of earnings per share or otherwise. All of the shares of common stock issued to the former security holders of MiaMed in connection with the closing of the acquisition have been registered under the Securities Act of 1933, as amended (the "Securities Act"), pursuant to automatic shelf registration statements on Form S-3 (File No. 333-212414) and may now be resold by the former security holders of MiaMed to investors in the general market.

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, 2018.

Location	Approximate Square Feet	Use	Lease expiry date
Cranbury, New Jersey, USA	90,000	Office and laboratory	September 2025
United Kingdom	46,617	Office	August 2028
Princeton, New Jersey, USA	21,922	Office	January 2022

In addition to the above, we also maintain offices in Germany, Netherlands, Italy, Spain, France, Japan, Canada, Denmark, and Australia. 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.

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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 following table sets forth the range of high and low closing sales prices of our common stock as quoted on the NASDAQ Global Market for the periods indicated.

	High	Low
2018		
First Quarter	\$17.12	\$13.76
Second Quarter	\$17.09	\$13.13
Third Quarter	\$16.54	\$11.60
Fourth Quarter	\$13.44	\$8.38
	High	Low
2017		
First Quarter	\$7.79	\$5.13
Second Quarter	\$10.44	\$6.65
Third Quarter	\$15.78	\$10.08
Fourth Quarter	\$16.24	\$12.51

The closing price for our common stock as reported by the NASDAQ Global Market on February 15, 2019 was \$11.42 per share. As of February 15, 2019, there were 28 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, 2018 in transactions that were not registered under the Securities Act.

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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.

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, 2018. We have not announced any plans or programs for the repurchase of our common stock. However, employees surrendered 182,396 shares to the Company, during the year ended December 31, 2018 at a weighted average price of \$15.51 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.

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## Item 6. SELECTED FINANCIAL DATA

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

	2018	2017	2016	2015	2014
Revenue:					
Net product sales	\$91,245	\$36,930	\$4,958	—	—
Research revenue	—	—	—	—	1,224
Total revenue	91,245	36,930	4,958	—	1,224
Total cost of goods sold	14,404	6,236	833	—	—
Gross profit	76,841	30,694	4,125	—	1,224
Operating expenses:					
Research and development	270,902	149,310	104,793	76,943	47,624
Selling, general and administrative	127,200	88,671	71,151	47,269	20,717
Changes in fair value of contingent consideration payable	3,300	(234,322 )	6,760	4,377	100
Loss on impairment of assets	—	465,427	—	—	—
Restructuring charges	—	—	69	15	(63 )
Depreciation and amortization	4,216	3,593	3,242	1,833	1,547
Total operating expenses	405,618	472,679	186,015	130,437	69,925
Loss from operations	(328,777 )	(441,985 )	(181,890 )	(130,437 )	(68,701 )
Other income (expense):					
Interest income	10,461	4,096	1,602	929	223
Interest expense	(22,402 )	(17,240 )	(5,398 )	(1,578 )	(1,484 )
Change in fair value of derivatives	(2,739 )	—	—	—	—
Loss on extinguishment of debt	—	—	(13,302 )	(952 )	—
Other income (expense)	(5,632 )	6,008	(4,793 )	(80 )	(77 )
Loss before income tax	(349,089 )	(449,121 )	(203,781 )	(132,118 )	(70,039 )
Income tax benefit	94	165,119	3,739	—	1,113
Net loss attributable to common stockholders	\$(348,995 )	\$(284,002 )	\$(200,042 )	\$(132,118 )	\$(68,926 )
Net loss attributable to common stockholders per common share — basic and diluted	\$(1.88 )	\$(1.85 )	\$(1.49 )	\$(1.20 )	\$(0.93 )
Weighted-average common shares outstanding — basic and diluted	185,790	153,355	134,402	109,924	74,444

## Balance Sheet Data (in thousands)

	As of December 31,				
	2018	2017	2016	2015	2014
Cash and cash equivalents and marketable securities	\$504,152	\$358,562	\$330,351	\$214,033	\$169,139
Working capital	464,971	321,925	229,105	142,985	134,392
Total assets	789,951	627,024	1,036,845	908,384	209,967
Total liabilities	447,039	274,174	676,694	560,550	87,789
Accumulated deficit	(1,412,222 )	(1,063,610 )	(779,608 )	(579,566 )	(447,448 )
Total stockholders' equity	342,912	352,850	360,151	347,834	122,178

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

Overview

We are a global patient-dedicated biotechnology company engaged in the discovery, development and commercialization of a diverse set of novel treatments for patients living with rare metabolic diseases. With one medicine for Fabry disease achieving global approval, a differentiated biologic for Pompe disease in late-stage clinical development and fourteen gene therapy programs in the pipeline, including two clinical stage gene therapies for Batten disease, we have a leading portfolio of therapies for lysosomal storage disorders ("LSDs").

The cornerstone of our portfolio is Galafold<sup>®</sup>, (also referred to as "migalastat"), the first and only approved oral precision medicine for people living with Fabry disease who have amenable genetic variants, or mutations. Migalastat is currently approved under the trade name Galafold<sup>®</sup> in the United States ("U.S."), European Union ("EU") and Japan, with additional approvals granted and applications pending in several geographies. During the third quarter of 2018, we initiated the commercial launch of Galafold<sup>®</sup> in the U.S. for the treatment of adult patients with a confirmed diagnosis of Fabry disease and an amenable genetic variant.

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. Our Chaperone-Advanced Replacement Therapy ("CHARP<sup>®</sup>") platform technology is leveraged to combine our novel Pompe biologic ATB200 with a pharmacological chaperone AT2221.

During the second half of 2018, we expanded our portfolio to include fourteen new gene therapy programs. During the third quarter of 2018, we acquired worldwide development and commercial rights for ten gene therapy programs for neurologic LSDs developed at The Center for Gene Therapy at The Research Institute at Nationwide Children's Hospital ("NCH") and The Ohio State University through the acquisition of Celenex, Inc. ("Celenex"), a private, clinical stage gene therapy company, for cash consideration of \$100.0 million and additional consideration payable upon the achievement of certain development and approval milestones. The acquisition establishes Amicus as a leading company in neurologic LSDs. The lead programs in CLN6, CLN3, and CLN8 Batten disease are potential first-to-market curative therapies for these rare, devastating diseases.

In October 2018, we further expanded our gene therapy portfolio through a collaboration agreement with the Gene Therapy Program in the Perelman School of Medicine at the University of Pennsylvania ("Penn") to pursue the research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, cyclin-dependent kinase-like 5 ("CDKL5") deficiency disorder ("CDD") and one additional undisclosed rare metabolic disorder. This relationship will combine our protein engineering and glycobiology expertise with Penn's adeno associated virus ("AAV") gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability.

In February 2019, we announced that the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy Designation ("BTD") to AT-GAA in late onset Pompe disease. AT-GAA is the first ever investigational product for Pompe disease to receive BTD. The BTD will facilitate multidisciplinary, comprehensive discussions of the AT-GAA development program with the FDA, including planned clinical trials and plans for expediting manufacturing development strategy. The BTD for AT-GAA is based on clinical efficacy results from the ongoing ATB200-02 Phase 1/2 clinical study, including improvements in six-minute walk distance in late onset Pompe patients and comparison to natural history of treated patients.

We believe that our platform technologies and our product pipeline uniquely position us and drive our commitment to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases.

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 estimated expenses payable by us. There are no warrants or any equity conversion features associated with the Senior Secured Term Loan. The proceeds from this financing were used to support the cost of the Celenex acquisition, its related development costs



and other general corporate purposes. For additional information, see " —Note 12. Debt" in our Notes to Consolidated Financial Statements.

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During the first quarter of 2018, we issued 20,239,839 shares of our common stock through an underwritten offering resulting in net proceeds of \$294.6 million after deducting underwriting discounts and commissions and offering expenses payable by us. The net proceeds of the offering were used for investment in the U.S. and international commercial infrastructure for Galafold®, investment in manufacturing capabilities for the ERT ATB200, the continued clinical development of our product candidates, research and development expenditures, clinical and pre-clinical trial expenditures, commercialization expenditures and for other general corporate purposes. For additional information, see “—Note 9. Stockholders’ Equity” in our Notes to Consolidated Financial Statements.

## Consolidated Results of Operations

Year Ended December 31, 2018 Compared to Year Ended December 31, 2017

The following table provides selected financial information for the Company:

(in thousands)	Years Ended December 31,		
	2018	2017	Change
Net product sales	\$91,245	\$36,930	\$54,315
Cost of goods sold	14,404	6,236	8,168
Cost of goods sold as a percentage of net product sales	15.8	% 16.9	% (1.1 )%
Operating expenses:			
Research and development	270,902	149,310	121,592
Selling, general and administrative	127,200	88,671	38,529
Changes in fair value of contingent consideration payable	3,300	(234,322 )	237,622
Loss on impairment of asset	—	465,427	(465,427 )
Depreciation	4,216	3,593	623
Other income (expense):			
Interest income	10,461	4,096	6,365
Interest expense	(22,402 )	(17,240 )	(5,162 )
Change in fair value of derivatives	(2,739 )	—	(2,739 )
Other (expense) income	(5,632 )	6,008	(11,640 )
Income tax benefit	94	165,119	(165,025 )
Net loss attributable to common stockholders	\$(348,995)	\$(284,002)	\$(64,993)

**Net Product Sales.** Net product sales increased \$54.3 million during the year ended December 31, 2018 compared to the same period in the prior year. Galafold® was approved for sale in the EU in May 2016 and has been approved for pricing and reimbursement in 22 countries, including the U.S. and Japan, as well as in select other European markets through reimbursed EAPs. The increase in revenue was related to the increase in the number of markets where we had obtained pricing and reimbursements and the corresponding increase in the number of patients being treated with Galafold®.

**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 decreased to 15.8% during the year ended December 31, 2018 compared to 16.9% during the same period in the prior year primarily due to the proportion of sales in countries subject to a higher royalty burden.

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

(in thousands)	Years Ended	
	December 31,	
Projects	2018	2017
Third party direct project expenses		
Migalastat (Fabry Disease)	\$ 12,665	\$ 11,107
AT-GAA (Pompe Disease)	55,919	49,890
SD-101 (EB-Epidermolysis Bullosa)	337	15,424
Gene therapy programs	137	—
Pre-clinical programs	1,225	539
Total third party direct project expenses	70,283	76,960
Other project costs		
Personnel costs	62,999	50,095
Other costs	30,620	22,255
Total other project costs	93,619	72,350
Business development transactions	107,000	—
Total research and development costs	\$ 270,902	\$ 149,310

The increase in research and development costs was primarily due to \$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. There were also increases in personnel and other costs with the advancement and enrollment of clinical studies and investments in manufacturing. The decrease in costs related to the EB program was due to the discontinuation of the program after the results of a Phase 3 study that did not meet the primary endpoint in September 2017.

Selling, General and Administrative Expense. Selling, general and administrative increased \$38.5 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.

Changes in Fair Value of Contingent Consideration Payable. The change in the fair value of the contingent consideration payable of \$237.6 million resulted from a decrease in the Scioderm, Inc. ("Scioderm") contingent consideration of \$250.0 million, partially offset by an increase in the Callidus Biopharma, Inc. ("Callidus") contingent consideration of \$12.4 million. The change in the fair value of the contingent consideration payable of \$3.3 million is the unrealized change in fair value. The fair value and change in fair value are impacted by updates to the estimated probability of achievement, assumed timing of milestones and adjustments to the discount periods and rates. The decrease in Scioderm contingent consideration was due to the results announced in September 2017 that the study did not meet the primary or secondary endpoints, and, as a result, the contingent consideration is no longer payable.

Loss on Impairment of Assets. For the year ended December 31, 2017, we recorded \$465.4 million as impairment charges to assets, which primarily included \$463.7 million in IPR&D. The impairment was assessed after the announcement of the results from the Phase 3 ESSENCE Scioderm study. There was no similar event in 2018.

Interest Income. Interest income increased \$6.4 million due to the overall higher average cash and investment balances as a result of our financing transactions.



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Change in Fair Value of Derivatives. Subsequent to the underwritten public offering on February 15, 2018, we did not have sufficient unissued authorized shares to cover a conversion of the Convertible Notes. The fair value of the derivative liability for the conversion feature and derivative asset for the capped call transactions 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. Following the approval by our stockholders on June 7, 2018, to increase the authorized shares of common stock to 500,000,000, we now have 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. Subsequent changes to fair value of the derivatives were recorded through earnings on our consolidated statements of operations resulting in a change in fair value of derivatives for the year ended December 31, 2018 of \$2.7 million.

Other Expense. The \$11.6 million increase in other expense was primarily due to unrealized losses on foreign exchange transactions.

Income Tax Benefit. The income tax benefit recorded during the year ended December 31, 2018 was primarily related to a provision to return variances. We are subject to income taxes in the United States, although currently not a tax payer, and in various foreign jurisdictions, and our foreign tax liabilities are largely dependent upon the distribution of pre-tax earnings among these different jurisdictions. The income tax benefit for the year ended December 31, 2017 was \$165.1 million and was primarily due to the reduction of the deferred tax liability related to Scioderm IPR&D as a result of announcement of the Phase 3 ESSENCE Study in 2017.

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Year Ended December 31, 2017 Compared to Year Ended December 31, 2016

The following table provides selected financial information for the Company:

(in thousands)	Years Ended December 31,		
	2017	2016	Change
Net product sales	\$36,930	4,958	\$31,972
Cost of goods sold	6,236	833	5,403
Cost of goods sold as a percentage of net product sales	16.9	% 16.8	% 0.1
Operating expenses:			
Research and development	149,310	104,793	44,517
Selling, general and administrative	88,671	71,151	17,520
Changes in fair value of contingent consideration payable	(234,322)	6,760	(241,082)
Loss on impairment of asset	465,427	—	465,427
Restructuring charges	—	69	(69 )
Depreciation	3,593	3,242	351
Other income (expense):			
Interest income	4,096	1,602	2,494
Interest expense	(17,240 )	(5,398 )	(11,842 )
Change in fair value of derivatives	—	(13,302 )	13,302
Other income (expense)	6,008	(4,793 )	10,801
Income tax benefit	165,119	3,739	161,380
Net loss attributable to common stockholders	(284,002)	(200,042)	(83,960 )

**Net Product Sales.** Net product sales were \$36.9 million for Galafold® for the year ended December 31, 2017 as compared to \$5.0 million for the year ended December 31, 2016. Galafold® was approved for sale in the EU in May 2016 and was approved for pricing and reimbursement in 18 countries, as well as in select other European markets through reimbursed EAPs. We began to recognize revenue in the third quarter of 2016.

**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 sales was 16.9% for the year ended December 31, 2017 as compared to 16.8% for the year ended December 31, 2016.

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

(in thousands)	Years Ended	
	December 31,	
Projects	2017	2016
Third party direct project expenses		
Migalastat (Fabry Disease)	\$ 11,107	\$ 14,055
AT-GAA (Pompe Disease)	49,890	20,548
SD-101 (EB-Epidermolysis Bullosa)	15,424	9,530
Pre-clinical programs	539	6,939
Total third party direct project expenses	76,960	51,072
Other project costs		
Personnel costs	50,095	36,624
Other costs	22,255	17,097
Total other project costs	72,350	53,721
Total research and development costs	\$ 149,310	\$ 104,793

The increase in research and development costs was primarily due to increases in clinical research and manufacturing costs of \$25.9 million, due to the advancement and enrollment of clinical studies and investments in manufacturing, for Pompe of \$29.4 million and EB of \$5.9 million. Other increases were in personnel costs of \$13.5 million.

Selling, General and Administrative Expense. Selling, general and administrative expense was \$88.7 million in 2017, an increase of \$17.5 million or 24.6% from \$71.2 million in 2016. The increase in 2017 was primarily from efforts to support the ongoing commercial launch of Galafold®.

Changes in Fair Value of Contingent Consideration Payable. For the year ended December 31, 2017, we recorded a gain of \$234.3 million representing a change of \$241.1 million from the \$6.8 million of expense for the year ended December 31, 2016. The change in the fair value resulted from a decrease in the change attributable to the Scioderm contingent consideration of \$257.3 million and an increase in the change attributable to the Callidus contingent consideration of \$16.2 million. The fair value and change in fair value are impacted by updates to the estimated probability of achievement, assumed timing of milestones and adjustments to the discount periods and rates. The decrease in Scioderm contingent consideration was due to the results announced in September 2017 that the study did not meet the primary endpoints or secondary endpoints in participants, and, as a result, the contingent consideration is no longer payable.

Loss on Impairment of Assets. For the year ended December 31, 2017, we recorded \$465.4 million as impairment charges to assets, which primarily included \$463.7 million in IPR&D. The impairment was assessed after the announcement of the results from the Phase 3 ESSENCE study.

Depreciation. Depreciation expense was \$3.6 million in 2017, representing an increase of \$0.4 million as compared to \$3.2 million in 2016. Depreciation was higher due to increased asset acquisitions, resulting in a higher depreciation base in 2016.

Interest Income. Interest income was \$4.1 million for the year ended December 31, 2017, representing an increase of \$2.5 million from \$1.6 million for the year ended December 31, 2016. The increase in interest income was due to the overall higher average cash and investment balances as a result of our financing transactions.

Interest Expense. Interest expense was \$17.2 million in 2017 as compared to \$5.4 million in 2016. Interest expense in 2017 reflected a full year interest expense amount as compared to only a partial year interest expense amount in 2016 as the debt was secured in December 2016.

Loss from Extinguishment of Debt. For the year ended December 31, 2016, we recognized a non-cash loss of \$13.3 million arising from the early extinguishment of the \$80 million secured loan in the fourth quarter of 2016. There was no such event in the year ended December 31, 2017.





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Other Income (Expense). Other income was \$6.0 million for the year ended December 31, 2017 as compared to other expense of \$4.8 million for the year ended December 31, 2016. The increase was primarily due to unrealized gains on foreign exchange transactions.

Income Tax Benefit. For the year ended December 31, 2017, we recorded an income tax benefit of \$165.1 million, as compared to a benefit of \$3.7 million in 2016. The increase was primarily due to the reduction of the deferred tax liability of \$164.7 million related to Scioderm IPR&D as a result of the announcement of the Phase 3 ESSENCE study. We recorded an income tax benefit of \$2.7 million in the Consolidated Statement of Operations, in connection with the reduction in the statutory corporate income tax rate.

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### 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<sup>®</sup> for the treatment of Fabry disease. We have recorded revenue on sales where Galafold<sup>®</sup> is available either on a commercial basis or through a reimbursed EAP. Orders for Galafold<sup>®</sup> 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<sup>®</sup>. 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<sup>®</sup> are 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 amount received and we evaluate these estimates each reporting period to reflect known changes in factors.

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.

#### Inventories and Cost of Goods Sold

Until regulatory approval of Galafold<sup>®</sup>, we expensed all manufacturing costs of Galafold<sup>®</sup> as research and development expense. Upon regulatory approval, we began capitalizing costs related to the purchase and manufacture of Galafold<sup>®</sup>.

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

#### Research and Development Expenses

We expect to continue to incur substantial research and development expenses as we continue to develop our product candidates and explore new uses for our pharmacological chaperone technology. Research and development expense consists of:

- internal costs associated with our research and clinical development activities;

payments we make to third party contract research organizations, contract manufacturers, investigative sites, and consultants;

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• 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.

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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. Beginning in the third quarter of 2017, the average expected life was determined 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. In earlier quarters, we 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 historical analysis of actual option forfeitures.

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

The RSUs awarded 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. We only recognize expense for those shares that are expected to vest.

### Warrants

In October 2015, we entered into the October 2015 Purchase Agreement with Redmile Capital fund, LP and certain funds and accounts managed or advised by it (collectively referred to as "Redmile"), who beneficially owned approximately 6.7% of our common stock as of December 31, 2015, as set forth in the October 2015 Purchase Agreement, whereby we sold, on a private placement basis, (a) \$50.0 million aggregate principal amount of its unsecured promissory notes and (b) 1.3 million warrants that have a term of five-years. The warrants are classified as equity and included in stockholder's equity. The fair value of the warrants were initially measured at \$8.8 million using the Black-Scholes valuation model. In accordance with applicable guidance, we allocated the proceeds received based on the relative fair value of the notes and warrants, which resulted in \$10.6 million being recorded as a debt discount

On February 19, 2016, we entered into a Note and Warrant Purchase Agreement (the "February 2016 Purchase Agreement") with Redmile whereby we sold, on a private placement basis, (a) \$50 million aggregate principal amount of unsecured promissory notes and (b) five-year warrants to purchase up to 37 shares of our common stock for every \$1,000 of the principal amount of notes purchased by each purchaser, for an aggregate of up to 1,850,000 shares of common stock issuable under the warrants. We agreed with Redmile that in full consideration of the purchase price for the notes issued under the October 2015 Purchase Agreement, Redmile surrendered for cancellation all notes and warrants acquired from the October 2015 Purchase Agreement and we paid Redmile any unpaid interest accrued thereunder.

On June 30, 2016, following the marketing approval for Galafold® in Europe, we entered into a Joinder to and Amendment of Note and Warrant Purchase Agreement (the "Amended Purchase Agreement") with Redmile. Such amendment joined GCM Grosvenor Special Opportunities Master Fund, Ltd ("GCM") to the February 2016 Purchase Agreement. There were no changes to the previously issued debt. Pursuant to the Amended Purchase Agreement, we sold an additional \$30 million unsecured promissory notes and five year warrants to purchase up to 42 shares of the our common stock for every \$1,000 of the principal amount of additional Notes purchased, for an aggregate of up to 1,260,000 shares of common stock issuable under the additional warrants.

On December 15, 2016, we entered into a Note Purchase Agreement ("Note Purchase Agreement") with GCM and RedMile, pursuant to which we agreed to prepay all outstanding principal and accrued and unpaid interest on the notes issued by us and held by GCM and Redmile. Such prepayment was made in December, 2016, which resulted in a

non-cash loss of \$13.3 million and is included as loss on extinguishment in the Consolidated Statement of Operations for the year ended December 31, 2016. The Note Purchase Agreement did not cancel the warrants under the Amended Purchase Agreement described above.

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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.

### 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 year ended December 31, 2018.

### Valuation of Contingent Consideration Payable

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.

### Accrued Expenses

When we are required to estimate accrued expenses because we have not yet been invoiced or otherwise notified of actual cost, we identify services that have been performed on our behalf and estimate the level of service performed and the associated cost incurred. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

- fees owed to contract research organizations in connection with preclinical, toxicology studies and clinical trials;
- fees owed to investigative sites in connection with clinical trials;
- fees owed to contract manufacturers in connection with the production of clinical trial materials;





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fees owed for professional services, and  
unpaid salaries, wages and benefits.

### Liquidity and Capital Resources

As a result of our significant research and development expenditures as well as expenditures to build a commercial organization to support the launch of Galafold®, we have not been profitable and have generated operating losses since we were incorporated in 2002. We have historically funded our operations principally through the issuance and sale of stock, collaborations, debt financings, grants and non-refundable license fees.

#### Sources of Liquidity

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 estimated expenses payable by us. There are no warrants or any equity conversion features associated with the Senior Secured Term Loan. The proceeds from this financing will be used to support the cost of the Celenex acquisition, its related development costs and other general corporate purposes. 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, 20,239,839 shares of our common stock resulting in net proceeds of \$294.6 million after deducting underwriting discounts and commissions and offering expenses payable by us. We expect to use the net proceeds of the offering for investment in the U.S. and international commercial infrastructure for Galafold®, investment in manufacturing capabilities for ATB200, the continued clinical development of our product candidates, research and development expenditures, clinical and pre-clinical trial expenditures, commercialization expenditures and for other general corporate purposes. For additional information, see "—Note 9. Stockholders' Equity" in our Notes to Consolidated Financial Statements.

In July 2017, we entered into an underwriting agreement ("the Underwriting Agreement") with J.P. Morgan Securities LLC and Goldman Sachs & Co. LLC, as representatives of the several underwriters set forth on Schedule 1 thereto, relating to an underwritten public offering of our common stock (the "Offering"). Under the terms of the Underwriting Agreement, we issued and sold 21,122,449 shares at a price to the public of \$12.25 per share, resulting in gross proceeds of \$258.8 million, before deducting underwriting discounts and commissions and offering expenses payable by us. The Offering closed on July 18, 2017 and we received net proceeds from the Offering, after deducting underwriting discounts and commissions and offering expenses payable by us of \$243.0 million.

In December 2016, we issued \$250 million aggregate principal amount of 3.00% unsecured Convertible Notes due 2023 (the "Convertible Notes"), in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act (the "Note Offering"). 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 net proceeds from the Note Offering were \$243.0 million, after deducting fees and estimated expenses payable by us. We also used approximately \$13.5 million of the net proceeds from the Note Offering to pay the cost of the capped call transactions ("Capped Call Confirmations") that we entered into in connection with the Note Offering.

#### Cash flow discussion

As of December 31, 2018, we had cash and cash equivalents and marketable securities of \$504.2 million. We invest cash in excess of our immediate requirements with 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.

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### Net Cash Used in Operating Activities

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 used in operations for the year ended December 31, 2017 was \$213.7 million. The components of net cash used in operations included the net loss for the year ended December 31, 2017 of \$284.0 million, an increase in operating assets of \$24.7 million and decrease in deferred reimbursements of \$12.6 million. The increase in operating assets was primarily due to the change in prepaid and other current assets of \$15.3 million for spending to support commercial activities for Galafold<sup>®</sup> launch and a corresponding increase in accounts receivable by \$7.7 million due to commercial sales of Galafold<sup>®</sup>. The decrease in deferred reimbursements was due to milestone payments made to GSK. The net cash used in operations was partially offset by an increase in accounts payable and accrued expenses of \$12.6 million, mainly related to program expenses and support for the commercial launch of Galafold<sup>®</sup>.

### Net Cash Used in Investing Activities

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 and 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 used in investing activities for the year ended December 31, 2017 was \$171.2 million. Our investing activities have consisted primarily of purchases and sales and maturities of investments and capital expenditures. Net cash used in investing activities reflects \$490.5 million for the purchase of marketable securities, \$4.5 million for the acquisition of property and equipment, partially offset by \$323.8 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, 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 payable by us, \$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.

Net cash provided by financing activities for the year ended December 31, 2017 was \$247.4 million. Net cash provided by financing activities reflects \$243.0 million from issuance of common stock, \$16.3 million from the exercise of stock options, partially offset by \$10.0 million from contingent consideration payments, \$1.6 million from the purchase of vested RSUs and \$0.3 million from payments on capital lease arrangements.

### 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;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the significant cost of manufacturing Pompe ERT and gene therapies;

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the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of LSDs 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, including our ability to obtain regulatory approvals and commercialize CDKL5 therapies and obtain market acceptance for such therapies;

the costs, timing and outcome of regulatory 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;

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 and obtain milestone, royalty or other payments from any such collaborators;

our ability to adjust to changes in European and United Kingdom markets as the United Kingdom leaves the European Union; and

fluctuations in foreign currency exchange rates; and changes in accounting standards.

While we have generated revenue from product sales in 2018, 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 proceeds from the recent equity offering and expected Galafold® revenues, is sufficient to fund ongoing Fabry, Pompe and gene therapy program operations into at least mid-2021. 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 - 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 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.

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.

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**Penn** - 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 four additional indications, including Pompe disease, Fabry disease, CDD and one additional undisclosed rare metabolic disorder. Under this collaboration agreement, Penn is eligible to receive certain milestone and royalty 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.

**MSSM** - We acquired exclusive worldwide patent rights to develop and commercialize Galafold<sup>®</sup> and other pharmacological chaperones for the prevention or treatment of human diseases or clinical conditions by increasing the activity of wild-type and mutant enzymes pursuant to a license agreement with Mount Sinai School of Medicine ("MSSM"). This agreement expires upon expiration of the last of the licensed patent rights, which occurred in 2018 in the U.S. and will be in 2019 in Europe and Japan for monotherapy. If we develop a product for combination therapy of specific pharmacological chaperone such as Galafold<sup>®</sup> plus an ERT for certain LSDs such as Fabry disease and a patent issues from the pending MSSM applications covering such a combination therapy(ies), expiration for the combination product(s) will be 2024.

**GSK** - In November 2013, we entered into a Revised Agreement (the "Revised Agreement") with GlaxoSmithKline ("GSK"), pursuant to which we have 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 (the "Original Collaboration Agreement"). Under the terms of the Revised Agreement, there was no upfront payment from us 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 United States. In addition, because we reacquired worldwide rights to Galafold<sup>®</sup>, we are no longer eligible to receive any milestones or royalties we would have been eligible to receive under the Original Collaboration Agreement.

Under our license and collaboration agreements, if we owe royalties on net sales for one of our products to more than one of the above licensors, we have the right to reduce the royalties owed to one licensor for royalties paid to another. The amount of royalties to be offset is generally limited in each license and can vary under each agreement. For the year ended December 31, 2018, under the MSSM and GSK license and collaboration agreements, we paid \$7.6 million in royalties and \$1.3 million in sales-based milestones.

**Callidus** - As part of the acquisition of Callidus, we will be obligated to make additional payments to the former stockholders of Callidus upon the achievement by us of certain clinical milestones of up to \$35 million and regulatory approval milestones of up to \$80 million as set forth in the merger agreement. We may, at our election, satisfy certain milestone payments identified in the merger agreement aggregating \$40 million in shares of our common stock (calculated based on a price per share equal to the average of the last closing bid price per share for the common stock on The NASDAQ Global Select Market for the ten trading days immediately preceding the date of payment). The milestone payments not permitted to be satisfied in common stock (as well as any payments that we are permitted to, but choose not to, satisfy in common stock), as a result of the terms of the merger agreement, the rules of The NASDAQ Global Select Market, or otherwise, will be paid in cash. During the second quarter of 2016, we reached the first clinical milestone for Callidus, which was the dosing of the first patient in a Phase 1 or 2 study. The milestone payment for this event was \$6.0 million which was paid in our common stock during the second quarter of 2016. During the fourth quarter of 2018, we 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 our common stock during the first quarter of 2019.

**MiaMed** - As part of the acquisition of MiaMed, Inc. ("MiaMed"), we will be obligated to make additional payments to the former stockholders of MiaMed upon the achievement by us of certain clinical milestones of up to \$8 million,

regulatory approval milestones of up to \$10 million, and commercial milestones up to \$65 million. Any milestone payment may be satisfied in cash, shares of our common stock, or a combination of both. The milestone payments not permitted to be satisfied in common stock (as well as any payments that we are permitted to, but choose not to, satisfy in common stock), as a result of the terms of the merger agreement, the rules of The NASDAQ Global Select Market, or otherwise, will be paid in cash. No milestone payments in connection with the acquisition of MiaMed have been paid.

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## Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2018 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>	\$30,887	\$6,244	\$7,623	\$6,982	\$10,038
Capital lease obligations, including interest <sup>(3)</sup>	331	194	107	30	—
Debt obligations, including interest <sup>(4)</sup>	508,067	22,430	45,149	440,488	—
Purchase obligations <sup>(5)</sup>	47,287	47,287	—	—	—
Total fixed contractual obligations <sup>(1)</sup>	\$586,572	\$76,155	\$52,879	\$447,500	\$10,038

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>(1)</sup> Represents the future payments on operating leases for properties, equipment and vehicles at the United States and international locations. For more details, refer to "— Note 13. Leases," in our Notes to Consolidated Financial Statements.

<sup>(2)</sup> Represents the future payments of principal and interest to be made on our capital leases. 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 \$250 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.

<sup>(4)</sup> 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. In the first quarter of 2019, we converted a portion of the Convertible Notes into equity. For more details, refer to "— Note 12. Debt," in our Notes to Consolidated Financial Statements.

<sup>(5)</sup> Represent 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, 2018 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, 2018 and 2017.

## Recent Accounting Pronouncements

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

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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 \$1.7 million as of December 31, 2018. 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, 2018, we had \$150 million aggregate principal amount of variable rate debt through our Senior Secured Term Loan. We do not currently hedge our variable interest rate debt. The average variable interest rate for our variable rate debt as of December 31, 2018 was 10.13%. A hypothetical 100 basis point increase or decrease in the average interest rate on our variable rate debt would not result in a material change in the interest expense.

We have operated primarily in the U.S. with international operations increasing since the last quarter of 2015. We do conduct some clinical activities with vendors outside the U.S. While most expenses are paid in U.S. dollars, we now have increased transactions of expenses and cash flows in foreign currencies that are exposed to changes in foreign currency rates.



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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, 2018. 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, 2018, 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, 2018 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report. This report appears on the following page.

Dated February 28, 2019

/s/ JOHN F. CROWLEY

Chairman and Chief Executive Officer

/s/ DAPHNE QUIMI

Chief Financial Officer

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Report of Independent Registered Public Accounting Firm  
To the Stockholders and 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, 2018, 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 control over financial reporting as of December 31, 2018, 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, 2018 and 2017, 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, 2018, and the related notes and our report dated February 28, 2019 expressed an unqualified opinion thereon.

### Basis for Opinion

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

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

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

### Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

Iselin, New Jersey

February 28, 2019

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Report of Independent Registered Public Accounting Firm  
To the Stockholders and 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, 2018 and 2017, and 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, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company as of December 31, 2018 and 2017, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with US 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, 2018, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2019 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 these 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 US 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 include evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

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

Iselin, New Jersey

February 28, 2019

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Amicus Therapeutics, Inc.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	\$79,749	\$49,060
Investments in marketable securities	424,403	309,502
Accounts receivable	21,962	9,464
Inventories	8,390	4,623
Prepaid expenses and other current assets	16,592	19,316
Total current assets	551,096	391,965
Property and equipment, less accumulated depreciation of \$15,671 and \$12,515 at December 31, 2018 and 2017, respectively	11,375	9,062
In-process research & development	23,000	23,000
Goodwill	197,797	197,797
Other non-current assets	6,683	5,200
Total Assets	\$789,951	\$627,024
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable, accrued expenses, and other current liabilities	\$80,625	\$53,890
Deferred reimbursements	5,500	7,750
Contingent consideration payable	—	8,400
Total current liabilities	86,125	70,040
Deferred reimbursements	10,156	14,156
Convertible notes	175,006	164,167
Senior secured term loan	146,734	—
Contingent consideration payable	19,700	17,000
Deferred income taxes	6,465	6,465
Other non-current liabilities	2,853	2,346
Total Liabilities	447,039	274,174
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$.01 par value, 500,000,000 shares authorized, 189,383,924 shares issued and outstanding at December 31, 2018 Common stock, \$.01 par value, 250,000,000 shares authorized, 166,989,790 shares issued and outstanding at December 31, 2017	1,942	1,721
Additional paid-in capital	1,740,061	1,400,758
Accumulated other comprehensive loss:		
Foreign currency translation adjustment	495	(1,659 )
Unrealized loss on available-for securities	(427 )	(436 )
Warrants	13,063	16,076
Accumulated deficit	(1,412,222)	(1,063,610)
Total stockholders' equity	342,912	352,850
Total Liabilities and Stockholders' Equity	\$789,951	\$627,024
See accompanying notes to consolidated financial statements		

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Amicus Therapeutics, Inc.

Consolidated Statements of Operations

(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2018	2017	2016
Revenue:			
Net product sales	\$91,245	\$36,930	\$4,958
Cost of goods sold	14,404	6,236	833
Gross profit	76,841	30,694	4,125
Operating expenses:			
Research and development	270,902	149,310	104,793
Selling, general and administrative	127,200	88,671	71,151
Changes in fair value of contingent consideration payable	3,300	(234,322)	6,760
Loss on impairment of assets	—	465,427	—
Restructuring charges	—	—	69
Depreciation	4,216	3,593	3,242
Total operating expenses	405,618	472,679	186,015
Loss from operations	(328,777)	(441,985)	(181,890)
Other income (expenses):			
Interest income	10,461	4,096	1,602
Interest expense	(22,402)	(17,240)	(5,398)
Change in fair value of derivatives	(2,739)	—	—
Loss on extinguishment of debt	—	—	(13,302)
Other income (expense)	(5,632)	6,008	(4,793)
Loss before income tax	(349,089)	(449,121)	(203,781)
Income tax benefit	94	165,119	3,739
Net loss attributable to common stockholders	\$(348,995)	\$(284,002)	\$(200,042)
Net loss attributable to common stockholders per common share — basic and diluted	\$(1.88)	\$(1.85)	\$(1.49)
Weighted-average common shares outstanding — basic and diluted	185,790,021	153,355,144	134,401,588
See accompanying notes to consolidated financial statements			

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Amicus Therapeutics, Inc.

Consolidated Statements of Comprehensive Loss

(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2018	2017	2016
Net loss	\$ (348,995)	\$ (284,002)	\$ (200,042)
Other comprehensive gain (loss):			
Foreign currency translation adjustment gain (loss), net of tax impact of \$0, \$0, \$0, respectively	2,537	(3,604 )	1,945
Unrealized gain (loss) on available-for-sale securities	9	(538 )	217
Other comprehensive income (loss)	2,546	(4,142 )	2,162
Comprehensive loss	\$ (346,449)	\$ (288,144)	\$ (197,880)

See accompanying notes to consolidated financial statements

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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, 2015	125,027,034	1,306	917,454	8,755	(115 )	(579,566 )	347,834
Stock issued from exercise of stock options, net	723,102	7	3,029	—	—	—	3,036
Stock issued from ATM transactions	14,989,027	150	96,918	—	—	—	97,068
Stock issued for MiaMed acquisition	825,603	8	4,599	—	—	—	4,607
Restricted stock tax vesting	268,425	—	(1,282 )	—	—	—	(1,282 )
Stock issued for contingent consideration	858,795	9	6,106	—	—	—	6,115
Receivable from investor	—	—	932	—	—	—	932
Warrants issued in debt financing	—	—	—	7,321	—	—	7,321
Equity component of the Convertible Notes issuance, net of issuance costs of \$2,709	—	—	88,346	—	—	—	88,346
Premium paid for Capped Call Confirmations	—	—	(13,450 )	—	—	—	(13,450 )
Stock-based compensation	—	—	17,504	—	—	—	17,504
Unrealized holding gain on available-for-sale securities	—	—	—	—	217	—	217
Foreign currency translation adjustment	—	—	—	—	1,945	—	1,945
Net loss	—	—	—	—	—	(200,042 )	(200,042 )
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 gain 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 )



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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
See accompanying notes to consolidated financial statements							

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

	Years Ended December 31,		
	2018	2017	2016
Operating activities			
Net loss	\$(348,995)	\$(284,002)	\$(200,042)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of debt discount and deferred financing	10,976	9,703	2,689
Depreciation	4,216	3,593	3,242
Stock-based compensation	29,260	23,101	17,504
Restructuring charges	—	—	69
Change in fair value of derivatives	2,739	(265)	265
Non-cash changes in the fair value of contingent consideration payable	3,300	(234,322)	6,760
Charges to research expense for stock issued in asset acquisition	—	—	4,607
Loss on extinguishment of debt	—	—	13,302
Foreign currency remeasurement (gain) loss	3,217	(5,620)	3,660
Non-cash deferred taxes	—	(167,305)	(3,742)
(Gain) loss on disposal of assets	59	(8)	17
Loss on impairment	—	465,427	—
Changes in operating assets and liabilities:			
Accounts receivable	(13,294)	(7,725)	(1,419)
Inventories	(4,205)	(897)	(3,651)
Prepaid expenses and other current assets	2,488	(15,329)	(394)
Other non-current assets	(1,039)	(729)	(970)
Account payable and accrued expenses	17,115	12,563	7,131
Non-current liabilities	458	720	825
Deferred reimbursements	(6,250)	(12,600)	—
Net cash used in operating activities	(299,955)	(213,695)	(150,147)
Investing activities			
Sale and redemption of marketable securities	463,502	323,753	221,374
Purchases of marketable securities	(578,394)	(490,468)	(219,932)
Capital expenditures	(6,308)	(4,526)	(5,951)
Net cash used in investing activities	(121,200)	(171,241)	(4,509)
Financing activities			
Proceeds from issuance of common stock and warrants, net of issuance costs	294,584	243,037	97,068
Payments of secured loan agreement	—	—	(80,000)
Payment of capital leases	(334)	(308)	(193)
Purchase of vested restricted stock units	(2,832)	(1,596)	(1,282)
Proceeds from exercise of stock options	9,144	16,301	3,036
Proceeds from exercise of warrants	3,617	—	—
Payment of contingent consideration	—	(10,000)	(5,000)
Proceeds from issuance of convertible notes, net of issuance costs	—	—	242,536
Premiums paid for Capped Call Confirmations	—	—	(13,450)
Proceeds from loan agreements, net of issuance costs	146,596	—	30,000
Net cash provided by financing activities	450,775	247,434	272,715

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Effect of exchange rate changes on cash, cash equivalents and restricted cash	1,518	1,326	(131 )
Net increase (decrease) in cash and cash equivalents and restricted cash	31,138	(136,176)	117,928
Cash and cash equivalents and restricted cash at beginning of year/period	51,237	187,413	69,485
Cash and cash equivalents and restricted cash at end of year/period	\$82,375	\$51,237	\$187,413
Supplemental disclosures of cash flow information			
Cash paid during the period for interest	\$7,500	\$7,424	\$2,990
Contingent consideration paid in shares	\$—	\$—	\$6,115
Capital expenditures unpaid at the end of period	\$106	\$—	\$—
Capital expenditures funded by capital lease borrowings	\$208	\$—	\$944
See accompanying notes to consolidated financial statements			

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements

1. Description of Business

Amicus Therapeutics, Inc. (the “Company”) is a global patient-dedicated biotechnology company engaged in the discovery, development and commercialization of a diverse set of novel treatments for patients living with rare metabolic diseases. With one medicine for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease in the clinic and the recent addition of fourteen new gene therapy programs into the pipeline, including two clinical stage gene therapies for Batten disease, the Company has a leading portfolio of medicines for lysosomal storage disorders (“LSDs”).

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 (“EU”) and Japan, with additional approvals granted and applications pending in several other geographies. During the third quarter of 2018, the Company initiated the commercial launch of Galafold® in the U.S. for the treatment of adult patients with a confirmed diagnosis of Fabry disease and an amenable genetic variant.

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. The Company’s Chaperone-Advanced Replacement Therapy (“CHART”) platform technology is leveraged to develop novel products for Pompe disease and potentially future other LSDs.

During the second half of 2018, the Company has expanded its portfolio to include fourteen new gene therapy programs. In September 2018, the Company acquired worldwide development and commercial rights for ten gene therapy programs for neurologic LSDs developed at The Center for Gene Therapy at The Research Institute at Nationwide Children’s Hospital and The Ohio State University through the acquisition of Celenex, Inc., (“Celenex”) a private, clinical stage gene therapy company, for cash consideration of \$100.0 million and additional consideration payable upon the achievement of certain development and approval milestones. The acquisition establishes the Company as a leading company in neurologic LSDs. The lead programs in CLN6, CLN3, and CLN8 Batten disease are potential first-to-market curative therapies for these rare, devastating diseases. For additional information see “—Note 3. Acquisitions.”

In October 2018, the Company further expanded its gene therapy portfolio through a collaboration agreement with the Gene Therapy Program in the Perelman School of Medicine at the University of Pennsylvania (“Penn”) to pursue the research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, CDKL5 deficiency disorder (“CDD”) and one additional undisclosed rare metabolic disorder. This relationship will combine the Company’s protein engineering and glycobiology expertise with Penn’s adeno associated virus (“AAV”) gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability.

The Company believes that its platform technologies and its product pipeline uniquely positions it and drives its commitment to advancing and expanding a robust pipeline of cutting-edge, first- or best-in-class medicines for rare metabolic diseases.

During the third quarter of 2018, the Company 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. The Company received net proceeds of \$146.6 million in September 2018, after deducting fees and estimated expenses payable by the Company. There are no warrants or any equity conversion features associated with the Senior Secured Term Loan. The proceeds from this financing were used to support the cost of the Celenex acquisition, its related development costs and other general corporate purposes. For additional information, see “—Note 12. Debt.”

During the first quarter of 2018, the Company issued 20,239,839 shares of its common stock through an underwritten offering resulting in net proceeds of \$294.6 million after deducting underwriting discounts and commissions and offering expenses payable by the Company. The Company expects to use the net proceeds of the offering for

investment in the U.S. and international commercial infrastructure for Galafold<sup>®</sup>, investment in manufacturing capabilities for the ERT ATB200, the continued clinical development of its product candidates, research and development expenditures, clinical and pre-clinical trial expenditures, commercialization expenditures and for other general corporate purposes. For additional information, see “—Note 9. Stockholders’ Equity.”

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

The Company had an accumulated deficit of approximately \$1.4 billion as of December 31, 2018 and anticipates incurring losses through the fiscal year ending December 31, 2019 and beyond. The Company has been able to fund its operating losses to date through stock offerings, debt issuances, payments from partners during the terms of the collaboration agreements, and other financing arrangements.

The current cash position, including expected Galafold<sup>®</sup> revenues, is sufficient to fund ongoing Fabry, Pompe and gene therapy program operations into at least mid-2021. 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 accompanying consolidated financial statements have been prepared 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.

Reclassification

Certain prior year amounts have been reclassified for comparative purposes. The reclassifications did not affect results of operations, net assets or cash flows.

Cash, Cash Equivalents, Restricted Cash and Marketable Securities

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 sheet. 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 sheet.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and 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 cash and cash equivalents or its 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, 2018 have arisen from product sales primarily in the EU and the United States. 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. To date, the Company has not incurred any credit losses.

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.

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 Company elected the portfolio approach practical expedient in applying ASC Topic 606, Revenue from Contracts with Customers, to its identified revenue streams. Contracts within each revenue stream have similar characteristics and the Company believes this approach would not differ materially from applying ASC Topic 606 to each individual contract.

Inventories and Cost of Goods Sold

Prior to regulatory approval of Galafold®, the Company expensed all manufacturing costs related to Galafold® as research and development expense. Upon regulatory approval, the Company began capitalizing costs related to the purchase and manufacture of Galafold®.

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.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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

**Fair Value Measurements**

The Company records certain asset and liability balances under the fair value measurements as defined by the 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 consists 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 and cash equivalents and marketable securities. Interest expense consists of interest incurred on debt and capital leases.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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

In the ordinary course of business, the Company enters into lease agreements for office space as well as leases for certain property and equipment. The leases have varying terms and expirations and have provisions to extend or renew the lease agreement, among other terms and conditions, as negotiated. Once the agreement is executed, the lease is assessed to determine whether the lease qualifies as a capital or operating lease.

When a non-cancelable operating lease includes any fixed escalation clauses and lease incentives for rent holidays or build-out contributions, rent expense is recognized on a straight-line basis over the initial term of the lease. The excess between the average rental amount charged to expense and amounts payable under the lease is recorded in accrued expenses.

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, 2018, 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.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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

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.

Recent Accounting Developments - Guidance Adopted in 2018

ASU 2018-07 - In June 2018, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Non-employee Share-Based Payment Accounting ("ASU 2018-07"). These amendments expand the scope of Topic 718, Compensation-Stock Compensation (which currently only includes share-based payments to employees) to include share-based payments issued to non-employees for goods or services. Consequently, the accounting for share-based payments to non-employees and employees will be substantially aligned. ASU 2018-07 supersedes Subtopic 505-50, Equity-Equity-Based Payments to Non-Employees, and is effective for all public entities for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. Early adoption is permitted, but no earlier than a company's adoption date of Topic 606, Revenue from Contracts with Customers. The Company early adopted ASU 2018-07 in the second quarter of 2018 and there was no material impact on its consolidated financial statements from the adoption.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

ASU 2018-02 - In February 2018, the FASB issued ASU 2018-02, Income Statement - Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income (“ASU 2018-02”). Prior to ASU 2018-02, U.S. GAAP required the remeasurement of deferred tax assets and liabilities as a result of a change in tax laws or rates to be presented in net income from continuing operations, even in situations in which the related income tax effects of items in accumulated other comprehensive income were originally recognized in other comprehensive income. As a result, such items, referred to as stranded tax effects, did not reflect the appropriate tax rate. Under ASU 2018-02, entities are permitted, but not required, to reclassify from accumulated other comprehensive income to retained earnings those stranded tax effects resulting from the Tax Cuts and Jobs Act of 2017. ASU 2018-02 is effective for all entities for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years. Early adoption is permitted. The Company adopted the new standard effective January 1, 2018. As a result of the adoption, the Company reclassified a gain of \$383,000 from the foreign currency translation adjustment in accumulated other comprehensive loss to accumulated deficit in the consolidated balance sheet as of December 31, 2018.

ASU 2017-09 - In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting (“ASU 2017-09”). The amendments in ASU 2017-09 provide guidance on determining which changes to the terms and conditions of share-based payment awards require an entity to apply modification accounting under ASU 2017-09. An entity should account for the effects of a modification unless all the following are met: (1) The fair value (or calculated value or intrinsic value, if such an alternative measurement method is used) of the modified award is the same as the fair value (or calculated value or intrinsic value, if such an alternative measurement method is used) of the original award immediately before the original award is modified. If the modification does not affect any of the inputs to the valuation technique that the entity uses to value the award, the entity is not required to estimate the value immediately before and after the modification; (2) The vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified; and (3) The classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. ASU 2017-09 is effective for all entities for annual periods, including interim periods within those annual periods, beginning after December 15, 2017. The Company adopted this standard on January 1, 2018 and the adoption did not have a material impact on its consolidated financial statements.

ASU 2017-01 - In January 2017, the FASB issued ASU 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business (“ASU 2017-01”). This ASU clarifies the definition of a business. The amendments affect all companies and other reporting organizations that must determine whether they have acquired or sold a business. The amendments in ASU 2017-01 are effective for public companies for annual periods beginning after December 15, 2017, including interim periods within those periods. The amendments should be applied prospectively as of the beginning of the period of adoption. The Company adopted ASU 2017-01 on January 1, 2018. The adoption of the standard did not have a material impact on its consolidated financial statements. For additional information see “—Note 3. Acquisitions.”

ASU 2016-18 - In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash (“ASU 2016-18”). The amendments of ASU 2016-18 require an entity to include amounts generally described as restricted cash and restricted cash equivalents with cash and cash equivalents when reconciling the beginning of period and end of period total amounts on the statement of cash flows. The amendments of ASU 2016-18 are effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual periods. The Company adopted the guidance in ASU 2016-18 effective January 1, 2018. In connection with the adoption of the standard, the Company applied the guidance retrospectively which resulted in an increase in cash flows from operations of \$1.8 million on the statement of cash flows for the year ended December 31, 2017.

ASU 2016-16 - In October 2016, the FASB issued ASU 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other Than Inventory (“ASU 2016-16”). ASU 2016-16 requires an entity to recognize the income tax consequences of an intra-entity transfer of an asset other than inventory when the transfer occurs. The amendments eliminate the exception for an intra-entity transfer of an asset other than inventory. The amendments in ASU 2016-16 are effective for public business entities for annual periods beginning after December 15, 2017, including interim reporting periods within those annual reporting periods. The Company adopted ASU 2016-16 on January 1, 2018 and there was no material impact from the adoption.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

ASU 2016-01 - In January 2016, the FASB issued ASU No. 2016-01, Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities (“ASU 2016-01”). ASU 2016-01 changes accounting for equity investments, financial liabilities under the fair value option, and presentation and disclosure requirements for financial instruments. ASU 2016-01 does not apply to equity investments in consolidated subsidiaries or those accounted for under the equity method of accounting. In addition, the FASB clarified guidance related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. Equity investments with readily determinable fair values will be measured at fair value with changes in fair value recognized in net income. Companies have the option to measure equity investments without readily determinable fair values at either fair value or at cost adjusted for changes in observable prices minus impairment. Companies that elect the fair value option for financial liabilities must recognize changes in fair value related to instrument-specific credit risk in other comprehensive income. Companies must assess valuation allowances for deferred tax assets related to available-for-sale debt securities in combination with their other deferred tax assets. ASU 2016-01 is effective beginning in the first quarter of 2018 and the Company adopted it in the first quarter of 2018. There was no impact on the Company’s consolidated financial statements and related disclosures upon adoption, as the Company does not have equity investments or liabilities with credit risk. In addition, the guidance relating to deferred tax assets did not result in a change in accounting treatment for the Company.

ASU 2014-09 - In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606) which along with amendments issued in 2015 and 2016, replaced substantially all current U.S. GAAP guidance on this topic and eliminated industry-specific guidance. The new revenue recognition standard requires entities to recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. Effective January 1, 2018, the Company adopted the new revenue recognition standard using the modified retrospective approach and applied this approach only to contracts that were not completed as of January 1, 2018. The timing of revenue recognition and treatment of contract costs remains unchanged under the new revenue recognition standard. As such, the adoption of the new revenue recognition standard did not have a material impact on the Company's consolidated financial statements. The information presented for the periods prior to January 1, 2018 has not been restated and is reported under the accounting standard in effect for those periods.

Recent Accounting Developments - Guidance Not Yet Adopted

In August 2018, the Securities Exchange Commission (“SEC”) issued Final Rule 33-10532, Disclosure Update and Simplification, which amends certain disclosure requirements that were redundant, duplicative, overlapping or superseded by other SEC disclosure requirements. The amendments generally eliminated or otherwise reduced certain disclosure requirements of various SEC rules and regulations. However, in some cases, the amendments require additional information to be disclosed, including changes in stockholders’ equity in interim periods. The rule is effective 30 days after its publication in the Federal Register. The rule was posted on October 4, 2018. On September 25, 2018, the SEC released guidance advising it will not object to a registrant adopting the requirement to include changes in stockholders’ equity in the Form 10-Q for the first quarter beginning after the effective date of the rule. The Company is currently assessing the impact that this standard will have on its consolidated financial statements upon adoption and expects to adopt the guidance in its Form 10-Q for the period ended March 31, 2019.

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 changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and 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. Early adoption is permitted. An entity is permitted to early adopt any removed or modified disclosures upon issuance of ASU 2018-13 and delay adoption of the additional disclosures until their effective date. The Company is currently assessing the impact that this standard will have on its consolidated financial statements upon adoption.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

ASU 2017-08 - In March 2017, the FASB issued ASU 2017-08, Receivables-Nonrefundable Fees and Other Costs (Subtopic 310-20), Premium Amortization on Purchased Callable Debt Securities (“ASU 2017-08”). The amendments in ASU 2017-08 shorten the amortization period for certain callable debt securities held at a premium. Specifically, the amendments require the premium to be amortized to the earliest call date. The amendments do not require an accounting change for securities held at a discount; the discount continues to be amortized to maturity. ASU 2017-08 is effective for public business entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018. Early adoption is permitted, including adoption in an interim period. If an entity early adopts in an interim period, any adjustments should be reflected as of the beginning of the fiscal year that includes that interim period. The amendments should be applied on a modified retrospective basis, with a cumulative-effect adjustment directly to retained earnings as of the beginning of the period of adoption. The Company is currently assessing the impact that this standard will have on its consolidated financial statements.

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”). To simplify the subsequent measurement of goodwill, ASU 2017-04 eliminates Step 2 from the goodwill impairment test. The annual, or interim, goodwill impairment test is performed by comparing the fair value of a reporting unit with its carrying amount. An impairment charge should be recognized for the amount by which the carrying amount exceeds the reporting unit’s fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. In addition, income tax effects from any tax deductible goodwill on the carrying amount of the reporting unit should be considered when measuring the goodwill impairment loss, if applicable. ASU 2017-04 also eliminates the requirements for any reporting unit with a zero or negative carrying amount to perform a qualitative assessment and, if it fails that qualitative test, to perform Step 2 of the goodwill impairment test. An entity still has the option to perform the qualitative assessment for a reporting unit to determine if the quantitative impairment test is necessary. ASU 2017-04 should be applied on a prospective basis. The nature of and reason for the change in accounting principle should be disclosed upon transition. A public business entity that is a U.S. SEC filer should adopt ASU 2017-04 for its annual or any interim goodwill impairment tests in fiscal years beginning after December 15, 2019. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. The Company is currently assessing the impact that this standard will have on its consolidated financial statements.

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. ASU 2016-02 will be effective for the Company for all annual and interim periods beginning after December 15, 2018, including interim periods within those fiscal years. In August 2018, the FASB issued ASU 2018-11, Leases (Topic 842): Targeted Improvements, (“ASU 2018-11”). ASU 2018-11 provide 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. The Company will adopt these standards effective January 1, 2019 and elect the transition method in ASU 2018-11. The Company will also elect certain of the practical expedients permitted, including the expedient that permits the Company to retain its existing lease assessment and classification. The Company is currently working through an adoption plan which includes the evaluation of lease contracts compared to the new standard and estimates that the impact that this standard will have on its consolidated financial statements will be an increase to lease liabilities and right-of-use assets of approximately \$15 million to \$18 million.





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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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. 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. The associated impairment of Scioderm IPR&D is discussed in "— Note 4. Goodwill and Intangible Assets."

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

The Company was previously developing SD-101 in late-stage development as a potential first-to-market therapy for the chronic, rare connective tissue disorder Epidermolysis Bullosa ("EB"). On September 13, 2017, the Company reported that top-line data from the randomized, double-blind, placebo-controlled Phase 3 clinical study ("ESSENCE" or "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. The Company plans to further analyze and share the Phase 3 ESSENCE results with key stakeholders in the EB community including physicians, patient organizations and regulators. In the interim, in consultation with their physicians, participants in the ongoing extension studies (SD-004 and -006) will have the opportunity to continue being treated with SD-101. Based on the 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 has 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 a privately-held biologics company focused on developing best-in-class ERTs for LSDs with its lead ERT ATB200 for Pompe disease in late preclinical development. The acquisition of the Callidus assets and technology complements Amicus' CHART® platform for the development of next generation ERTs.

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 \$28.7 million at December 31, 2018, of which \$9.0 million is payable over the next twelve months and \$19.7 million 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, 2018. 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.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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, 2018 and 2017, respectively:

	(in millions)
Beginning balance	\$ 486.7
Impairment in IPR&D related to Scioderm	(463.7 )
Balance at December 31, 2017	\$ 23.0
Change in IPR&D	—
Balance at December 31, 2018	\$ 23.0

The following table represents the changes in Goodwill for the years ended December 31, 2018 and 2017, respectively:

	(in millions)
Beginning balance	\$ 197.8
Change in goodwill	—
Balance at December 31, 2017	\$ 197.8
Change in goodwill	—
Balance at December 31, 2018	\$ 197.8

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

As of December 31, 2018, the Company held \$79.7 million in cash and cash equivalents and \$424.4 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, while investments that have maturities greater than one year are classified as long-term.

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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, 2018			
	Cost	Unrealized Gain	Unrealized Loss	Fair Value
Cash and cash equivalents	\$79,749	\$ —	\$ —	\$79,749
Corporate debt securities, current portion	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
Certificate of deposit	51	—	—	51
	\$504,579	\$ 11	\$ (438)	) \$504,152
Included in cash and cash equivalents	\$79,749	\$ —	\$ —	\$79,749
Included in marketable securities, current	424,830	11	(438)	) 424,403
Total cash, cash equivalents and marketable securities	\$504,579	\$ 11	\$ (438)	) \$504,152

(in thousands)	As of December 31, 2017			
	Cost	Unrealized Gain	Unrealized Loss	Fair Value
Cash and cash equivalents	\$49,060	\$ —	\$ —	\$49,060
Corporate debt securities, current portion	199,314	1	(303)	) 199,012
Commercial paper	79,878	—	(75)	) 79,803
Asset-backed securities	30,346	—	(59)	) 30,287
Money market	350	—	—	350
Certificate of deposit	50	—	—	50
	\$358,998	\$ 1	\$ (437)	) \$358,562
Included in cash and cash equivalents	\$49,060	\$ —	\$ —	\$49,060
Included in marketable securities, current	309,938	1	(437)	) 309,502
Total cash, cash equivalents and marketable securities	\$358,998	\$ 1	\$ (437)	) \$358,562

For the years ended December 31, 2018 there were nominal realized gains. For the fiscal year ended December 31, 2017, there were no realized gains or losses. 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, 2018 and December 31, 2017 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 \$403.1 million and \$295.1 million as of December 31, 2018 and 2017, respectively.

The following table provides a reconciliation of cash and cash equivalents, and restricted cash reported within the consolidated balance sheet that sum to the total of the same such amounts shown in the Statement of Cash Flows:

(in thousands)	December 31, 2018	December 31, 2017	December 31, 2016
Cash and cash equivalents	\$79,749	\$49,060	\$187,026
Restricted cash	2,626	2,177	387
Cash and cash equivalents and restricted cash shown in the statement of cash flows	\$82,375	\$51,237	\$187,413

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

## 6. Inventories

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

(in thousands)	December	
	31, 2018	31, 2017
Raw materials	\$ 1,291	\$ 2,393
Work-in-process	3,485	1,450
Finished goods	3,614	780
Total inventories	\$ 8,390	\$ 4,623

The Company recorded a reserve for inventory of \$0.2 million of December 31, 2018. There was no reserve as of December 31, 2017.

## 7. Property and Equipment

Property and equipment consist of the following:

(in thousands)	December 31,	
	2018	2017
Property and equipment consist of the following:		
Computer equipment	\$4,691	\$3,746
Computer software	1,298	1,236
Research equipment	8,445	6,379
Furniture and fixtures	4,876	2,992
Leasehold improvements	7,425	7,193
Vehicles	209	—
Construction in progress	102	31
Gross property and equipment	27,046	21,577
Less accumulated depreciation	(15,671 )	(12,515)
Net property and equipment	\$11,375	\$9,062

Depreciation expense was \$4.2 million and \$3.6 million for the years ended December 31, 2018 and 2017, respectively, and includes depreciation expenses related to capital lease obligations.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

## 8. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

(in thousands)	December 31,	
	2018	2017
Accounts payable	\$6,606	\$7,867
Accrued professional fees	2,276	5,845
Accrued contract manufacturing & contract research costs	5,890	4,632
Accrued compensation and benefits	21,731	19,620
Accrued facility costs	2,102	1,665
Accrued program fees	16,674	5,707
Royalties payable	4,463	2,529
Accrued interest	4,189	313
Milestone payments	9,000	—
Accrued sales rebates and discounts	3,636	1,957
Other	4,058	3,755
	\$80,625	\$53,890

## 9. Stockholders' Equity

## Common Stock and Warrants

As of December 31, 2018, 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.

On February 15, 2018, the Company announced the pricing of an underwritten offering of 19,354,839 shares of its common stock at \$15.50 per share, resulting in gross proceeds of \$300.0 million. 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 2,903,225 shares of the Company's common stock, which was exercised with respect to 885,000 shares of the Company's common stock at a purchase price of \$15.50 per share. The Company received net proceeds of \$294.6 million from these offerings, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

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.

On June 7, 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 250,000,000 shares to 500,000,000 shares.

In July 2017, the Company entered into an underwriting agreement whereby the Company issued and sold 21,122,449 shares at a price to the public of \$12.25 per share, resulting in gross proceeds of \$258.8 million, before deducting underwriting discounts and commissions and offering expenses payable by the Company. The offering closed on July 18, 2017 and the Company received net proceeds, after deducting underwriting discounts and commissions and offering expenses payable by the Company of \$243.0 million.



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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

As discussed in “— Note 12. Debt”, in December 2016, the Company issued \$250 million aggregate principal amount of 3.0% unsecured Convertible Senior Notes due 2023 (the “Convertible Notes”), in a private offering. The Notes will mature on December 15, 2023, unless earlier repurchased, redeemed, or converted in accordance with their terms. The 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 (“common stock”), or a combination thereof. Prior to the close of business on the business day immediately preceding September 15, 2023, the Notes are convertible at the option of the holders of the Notes only under certain conditions. On or after September 15, 2023, until the close of business on the second business day immediately preceding the maturity date, holders of the Notes may convert their Notes at their option at the conversion rate then in effect, irrespective of these conditions. The Company will settle conversions of the Notes by paying or delivering, as the case may be, cash, shares of common stock, or a combination of cash and shares of common stock, at the Company’s election. The conversion rate will initially be 163.3987 shares of common stock per \$1,000 principal amount of Notes (equivalent to an initial conversion price of approximately \$6.12 per share of common stock). The conversion rate is subject to customary adjustments upon the occurrence of certain events.

During the first quarter of 2019, the Company entered into separate, privately negotiated exchange agreements with a limited number of holders (the “Holders”) of the Convertible Notes. Under the terms of the exchange agreements (the “Exchange Agreements”), the Holders agreed to exchange an aggregate principal amount of approximately \$184.6 million of Convertible Notes held by them in exchange for an aggregate of approximately 33.0 million shares of the our common stock, par value \$0.01 per share. In addition, pursuant to the Exchange Agreements, the Company made aggregate cash payments of approximately \$0.7 million to the Holders to satisfy accrued and unpaid interest to the closing date of the transaction, along with cash in lieu of fractional shares.

**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 \$2.7 million and \$2.2 million as of December 31, 2018 and 2017, 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, 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

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, 2018, the Company has reserved up to 9,457,741 shares for issuance under the Plan and the 2007 Director Plan.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

10. Share based Compensation

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 units and options to purchase common stock in the Company to employees, 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 adopted 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 was 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,		
	2018	2017	2016
Expected stock price volatility	78.6 %	82.8 %	81.3 %
Risk free interest rate	2.4 %	2.0 %	1.5 %
Expected life of options (years)	5.62	6.18	6.25
Expected annual dividend per share	\$0.00	\$0.00	\$0.00

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Notes To Consolidated Financial Statements — (Continued)

The weighted average grant-date fair value per share of options granted during 2018, 2017 and 2016 were \$10.19, \$5.09 and \$5.28, respectively.

A summary of the Company's stock options for the year ended December 31, 2018 were as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value
	(in thousands)			(in millions)
Options outstanding, December 31, 2015	11,729.2	\$ 7.11		
Granted	5,114.1	\$ 7.67		
Exercised	(723.1 )	\$ 4.20		
Forfeited	(622.7 )	\$ 8.62		
Options outstanding, December 31, 2016	15,497.5	\$ 7.37		
Granted	3,695.3	\$ 7.17		
Exercised	(2,878.7 )	\$ 5.67		
Forfeited	(1,133.0 )	\$ 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	(8.0 )	10.76		
Options outstanding, December 31, 2018	15,810.0	\$ 8.63	6.7 years	\$ 37.6
Vested and unvested expected to vest, December 31, 2018	15,152.6	\$ 8.51	6.6 years	\$ 36.8
Exercisable at December 31, 2018	9,977.0	\$ 7.43	5.8 years	\$ 28.8

The aggregate intrinsic value of options exercised during the years ended December 31, 2018, 2017 and 2016 was \$11.9 million, \$20.8 million and \$2.6 million respectively. Cash proceeds from stock options exercised during the years ended December 31, 2018, 2017 and 2016 were \$9.1 million, \$16.3 million, and \$3.0 million, respectively. As of December 31, 2018, the total unrecognized compensation cost related to non-vested stock options granted was \$33.3 million and is expected to be recognized over a weighted average period of 2.4 years.

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Notes To Consolidated Financial Statements — (Continued)

## Restricted Stock Units (“RSUs”) and Performance-Based Restricted Stock Units

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, 2018 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, 2016	744.4	\$ 7.86		
Granted	2,348.7	\$ 5.69		
Vested	(318.2 )	\$ 9.23		
Forfeited	(199.8 )	\$ 6.24		
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	2.57	\$ 36.3

On December 30, 2016, the Compensation Committee approved a form of Performance-Based Restricted Stock Unit Award Agreement (the “Performance-Based RSU Agreement”), to be used for performance-based RSUs granted to participants under the Amended and Restated 2007 Equity Incentive Plan, including named executive officers. Certain awards under the Performance- Based RSU Agreement were granted in January 2017 and 2018. The grants include performance-based restricted stock units and market performance-based restricted stock units (“MPRSUs”). The performance-based awards vest over three years based on the Company achieving certain clinical milestones. Each reporting period the Company estimates the amount of the award that will vest based on the probability of achieving the clinical milestones and adjusts the expense, prospectively, when a change occurs. For the MPRSUs, vesting of these awards is contingent upon the Company meeting certain total shareholder return (“TSR”) levels as compared to a select peer group over three years. The MPRSUs cliff vest at the end of the three-year period and have a maximum potential to vest at 200% based on TSR performance. 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, irrespective of the actual TSR performance. The estimated fair value per share of the MPRSUs was calculated using a Monte Carlo simulation model.

For the year ended December 31, 2018, 530,035 RSUs have vested and all non-vested units are expected to vest over their normal term. As of December 31, 2018, there was \$25.8 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 2.5 years.

## Compensation Expense Related to Equity Awards

The following table summarizes information related to compensation expense recognized in the statements of operations related to the equity awards:

	Years Ended		
	December 31,		
	2018	2017	2016
Equity compensation expense recognized in:			
Research and development expense	\$11,740	\$10,328	\$8,071
Selling, general and administrative expense	17,520	12,773	9,433
Total equity compensation expense	\$29,260	\$23,101	\$17,504

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Notes To Consolidated Financial Statements — (Continued)

## 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.

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		
Assets:				
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		
	\$427,084	\$427,084		
			Level 2	Level 3
				Total
Liabilities:				
Contingent consideration payable	\$—	\$19,700	\$19,700	
Deferred compensation plan liability	2,732	—	2,732	
	\$2,732	\$19,700	\$22,432	

A summary of the fair value of the Company's assets and liabilities aggregated by the level in the fair value hierarchy within which those measurements fall as of December 31, 2017 are identified in the following table:

(in thousands)	Level 2	Total		
Assets:				
Commercial paper	\$79,803	\$79,803		
Asset-back securities	30,287	30,287		
Corporate debt securities	199,012	199,012		
Money market funds	2,598	2,598		
	\$311,700	\$311,700		
			Level 2	Level 3
				Total
Liabilities:				
Contingent consideration payable	\$—	\$25,400	\$25,400	
Deferred compensation plan liability	2,258	—	2,258	
	\$2,258	\$25,400	\$27,658	



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Notes To Consolidated Financial Statements — (Continued)

The Company's Convertible Notes are classified in 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 debt at December 31, 2018 was approximately \$437.1 million.

The Company's Senior Secured Term Loan are classified in 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, 2018 or December 31, 2017.

Cash, Money Market Funds and Marketable Securities

The Company classifies its cash and money market funds within the fair value hierarchy as Level 1 as these assets are valued using quoted prices in active market for identical assets at the measurement date. The Company considers its investments in marketable securities as available for sale and classifies these assets within the fair value hierarchy as Level 2 primarily utilizing broker quotes in a non-active market for valuation of these securities. No changes in valuation techniques or inputs occurred during the year ended December 31, 2018. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2018.

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 statement 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, including expenses related to CDD.

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

Contingent Consideration Liability	Fair value as of December 31, 2018	Valuation Technique	Unobservable Input	Range
Clinical and regulatory milestones	\$19.2 million	Probability weighted discounted cash flow	Discount rate Probability of achievement of milestones Projected year of payments	10% 71.0% - 100.0% 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.



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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

The following table shows the change in the balance of contingent consideration payable for the year ended December 31, 2018 and 2017, respectively:

(in thousands)	Year ended	
	December 31, 2018	2017
Balance, beginning of the period	\$25,400	\$269,722
Payment of contingent consideration in cash	—	(10,000 )
Milestone payable, included in accrued expenses	(9,000 )	—
Unrealized change in fair value change during the period, included in Statement of Operations	3,300	(234,322 )
Balance, end of the period	\$19,700	\$25,400

## 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 five years. 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 payable by the Company.

## Convertible Notes due 2023

In December 2016, the Company issued at par value \$250 million aggregate principal amount of unsecured Convertible Senior Notes due 2023 (the “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 payable by the Company. 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.

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Notes To Consolidated Financial Statements — (Continued)

The Convertible Notes are initially convertible into approximately 40,849,675 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.

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 second quarter. As a result, the Convertible Notes are currently convertible into the Company's common stock.

As further described in "Note 9. Stockholders' Equity," on February 15, 2018, the Company entered into an underwriting agreement relating to an underwritten public offering of 19,354,839 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 2,903,225 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.

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Notes To Consolidated Financial Statements — (Continued)

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

Liability component (in thousands)	2018	2017
Principal	\$400,000	\$250,000
Less: debt discount <sup>(1)</sup>	(74,145 )	(81,566 )
Less: deferred financing <sup>(1)</sup>	(4,115 )	(4,267 )
Net carrying value of the debt	\$321,740	\$164,167

Included in the consolidated balance sheets within convertible notes and senior secured term loan and amortized to (1) 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 total interest expense recognized related to the Convertible Notes and Senior Secured Term Loan for the year ended December 31, 2018, respectively:

Components (in thousands)	2018	2017
Contractual interest expense	\$11,426	\$7,528
Amortization of deferred financing	555	470
Amortization of debt discount	10,421	9,241
Total	\$22,402	\$17,239
Effective interest rate of the liability component, convertible debt	10.85 %	10.85 %
Effective interest rate of the liability component, senior secured term loan	10.48 %	— %

The Capped Call Confirmations of \$13.5 million are 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 Notes in the event that the market price of the common stock is greater than the strike price of the Capped Call Confirmations (which initially corresponds 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 have an initial cap price of \$7.20 per share, which represents 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 is subject to certain adjustments under the terms of the Capped Call Confirmations. The Capped Call Confirmations will cover, subject to anti-dilution adjustments substantially similar to those applicable to the Convertible Notes, the number of shares of common stock that will underlie the Convertible Notes. The Capped Call Confirmations do not meet the criteria for separate accounting as a derivative as they are indexed to the Company's common stock. The premiums paid for the Capped Call Confirmations have been included as a net reduction to additional paid-in capital.

During the first quarter of 2019, the Company entered into separate, privately negotiated exchange agreements with a limited number of holders (the "Holders") of the Convertible Notes. Under the terms of the exchange agreements (the "Exchange Agreements"), the Holders agreed to exchange an aggregate principal amount of approximately \$184.6 million of Convertible Notes held by them in exchange for an aggregate of approximately 33.0 million shares of the our common stock, par value \$0.01 per share. In addition, pursuant to the Exchange Agreements, the Company made aggregate cash payments of approximately \$0.7 million to the Holders to satisfy accrued and unpaid interest to the closing date of the transaction, along with cash in lieu of fractional shares.

During the first quarter of 2019, the Company also terminated the proportion of the Capped Call Confirmations related to the exchange of the Convertible Notes in 2019 for proceeds of approximately \$14.6 million.

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## 13. Leases

## Operating Leases

The Company currently leases office and research laboratory space, equipment and vehicles in various facilities under operating agreements expiring at various dates through 2028.

The following table contains information about our current significant leased properties as of December 31, 2018:

Location	Approximate Square Feet	Use	Lease expiry date
Cranbury, New Jersey	90,000	Office and laboratory	September 2025
United Kingdom	46,617	Office	August 2028
Princeton, New Jersey	21,922	Office	January 2022

In addition to the above, we also maintain offices in Germany, Netherlands, Italy, Spain, France, Japan, Canada, Denmark, and Australia. 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.

Rent expenses for the Company's facilities are recognized over the term of the lease. The Company recognizes rent starting when possession of the facility is taken from the landlord. When a lease contains a predetermined fixed escalation of the minimum rent, the Company recognizes the related rent expense on a straight-line basis and records the difference between the recognized rental expense and the amounts payable under the lease as deferred rent liability. Tenant leasehold improvement allowances are reflected in accrued expenses on the consolidated balance sheets and are amortized as a reduction to rent expense in the statement of operations over the term of the lease.

At December 31, 2018, aggregate annual future minimum lease payments under these leases are as follows:

(in thousands)	2019	2020	2021	2022	2023 and beyond	Total
Minimum lease payments	\$6,244	\$4,063	\$3,560	\$3,371	\$13,649	\$30,887

Rent expense, including fees for utilities and common area maintenances for the years ended December 31, 2018, 2017 and 2016 were \$5.7 million, \$3.9 million and \$3.5 million, respectively.

Subsequent to December 31, 2018, the Company entered into several new lease arrangements for additional office and research laboratory space in the U.S. and internationally. These leases will be accounted for under ASU 2016-02, Leases (Topic 842) during the first quarter of 2019. The future minimum lease payments of these leases range from approximately \$1.5 million to \$6.1 million annually over the next five years.

## Capital Leases

In 2018, the Company purchased vehicles of approximately \$0.2 million through financing arrangements. These financing arrangements include interest of approximately 5.0%-7.0%, and lease terms of 36-48 months.

In 2016, the Company purchased equipment of approximately \$0.9 million through financing arrangements. These financing arrangements include interest of approximately 2.0%-5.7%, and lease terms of 36-48 months.

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At December 31, 2018, aggregate annual future minimum lease payments under these leases, including interest, are as follows (in thousands):

Years ending December 31:

2019	\$194
2020	60
2021	47
2022	30
2023 and beyond	—
Total principal obligation	\$331

## 14. Income Taxes

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

	Years Ended December 31,		
(in thousands)	2018	2017	2016
United States	\$(309,183)	\$(440,696)	\$(174,913)
Foreign	(39,906 )	(8,425 )	(28,868 )
Total	\$(349,089)	\$(449,121)	\$(203,781)

Following were the components of income tax expense (benefit) for the years ended December 31, 2018, 2017 and 2016:

(in thousands)	2018	2017	2016
Current			
Federal	\$—	\$—	\$—
State	6	9	7
Foreign	(100)	2,276	—
Deferred			
Federal	—	(150,015 )	(1,101 )
State	—	(17,389 )	(2,645 )
Foreign	—	—	—
Total	\$(94)	\$(165,119)	\$(3,739)

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2018, 2017 and 2016 are as follows:

	Years Ended		
	December 31,		
	2018	2017	2016
Statutory rate	(21)%	(34)%	(34)%
State taxes, net of federal benefit	(4 )	(5 )	(5 )
Nondeductible IPR&D	6	(1 )	3
Contingent consideration	1	(18)	—
Tax credits	(10)	(2 )	(3 )
Foreign income tax rate differential	2	5	2
Impact of 2017 Act	—	27	—
Other	—	5	(1 )
Valuation allowance	26	(14)	36
Net	— %	(37)%	(2 )%

On December 22, 2017, the U.S. government enacted the 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 and the Company does not have any significant offshore earnings from which to record the mandatory transition tax. The Company recorded an income tax benefit of \$0.1 million in the Consolidated Statement of Operations, in connection with the reduction in the statutory corporate income tax rate. The Company operates in a consolidated loss position in its foreign operations, and does not have a one-time tax on accumulated earnings of foreign subsidiaries.

As of December 31, 2017, we 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 our consolidated financial statements. Our accounting for the effects of the enactment of the Tax Act is now complete.

The Company recorded an income tax benefit of \$0.1 million in 2018 for taxes in foreign and state jurisdictions. The Company did not recognize interest or penalties related to income tax during the period ended December 31, 2018 and did not accrue for interest or penalties as of December 31, 2018. The Company does not have an accrual for uncertain tax positions as of December 31, 2018. Tax returns for all years 2010 and thereafter are subject to future examination by tax authorities.

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Notes To Consolidated Financial Statements — (Continued)

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:

(in thousands)	For Years Ended	
	December 31,	
	2018	2017
Deferred tax assets		
Intellectual property	\$48,339	\$44,573
Amortization/depreciation	3,732	3,082
Research tax credit	96,509	43,382
Net operating loss carry forwards	248,398	221,912
Deferred revenue	4,401	6,158
Non-cash stock issue	16,850	10,751
Interest carry forward limitation	1,032	—
Others	10,852	7,328
Gross deferred tax assets	430,113	337,186
Deferred tax liabilities		
Business acquisition	(6,465 )	(6,465 )
Royalty payable	(48,339 )	(44,573 )
Convertible notes	(16,666 )	(18,991 )
Advanced R&D payments	(2,103 )	(3,069 )
Total net deferred tax assets	356,540	264,088
Less: valuation allowance	(363,005)	(270,553)
Net deferred tax liability	\$(6,465 )	\$(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, 2018 and 2017, the Company recorded valuation allowances of \$363.0 million and \$270.6 million, respectively, representing an increase in the valuation allowance of \$92.4 million in 2018 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, 2018, the Company had federal, state, and foreign net operating loss carry forwards ("NOLs") of approximately \$858.4 million, \$943.5 million, and \$35.0 million, respectively. The federal carry forward for losses generated prior to 2018 will expire in 2030 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the 2017 Tax Cut & Jobs Act. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2018 will expire in 2030 through 2038. The foreign NOLs have indefinite expiration. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of 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.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

The Company also has research and experimentation and orphan drug credit carryforwards of approximately \$23.7 million and \$72.8 million, respectively, which will expire in the years 2023 through 2037. Deferred tax assets for these carryforwards are subject to a full valuation allowance.

15. Licenses

The Company acquired rights to develop and commercialize its product candidates through licenses granted by various parties. The following summarizes the Company's material rights and obligations under those licenses: Nationwide Children's Hospital — As discussed in "— Note 3. Acquisitions," 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.

University of Pennsylvania — For discussion of the royalties and milestone payments potentially due to University of Pennsylvania ("Penn"), see "— Note 16. Collaborative Agreements."

GSK — For discussion of the royalties and milestone payments potentially due to GSK, see "— Note 16. Collaborative Agreements."

Mt. Sinai School of Medicine of New York University ("MSSM") — The Company acquired exclusive worldwide patent rights to develop and commercialize Galafold<sup>®</sup> and other pharmacological chaperones for the prevention or treatment of human diseases or clinical conditions by increasing the activity of wild-type and mutant enzymes pursuant to a license agreement with Mt. Sinai School of Medicine ("MSSM") of New York University. Under this agreement, to date, the Company has paid no upfront or annual license fees and there are no milestone or future payments other than royalties on net sales. This agreement expires upon expiration of the last of the licensed patent rights, which will be in 2019, subject to any patent term extension that may be granted, or 2024 if the Company develops a product for combination therapy (pharmacological chaperone plus/ERT) and a patent issues from the pending application covering the combination therapy, subject to any patent term extension that may be granted. Under its license agreements, if the Company owes royalties on net sales for one of its products to more than one of the above licensors, then the Company has the right to reduce the royalties owed to one licensor for royalties paid to another. The amount of royalties to be offset is generally limited in each license and can vary under each agreement. For the year ended December 31, 2018, under the MSSM and GSK license and collaboration agreements, we paid \$7.6 million in royalties.

The Company's rights with respect to these agreements to develop and commercialize Galafold<sup>®</sup> may terminate, in whole or in part, if the Company fails to meet certain development or commercialization requirements or if the Company does not meet its obligations to make royalty payments.

16. Collaborative Agreements

University of Pennsylvania

In October 2018, the Company further 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. This relationship will combine the Company's protein engineering and glycobiology expertise with Penn's AAV gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability. In connection with the collaboration agreement, the Company made an upfront payment of \$7 million in cash to Penn in October 2018, which was expensed to research and development expense in the Consolidated Statements of Operations. The Company agreed to certain milestone payments following the achievement of certain developmental and commercial milestone events by a licensed product in each indication up to an aggregate of \$86.5 million per indication.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

GSK

In November 2013, Amicus entered into the Revised Agreement with 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. 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, 2018, the Company incurred approximately \$6.9 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, 2018, under the GSK collaboration agreements, we paid \$1.3 million in sales-based milestones. As of December 31, 2018, the Company recognized a liability of \$15.7 million as deferred reimbursements, in addition to \$3.4 million related to royalties payable to GSK in accounts payable, accrued expenses, and other current liabilities 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.





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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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.

## 17. 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,		
Historical	2018	2017	2016
Numerator:			
Net loss attributable to common stockholders	\$(348,995)	\$(284,002 )	\$(200,042 )
Denominator:			

Weighted average common shares outstanding — basic and diluted 85,790,021 153,355,144 134,401,588

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 2018 there was 40.9 million potential common shares outstanding as a result of the convertible debt that was 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,		
	2018	2017	2016
Options to purchase common stock	15,810	15,181	15,528
Convertible debt	40,850	40,850	40,850
Outstanding warrants, convertible to common stock	2,657	3,110	3,110
Unvested restricted stock units	3,712	2,575	744
Vested restricted stock units, unissued	91	50	—
Total number of potentially issuable shares	63,120	61,766	60,232

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

## 18. Selected Quarterly Financial Data (Unaudited — in thousands except per share data)

	Quarters Ended			
	March 31	June 30	September 30	December 31
2018				
Net loss	\$(49,916)	\$(61,833)	\$(159,163 )	\$(78,083 )
Basic and diluted net loss per common share (1)	\$(0.28 )	\$(0.33 )	\$(0.84 )	\$(0.43 )
2017				
Net loss	\$(54,992)	\$(48,136)	\$(111,666 )	\$(69,208 )
Basic and diluted net loss per common share (1)	(0.39 )	(0.34 )	(0.69 )	(0.42 )

(1) 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.

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Amicus Therapeutics, Inc.

Notes To Consolidated Financial Statements — (Continued)

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, 2018. 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, 2018, 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, 2018 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.

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**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 2019 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.

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## PART IV

## 1 Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULE

## (a) 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			Filed with this Form 10-K
		Form	Date	Exhibit No.	
2.1	<u>Agreement and Plan of Merger, dated November 19, 2013, by and among Amicus Therapeutics, Inc., CB Acquisition Corp., Callidus BioPharma, Inc., and Cuong Do</u>	Form 8-K	2/12/2014	2.1	
2.2	<u>Amendment to Agreement and Plan of Merger, dated September 30, 2015, by and among the Registrant, Titan Merger Sub Corp. and Scioderm, Inc.</u>	Form 8-K	9/30/2015	2.2	
+2.3	<u>Agreement and Plan of Merger, dated July 5, 2016, by and among MiaMed, Inc., the Registrant and Minervas Merger Sub, Inc.</u>	Form 8-K	7/6/2016	2.1	
+2.4	<u>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</u>	Form 8-K	9/25/2018	2.1	
3.1	<u>Restated Certificate of Incorporation of the Registrant.</u>	Form 10-K	2/28/2012	3.1	
3.2	<u>Restated By-laws of the Registrant.</u>	S-1/A (333-141700)	4/27/2007	3.4	
3.3	<u>Certificate of Amendment to the Registrant's Restated Certificate of Incorporation, as amended.</u>	Form 8-K	6/10/2015	3.1	
3.4	<u>Certificate of Amendment to the Restated Certificate of Incorporation</u>	Form 8-K	6/8/2018	3.1	
4.1	<u>Specimen Stock Certificate evidencing shares of common stock</u>	S-1 (333-141700)	3/30/2007	4.1	
4.2	<u>Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended</u>	S-1 (333-141700)	3/30/2007	4.2	
4.3	<u>Form of Warrant, issued on October 1, 2015</u>	Form 8-K	10/1/2015	4.1	
4.4	<u>Form of Warrant to Purchase Common Stock</u>	Form 8-K	2/22/2016	4.1	

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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
4.5	<u>Form of Warrant to Purchase Common Stock</u>	Form 8-K	7/1/2016	4.1	
4.6	<u>Form of Indenture</u>	Form S-3ASR	4/29/2016	4.7	
4.7	<u>Indenture, dated December 21, 2016, by and between the Registrant and Wilmington Trust, National Association</u>	Form 8-K	12/21/2016	4.1	
*10.1	<u>2002 Equity Incentive Plan, as amended, and forms of option agreements thereunder</u>	S-1/A (333-141700)	4/27/2007	10.1	
+10.2	<u>Amended and Restated License Agreement, dated October, 31, 2008, by and between the Registrant and Mount Sinai School of Medicine of New York University</u>	Form 10-K	2/6/2009	10.3	
+10.3	<u>Exclusive License Agreement, dated as of June 8, 2005, by and between the Registrant and Novo Nordisk, A/S</u>	S-1 (333-141700)	3/30/2007	10.5	
10.4	<u>Form of Director and Officer Indemnification Agreement</u>	S-1 (333-141700)	3/30/2007	10.17	
*10.5	<u>Amended and Restated 2007 Director Option Plan and form of option agreement</u>	Form 8-K	6/18/2010	10.2	
*10.6	<u>2007 Employee Stock Purchase Plan</u>	S-1/A (333-141700)	5/17/2007	10.24	
*10.7	<u>Management Bonus Program Summary</u>	Form 8-K	6/9/2016	10.1	
10.8	<u>Lease Agreement dated August 16, 2011 between the Registrant and Cedar Brook 3 Corporate Center, L.P.</u>	Form 8-K	8/16/2011	10.1	

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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
10.9	<u>Securities Purchase Agreement, dated November 20, 2013 by and among the Company and the purchasers identified therein</u>	Form 8-K	11/20/2013	10.1	
10.10	<u>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</u>	Form 8-K	12/30/2013	10.1	
+10.11	<u>Second Restated Agreement, dated November 19, 2013 by and between the Registrant and Glaxo Group Limited</u>	Form 10-K	3/3/2014	10.46	
*10.12	<u>Amicus Therapeutics, Inc. Cash Deferral Plan</u>	Form 8-K	7/2/2014	10.1	
10.13	<u>Amendment No.1 to the Amicus Therapeutics, Inc. Cash Deferral Plan</u>	Form 8-K	10/16/2014	10.1	
*10.14	<u>Employment Agreement dated April 23, 2014, between the Registrant and John F. Crowley</u>	Form 8-K	4/25/2014	10.1	
*10.15	<u>Employment Agreement dated April 23, 2014, between the Registrant and William D. Baird, III</u>	Form 8-K	4/25/2014	10.2	
*10.16	<u>Employment Agreement dated April 23, 2014, between the Registrant and Bradley L. Campbell</u>	Form 8-K	4/25/2014	10.3	
*10.17	<u>Employment Agreement dated April 23, 2014, between the Registrant and Jay Barth, M.D.</u>	Form 10-Q	5/5/2014	10.6	
*10.18	<u>Letter Agreement dated April 30, 2014, between the Registrant and Daphne Quimi</u>	Form 10-Q	5/5/2014	10.8	
*10.19	<u>Amended and Restated 2007 Equity Incentive Plan</u>	Form 8-K	6/13/2016	10.1	
*10.20	<u>Amicus Therapeutics, Inc. Cash Deferral Plan</u>	Form 8-K	10/28/2016	10.1	
*10.21	<u>Employment Agreement dated December 17, 2015 between the Registrant and Hung Do</u>	Form 10-K	2/29/2016	10.37	

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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
*10.22	<u>Amendment No. 1 to the Amicus Therapeutics, Inc. Cash Deferral Plan</u>	Form 8-K	10/16/2014	10.1	
10.23	<u>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.</u>	Form 8-K	4/28/2015	10.1	
10.24	<u>Note and Warrant Purchase Agreement by and among the Registrant and the purchasers identified on the signature pages thereto, dated October 1, 2015</u>	Form 8-K	10/1/2015	10.1	
10.25	<u>First Amendment to Lease, dated September 9, 2015, by and between Cedar Brook 3 Corporate Center, L.P. and the Registrant</u>	Form 8-K	9/14/2015	10.1	
*10.26	<u>Retention Bonus Letter, dated March 10, 2016, by and between the Registrant and Jay Barth, M.D.</u>	Form 8-K	3/15/2016	10.1	
10.27	<u>Note and Warrant Purchase Agreement by and among the Registrant and the purchasers identified on the signature pages thereto, dated February 19, 2016.</u>	Form 8-K	2/22/2016	10.1	
10.28	<u>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</u>	Form 8-K	7/1/2016	10.2	
*10.29	<u>Amendment No. 1 to the Amended and Restated Amicus Therapeutics, Inc. 2007 Equity Incentive Plan</u>	Form 8-K	7/29/2016	10.1	



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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
*10.30	<u>Secondment Letter, dated August 22, 2016 by and between the Registrant and Bradley Campbell</u>	Form 8-K	8/23/2016	10.1	
10.31	<u>Base Capped Call Transaction, dated December 15, 2016, by and between the Registrant and Goldman, Sachs &amp; Co.</u>	Form 8-K	12/21/2016	10.1	
10.32	<u>Base Capped Call Transaction, dated December 15, 2016, by and between the Registrant and JPMorgan Chase Bank, National Association</u>	Form 8-K	12/21/2016	10.2	
10.33	<u>Base Capped Call Transaction, dated December 15, 2016, by and between the Registrant and Royal Bank of Canada</u>	Form 8-K	12/21/2016	10.3	
10.34	<u>Additional Capped Call Transaction, dated December 19, 2016, by and between the Registrant and Goldman, Sachs &amp; Co.</u>	Form 8-K	12/21/2016	10.4	
10.35	<u>Additional Capped Call Transaction, dated December 19, 2016, by and between the Registrant and JPMorgan Chase Bank, National Association</u>	Form 8-K	12/21/2016	10.5	
10.36	<u>Additional Capped Call Transaction, dated December 19, 2016, by and between the Registrant and Royal Bank of Canada</u>	Form 8-K	12/21/2016	10.6	
10.37	<u>Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and P Redmile Ltd.</u>	Form 8-K	12/21/2016	10.7	
10.38	<u>Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund, Ltd.</u>	Form 8-K	12/21/2016	10.8	
10.39	<u>Note Purchase Agreement, dated December 15, 2016, by among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund II, Ltd.</u>	Form 8-K	12/21/2016	10.9	

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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
10.40	<u>Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Special Opportunities Fund, Ltd.</u>	Form 8-K	12/21/2016	10.10	
10.41	<u>Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Fund, LP</u>	Form 8-K	12/21/2016	10.11	
10.42	<u>Note Purchase Agreement, dated December 15, 2016, by and between Amicus Therapeutics International Holding LTD and GCM Grosvenor Special Opportunities Master Fund, Ltd.</u>	Form 8-K	12/21/2016	10.12	
*10.43	<u>Form of Performance-Based Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan</u>	Form 8-K	12/30/2016	10.1	
10.44	<u>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</u>	Form 8-K	9/25/18	10.1	
10.45	<u>Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023</u>	Form 8-K	1/24/19	10.1	
10.46	<u>Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023</u>	Form 8-K	2/8/19	10.1	
10.47	<u>Amendment #1 to the Amended and Restated Amicus Therapeutics, Inc. 2007 Equity Incentive Plan</u>	Form 8-K	12/26/18	10.1	
++10.48	<u>Research, Collaboration and License Agreement with The Trustees of the University of Pennsylvania dated October 8, 2018</u>				X
10.49	<u>Separation Agreement with William D. Baird III dated as of February 8, 2019</u>				X
21	<u>List of Subsidiaries</u>				X
23.1	<u>Consent of Independent Registered Public Accounting Firm.</u>				X
31.1	<u>Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.</u>				X
31.2	<u>Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.</u>				X
32.1	<u>Certificate of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.</u>				X
32.2	<u>Certificate of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.</u>				X

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Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Filed with this Form 10-K
		Form	Date	
101	The following financial information from this Annual Report on Form 10-K for the year ended December 31, 2018, formatted in 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

+ 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.

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.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on February 28, 2019.

AMICUS

THERAPEUTICS, INC.

(Registrant)

By: /s/ John F. Crowley

John F. Crowley

Chief Executive Officer

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

Signature	Title	Date
/s/ John F. Crowley (John F. Crowley)	Chairman and Chief Executive Officer (Principal Executive Officer)	February 28, 2019
/s/ Daphne Quimi (Daphne Quimi)	Chief Financial Officer (Principal Financial Officer)	February 28, 2019
/s/ Samantha Prout (Samantha Prout)	Global Controller (Principal Accounting Officer)	February 28, 2019
/s/ Robert Essner (Robert Essner)	Director	February 28, 2019
/s/ Ted W. Love, M.D. (Ted W. Love, M.D.)	Director	February 28, 2019
/s/ Margaret G. McGlynn, R.Ph. (Margaret G. McGlynn, R.Ph.)	Director	February 28, 2019

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Signature	Title	Date
/s/ Michael G. Raab (Michael G. Raab)	Director	February 28, 2019
/s/ Glenn Sblendorio (Glenn Sblendorio)	Director	February 28, 2019
/s/ Craig Wheeler (Craig Wheeler)	Director	February 28, 2019
/s/ Lynn Bleil (Lynn Bleil)	Director	February 28, 2019

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