



EXTRAORDINARY PATIENT FOCUS.

2020
ANNUAL REPORT

Noah, Age 10
Whitby, Ontario
Living with Pompe Disease



A RARE COMPANY.

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

As of December 31, 2020

~\$261M
NET PRODUCT SALES

**GLOBAL
FOOTPRINT**

ROBUST PIPELINE
OF PROGRAMS FOR
RARE METABOLIC DISEASES

\$483M
CASH ON HAND

480+
DEDICATED EMPLOYEES

FIRST ORAL PRECISION
MEDICINE FOR FABRY DISEASE:
GALAFOLD

Kiera, Age 14
Dexter, MI

Living with CDKL5 Deficiency Disorder

Our dedication to patients goes hand in hand with our commitment to our environmental, social and governance (ESG) responsibilities.

Building strong ESG practices and oversight into our scientific and business activities creates a culture of integrity at every level of our organization while safely and effectively delivering on our founding beliefs:

Be at the forefront of therapies for rare and orphan diseases

Create long-term value for our stakeholders

Foster teamwork and respect for individual contributions

To access the full ESG report, please visit the Responsibility section of our corporate website.

RESPONSIBILITY

Diversity, Equity, Inclusion

Our "Three Pillars of DEI" are interwoven into Amicus culture. For our employees, these three pillars are a touchstone for inspiration, guidance and encouragement.

PEOPLE

Embed DEI into activities of our business units, Amicus Belief Statement, and Mission-focused Behaviors

Ensure diverse representation in next generation Talent initiatives

Attract talent through a diverse lens (candidate slates, interview teams, inclusive hiring processes)

Ensure diversity in Board of Directors and Senior Leadership Team representation

PATIENTS

Ensure diverse representation in our clinical trials

Create patient education to impact health literacy

Address the impact of socioeconomics and access through advocacy

Work towards global access to treatments for patients

PHILANTHROPY

Support non-profits that impact diverse communities

Invest in the next generation of innovators through partnerships with STEM programs

Build awareness of rare diseases as diverse populations

Galafold® Remains Cornerstone of Amicus' Success

- 1,400+ patients and ~\$261M global sales in FY20
- FY21 revenue guidance of \$300M-\$315M
- \$1B+ addressable market opportunity at peak

AT-GAA in Pompe: Potential to Become Standard of Care

- Advancing key global regulatory submissions for approval throughout 2021
- 150+ Pompe patients treated with AT-GAA by YE20
- \$1B-\$2B+ market opportunity

Advancing Our Industry Leading Rare Disease Gene Therapy Portfolio

- Gene therapy platform with rights to 50+ lysosomal disorders and 12 additional rare diseases
- Two clinical-stage gene therapy programs in CLN6 and CLN3 Batten disease
- \$1B+ peak recurring market opportunity

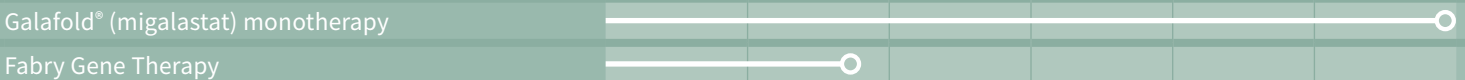


Megan Crowley, Age 24
Princeton, NJ
Living with Pompe Disease

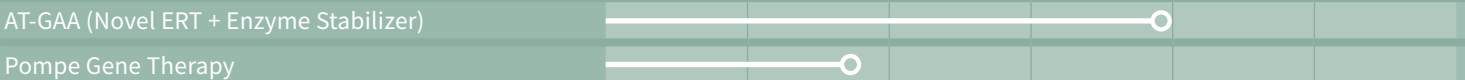
A leading, fully integrated, global rare disease biotechnology company

DISCOVERY PRECLINICAL PHASE 1/2 PHASE 3 REGULATORY COMMERCIAL

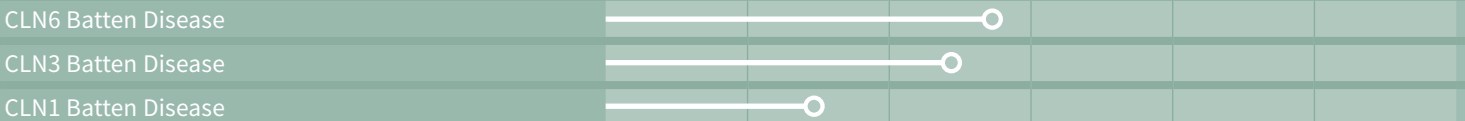
FABRY FRANCHISE



POMPE FRANCHISE



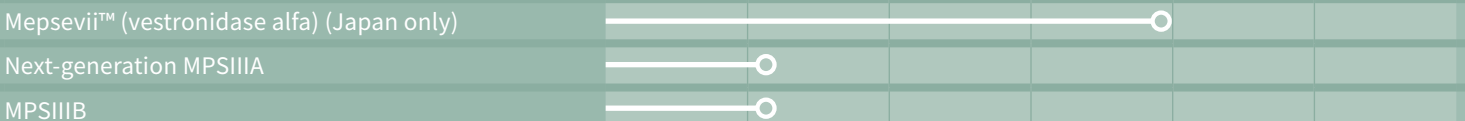
ADDITIONAL GENE THERAPY PROGRAMS



NEXT-GENERATION RESEARCH PROGRAMS AND CNS GENE THERAPIES



MPS FRANCHISE



**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K**

(Mark One)

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

For the fiscal year ended December 31, 2020

OR

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

For the transition period from _____ to _____

Commission file number 001-33497

Amicus Therapeutics, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)
3675 Market Street, Philadelphia, PA
(Address of Principal Executive Offices)

71-0869350
(I.R.S. Employer
Identification Number)
19104
(Zip Code)

(215) 921-7600

(Registrant's Telephone Number, Including Area Code)

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

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

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

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

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

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

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

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

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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

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

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

The aggregate market value of the 255,379,926 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, 2020) was \$3,851,129,284. Shares of voting and non-voting stock held by executive officers, directors, and holders of more than 10% of the outstanding stock have been excluded from this calculation because such persons or institutions may be deemed affiliates. This determination of affiliate status is not a conclusive determination for other purposes.

The number of shares outstanding of the registrant's common stock, \$0.01 par value per share, as of February 19, 2021 was 264,316,074 shares.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2021 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

- the scope, progress, results and costs of our clinical trials of our drug candidates and gene therapy candidates, including but not limited to AT-GAA, CLN6 and CLN3;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200" or "cipaglucosidase alfa") and gene therapies;
- the future results of on-going preclinical research and subsequent clinical trials for cyclin-dependent kinase-like 5 ("CDKL5") deficiency disorder, Pompe gene therapy, Fabry gene therapy, Mucopolysaccharidosis Type IIIB ("MPS IIIB"), next generation Mucopolysaccharidosis Type IIIA ("MPS IIIA") and other pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates;
- 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[®] (also referred to as "migalastat HCl") and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold[®], AT-GAA and our gene therapy candidates;
- our ability to obtain reimbursement for Galafold[®] and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold[®];
- our ability to obtain market acceptance of Galafold[®] and, if our regulatory filings are accepted and approved, AT-GAA;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- the extent to which we acquire or invest in businesses, products, and technologies;
- our ability to successfully integrate our acquired products and technologies into our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;

- our ability to adjust to changes in the European and United Kingdom markets in the wake of the United Kingdom leaving the European Union;
- the extent to which our business could be adversely impacted by the effects of the novel coronavirus ("COVID-19") outbreak, including due to actions by us, governments, our customers or suppliers or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

In light of these risks and uncertainties, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A "— Risk Factors", a summary of which may be found below, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Those factors and the other risk factors described herein are not necessarily all of the important factors that could cause actual results or developments to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors also could harm our results. Our forward-looking statements do not reflect the potential impact of any future 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.

Summary Risk Factors

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

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

- If we are unable to obtain marketing approval, or if approved unable to successfully commercialize AT-GAA, our business could be materially harmed.
- Our gene therapy product candidates are based on novel technologies, which makes it difficult to predict the time and cost of their development and subsequently obtaining regulatory approval.
- We may encounter difficulties manufacturing our gene therapy which could impact timing and availability of clinical and commercial supply.
- 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 rely on third parties to conduct certain preclinical development activities and our clinical trials, and those third parties may not perform satisfactorily.
- We may not be successful in maintaining or establishing collaborations, which could adversely affect our ability to develop and, particularly in international markets, commercialize products.
- Materials necessary to manufacture our product or product candidates may not be available on commercially reasonable terms, which may delay their development and commercialization.
- Manufacturing issues may arise that could increase costs or delay commercialization.
- We have incurred significant losses and anticipate that we will continue to incur losses in the future.
- We may never become profitable even though we currently generate revenue from the sale of products.
- If we require, and fail to obtain, additional necessary financing, we may be unable to complete the development and commercialization of our product and product candidates.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies, Galafold® or product candidates.
- We may not have sufficient cash flow from our business to pay our substantial debt.
- Foreign currency exchange rate fluctuations could harm our financial results.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- Our executive officers, directors and principal stockholders maintain the ability to exert significant influence and control over matters submitted to our stockholders for approval.
- 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.
- If we are unable to obtain and maintain sufficiently broad patent protection, our ability to successfully commercialize our technology and products may be adversely affected.
- We may become involved in lawsuits to protect or enforce our patents or other intellectual property.
- Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights which could have a material adverse effect on the success of our business.
- We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.
- If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.
- Failure to secure trademark registrations could adversely affect our business.
- Our rights to develop and commercialize our gene therapy product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.
- The novel coronavirus ("COVID-19") pandemic may negatively impact our business and operations.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- Our employees, independent contractors, principal investigators, consultants and vendors may engage in misconduct or improper activities which could lead to significant liability and harm our reputation.
- If our enterprise risk program, global risk committee and other compliance methods are not effective, our business, financial condition and operating results may be adversely affected.

PART I

Item 1. BUSINESS

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We have a portfolio of product opportunities led by the first, oral monotherapy for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease, and an industry leading rare disease gene therapy portfolio.

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. We initiated the rolling Biologic License Application ("BLA") submission to the FDA in the fourth quarter of 2020.

We have established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children's Hospital ("Nationwide Children's") and an expanded collaboration with the University of Pennsylvania ("Penn"). Our pipeline includes gene therapy programs in rare, neurologic lysosomal disorders ("LDs"), specifically: CLN6, CLN3, and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Mucopolysaccharidosis Type IIIB ("MPS IIIB"), as well as a next generation program in Mucopolysaccharidosis Type IIIA ("MPS IIIA"). Our expanded collaboration with Penn also provides us with exclusive disease-specific access and the option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. In the first quarter of 2020, the FDA granted Fast Track designation to the CLN3 Batten disease gene therapy, AT-GTX-502, for the treatment of pediatric patients less than 18 years of age. In September 2020 and February 2021, the European Medicines Agency ("EMA") granted Priority Medicines ("PRIME") designation and the FDA granted Fast Track designation, respectively, to the CLN6 Batten disease gene therapy, AT-GTX-501, for the treatment of patients with variant late infantile neuronal ceroid lipofuscinosis 6 ("vLINCL6").

In July 2020, we entered into a definitive agreement for a \$400 million credit facility with Hayfin Capital Management ("Senior Secured Term Loan due 2026") with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum and requires interest-only payments until mid-2024 and matures in six years in 2026. This transaction resulted in net proceeds of \$385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. Additionally, we used \$156.3 million of the proceeds to voluntarily settle the principal amount, accrued interest, and early settlement premiums of the Senior Secured Term Loan with BioPharma Credit PLC that was due in 2023 ("Senior Secured Term Loan due 2023").

Our Strategy

Our strategy is to create, manufacture, test, and deliver the highest quality medicines for people living with rare metabolic diseases through internally developed, acquired, or in-licensed products and product candidates that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. In addition to our programs in Fabry and Pompe diseases, we are leveraging our global capabilities to develop and expand our robust pipeline in genomic medicine. We have made significant progress toward fulfilling our vision of building a leading global biotechnology company focused on rare metabolic diseases.

Our operations have not been significantly impacted from the novel coronavirus (“COVID-19”) pandemic in 2020; however, we observed increased lag times between patient identification and Galafold[®] initiation due to the resurgence of COVID-19 in the fourth quarter. We have maintained operations in all geographies, secured our global supply chain for our commercial and clinical products, as well as maintained the operational integrity of our clinical trials, with minimum disruptions. Our ability to continue to operate without any significant disruptions will depend on the continued health of our employees, the ongoing demand for Galafold[®] and the continued operation of our global supply chain. We have continued to provide uninterrupted access to medicines for those in need of treatment, while prioritizing the health and safety of our global workforce. However, our results of operations in future periods may be negatively impacted by unknown future impacts from the COVID-19 pandemic.

Highlights of our progress include:

- *Commercial and regulatory success in Fabry disease.* For the year ended December 31, 2020, Galafold[®] revenue totaled \$260.9 million, an increase of \$78.6 million compared to the prior year. We continue to see strong commercial momentum and expansion into additional geographies. In countries where we have been operating the longest, such as Germany and the U.K., we see an increasing proportion of previously untreated patients come onto Galafold[®]. In the U.S., we continue to see a significant increase in patients from a growing and very wide prescriber base. Across all markets, we see a high rate of compliance and adherence to this oral treatment option.
- *Pompe clinical program milestones.* In December 2020, we completed last patient, last visit in our global Phase 3 pivotal study of AT-GAA (ATB200-03, also known as "PROPEL") with 123 patients at 62 sites in 24 countries and initiated the rolling BLA submission to the FDA for AT-GAA. In February 2021, we subsequently reported topline results for the PROPEL study. Additionally, in 2020, orphan drug designation was received in Japan and the British Medicines and Healthcare Products Regulatory Agency issued a Promising Innovative Medicine ("PIM") designation for AT-GAA for the treatment of late-onset Pompe disease. Previously, the U.S. FDA granted BTB for AT-GAA for the treatment of late-onset Pompe disease.
- *Pipeline advancement and growth.* We have established an industry leading gene therapy portfolio of medicines for people living with rare metabolic diseases through a license with Nationwide Children’s and an expanded collaboration with Penn. During the first quarter of 2020, we initiated the long-term follow-up of the initial participants in the CLN6 Phase 1/2 study. In October 2020, we reported additional positive interim safety and efficacy data in our ongoing CLN6 clinical study. Additionally, the research collaboration with Penn was expanded to pursue research and development of novel gene therapies for Pompe disease, Fabry disease, CDD, CLN1, MPS IIIB, as well as a next generation program in MPS IIIA.
- *Manufacturing.* We continued to manufacture our Pompe biologic at commercial scale (1,000L) for our clinical studies, including our pivotal PROPEL study, and early commercial inventory. Our supply agreement with WuXi Biologics and current capacity are expected to produce sufficient quantities to support commercial needs after receipt of applicable regulatory approvals if obtained. For gene therapy, we are working with our strategic partners to support our clinical manufacturing capabilities. During 2020 and thus far in 2021, our global supply chains have not been interrupted and we have thus far maintained our ability to manufacture Galafold[®] as well as our clinical supply during the COVID-19 pandemic.
- *Financial strength.* Total cash, cash equivalents, and marketable securities as of December 31, 2020 was \$483.3 million. Based on current operating models, we believe that the current cash position, which includes the net proceeds from the Senior Secured Term Loan due 2026 and expected revenues is sufficient to fund our operations and ongoing research programs to achieve self-sustainability. Potential impacts of the COVID-19 pandemic, business development

collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

Our Commercial Product and Product Candidates

Galafold® (Migalastat HCl) for Fabry Disease

Our oral precision medicine Galafold® was granted accelerated approval by the FDA in August 2018 under the brand name Galafold® for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene ("GLA") variant based on in vitro assay data. The FDA approved Galafold® for 348 amenable GLA variants. Galafold® was approved in the E.U. and U.K. in May 2016 as a first-line therapy for long-term treatment of adults and adolescents, aged 16 years and older, with a confirmed diagnosis of Fabry disease and who have an amenable mutation (variant). The approved E.U. and U.K. labels include 1,384 mutations amenable to Galafold® treatment, which represent up to half of all patients with Fabry disease. In countries where mutations are provided only on the amenability website, these 1,384 amenable mutations are now available. Marketing authorization approvals have been granted in over 40 countries around the world, including the U.S., E.U., U.K., Japan, and others. We plan to continue to launch Galafold® in additional countries during 2021.

As an orally administered monotherapy, Galafold® is designed to bind to and stabilize an endogenous alpha-galactosidase A ("alpha-Gal A") enzyme in those patients with genetic variants identified as amenable in a GLP cell-based amenability assay. Galafold® is an oral precision medicine intended to treat Fabry disease in patients who have amenable genetic variants, and at this time, it is not intended for concomitant use with ERT.

Gene Therapy for Fabry Disease

We are committed to continued innovation for all people living with Fabry disease. For people living with Fabry disease who have non-amenable variants, which are not suitable for Galafold® as a monotherapy, our strategy is to develop a Fabry gene therapy. In October 2018, we expanded our gene therapy portfolio through a collaboration agreement with Penn to pursue research and development of novel gene therapies, including Fabry disease, and other indications. In October 2019, we disclosed preliminary data from a Fabry adeno-associate viral ("AAV") gene therapy using an Amicus-engineered transgene that demonstrated high levels of GLA activity and robust GL-3 reduction in a mouse model of Fabry disease. In February 2021, we presented initial preclinical data from our investigational AAV gene therapy program. This initial preclinical study assessed a range of single doses of AAV in *Gla* knockout mice with either wild-type hGLA ("unmodified hGLA") or an Amicus/Penn engineered hGLA transgenes ("engineered hGLA" or "AT-GTX-701"). The engineered hGLA AAV gene therapy demonstrated stable homodimer formation, enhanced temperature, plasma and neutral pH stability compared to the unmodified hGLA AAV gene therapy. In the lowest tested dose of AT-GTX-701, *Gla* knockout mice showed partial substrate reduction, while highest tested dose resulted in near complete substrate reduction. Additionally, AT-GTX-701 demonstrated significantly greater lyso-Gb3/GL-3 substrate reduction across all Fabry disease relevant tissues including the dorsal root ganglia ("DRG"), kidney, and heart, with reductions at low dose being equal to or greater than the reductions observed at higher doses with wildtype transgene and provided the first evidence for DRG storage reduction in a Fabry mouse model treated with an AAV gene therapy.

Fabry Disease Background

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

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

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

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

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

Novel ERT for Pompe Disease

We are leveraging our biologics capabilities to develop AT-GAA, a novel treatment paradigm for Pompe disease. AT-GAA consists of a uniquely engineered rhGAA enzyme, ATB200, or cipaglucoisidase alfa, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with AT2221, or miglustat, that functions as an enzyme stabilizer.

The small molecule enzyme stabilizer, miglustat or AT2221, binds to and stabilizes ATB200, or cipaglucoisidase alfa, in circulation to improve the uptake of active enzyme in key disease-relevant tissues, resulting in increased clearance of accumulated substrate, glycogen. Miglustat is not an active ingredient that contributes directly to substrate reduction ("glycogen").

We initiated ATB200-03 (or "PROPEL"), a global Phase 3 clinical study of AT-GAA in adult patients with late onset Pompe disease in December 2018 and completed last patient, last visit in December 2020. In February 2021, we reported topline results from the Phase 3 PROPEL study.

Patients enrolled in PROPEL were randomized 2:1 so that for every two patients randomized to be treated with AT-GAA, one was randomized to be treated with alglucosidase alfa. Of the Pompe patients enrolled, 77% were being treated with alglucosidase alfa (n=95) immediately prior to enrollment ("Switch") and 23% had never been treated with any ERT (n=28) ("Naïve"). 117 patients completed the PROPEL study and all 117 voluntarily enrolled in the long-term extension study.

The primary endpoint of the study was the mean change in 6-minute walk distance as compared with baseline measurements at 52 weeks across the combined ERT Switch and ERT Naïve patient populations. In this combined population patients taking AT-GAA (n=85) walked on average 21 meters farther at 52 weeks compared to 7 meters with those treated with alglucosidase alfa (n=37). This primary endpoint in the combined population was assessed for superiority and while numerically greater, statistical significance for superiority on this combined population was not achieved for the AT-GAA arm as compared to the alglucosidase alfa arm (p=0.072).

Per the hierarchy of the statistical analysis plan, the first key secondary endpoint of the study was the mean change in percent-predicted Forced Vital Capacity ("FVC") at 52 weeks across the combined population. In this combined population patients taking AT-GAA demonstrated a nominally statistically significant and clinically meaningful difference for superiority over those treated with alglucosidase alfa. AT-GAA significantly slowed the rate of respiratory decline in patients after 52

weeks. Patients treated with AT-GAA showed a 0.9% absolute decline in percent-predicted FVC, compared to a 4.0% absolute decline in the alglucosidase alfa arm ($p=0.023$).

Patients within the combined study population demonstrated statistically significant improvements on the GSGC (“Gait, Stairs, Gower’s Chair”) key secondary endpoint, which captures strength, coordination and mobility, compared to a worsening for alglucosidase alfa treated patients in the overall population ($p<0.05$). Additionally, lower MMT (Manual Muscle Testing), Patient-Reported Outcomes Measurement Information System (“PROMIS”) physical function and PROMIS fatigue secondary endpoints favored AT-GAA treated patients over alglucosidase alfa treated patients. Results also showed improvements in the two important biomarker endpoints of Pompe disease (Hex-4 and CK), which significantly favored AT-GAA compared to alglucosidase alfa ($p<0.001$). AT-GAA demonstrated a similar safety profile to alglucosidase alfa.

The PROPEL Switch patients entered the study having been treated with alglucosidase alfa for a minimum of two years. More than two thirds (67%+) of those patients had been on ERT treatment for more than five years prior to entering the PROPEL study (mean of 7.4 years). A pre-specified analysis of the patients switching from alglucosidase alfa on 6-minute walk distance showed that after 52 weeks from switching, AT-GAA treated patients ($n=65$) walked 16.9 meters farther than their baseline, compared to 0.0 meters for those patients who were randomized to remain on alglucosidase alfa ($n=30$) ($p=0.046$).

A pre-specified analysis of the patients switching from alglucosidase alfa on percent-predicted FVC showed that AT-GAA treated patients stabilized and slightly improved their respiratory function on this important measure while those patients remaining on alglucosidase alfa continued to significantly decline in respiratory muscle function. AT-GAA patients showed a 0.1% absolute increase in percent-predicted FVC while the alglucosidase alfa patients showed a 4.0% absolute decline over the course of the year ($p=0.006$).

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

Gene Therapy for Pompe Disease

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

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

In May 2020, we presented preclinical data with the engineered hGAA AAV in single and combined central nervous system (“CNS”) and systemic directed gene therapy in a mouse model of Pompe disease with advanced disease at treatment. The engineered hGAA AAV showed better targeting and clearance of glycogen storage at low doses in Pompe mice compared to unmodified hGAA AAV. High dose IV therapy showed strength rescue and the addition of high dose intracerebroventricular (“ICV”) therapy to high dose IV provided incremental benefit.

Pompe Disease Background

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

According to reported estimates of the Acid Maltase Deficiency Association, the United Pompe Foundation, and the Lysosomal Disease Program at Massachusetts General Hospital, there are 5,000-10,000 patients with Pompe disease worldwide.

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

Gene Therapy for Various Types of Batten Disease

Through our license with Nationwide Children's and expanded collaboration with Penn, 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 ("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 ceroid lipofuscinosis, neuronal ("CLN") and given a different number designation as its subtype. There are 13 known forms of Batten disease often referred to as CLN1-8; 10-14. The various types of Batten disease have similar features and symptoms but vary in severity and age of onset.

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

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

Our Phase 1/2 study in CLN6 Batten disease enrolled thirteen patients who received a single one-time intrathecal administration of AAV-CLN6 gene therapy. In October 2020, we reported additional positive interim results from our CLN6 Batten disease AAV-CLN6 gene therapy program, AT-GTX-501. Interim safety data are available for 13 patients with CLN6 Batten disease. Interim safety data demonstrated the treatment with AT-GTX-501 was generally well tolerated. The majority of adverse events ("AEs") were mild and unrelated to treatment. No pattern of adverse events related to AAV or CLN6 immunogenicity was observed. Interim efficacy data are available within the Hamburg Motor and Language scores and showed a meaningful effect in slowing disease progression for twelve patients reaching the 12-month timepoint and for eight patients up to 24 months, post-administration of the AAV-CLN6 gene therapy. Additionally, in October 2019, we reported interim clinical data that suggested stabilization of various components of Hamburg Seizure and Vision scores in most patients from baseline to month 12 or 24, in particular those patients treated at a younger age, compared to the progression expected in matched untreated patients. The CLN6 Batten population is approximately 1,000 patients across our commercial landscape today and there are no approved therapies for this disorder.

In the fourth quarter of 2018, we announced the initiation of a Phase 1/2 study to evaluate the safety and efficacy of a single intrathecal administration of an AAV serotype AT-GTX-502 gene therapy in patients with CLN3 Batten disease. In the Phase 1/2 study, a total of three patients were dosed in the low-dose group, and based on the safety profile to date, the data safety monitoring board cleared us to begin enrollment in the high-dose cohort. One patient is currently dosed in the high-dose cohort. In February 2021, we announced initial safety for the first four patients up to 15 months post-administration of AT-GTX-502 and preliminary efficacy data for the first three patients in the low-dose cohort for up to 15 months post-administration of AT-GTX-502, as well as one patient in the high-dose cohort for up to 3 months post-administration of AT-GTX-502. Initial results of the study suggest that AT-GTX-502 was well tolerated and demonstrated potential early signs of disease stabilization compared to a natural history dataset. CLN3 impacts approximately 5,000 patients across our commercial landscape today and there are no approved therapies for this disorder.

CDKL5 Deficiency Disorder

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

Other Preclinical Gene Therapies

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

Strategic Alliances and Arrangements

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

Acquisitions

Celenex, Inc.

In September 2018, we expanded our pipeline by acquiring the rights and related intellectual property of ten gene therapy programs through the acquisition of Celenex, Inc. ("Celenex"). Celenex is a private, clinical stage gene therapy company whose lead programs are ten gene therapy programs including CLN6 and CLN3, which are in clinical stage, and several programs in pre-clinical stage. Pursuant to the terms of the agreement, we agreed to pay up to an additional \$10 million in connection with the achievement of certain development milestones, \$220 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to \$75 million in tiered sales milestone payments. Celenex has an exclusive license agreement with Nationwide Children's Hospital ("Nationwide Children's"). Under this license agreement, Nationwide Children's is eligible to receive development and sales-based milestones of up to \$7.8 million for each product.

MiaMed, Inc.

In July 2016, we acquired MiaMed, Inc., ("MiaMed"), which is a pre-clinical biotechnology company focused on developing protein replacement therapy for CDD and related diseases. As part of the transaction, we may be obligated to pay up to an additional \$83.0 million in connection with the achievement of certain clinical, regulatory, and commercial milestones, for a potential aggregate deal value of \$89.5 million.

Callidus Biopharma, Inc.

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

Intellectual Property

Patents and Trade Secrets

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

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

- We own issued U.S. patents that cover the use of migalastat, the active pharmaceutical ingredients in Galafold[®], in the treatment of Fabry disease, which expire in 2027, 2028, 2029, 2037 or 2038 and are listed in the FDA Orange Book. Foreign counterparts of the U.S. patents are pending or issued in Europe, Japan, and certain other jurisdictions. Further, we have pending U.S. patent applications covering various aspects of Galafold[®], including methods of treating a patient diagnosed with Fabry disease with migalastat and their foreign counterparts. Any patents issuing from these applications will expire in 2036, 2038, 2039, 2040, or 2041 and we anticipate listing these patents in the FDA Orange Book if issued.
- We own several issued U.S. patents that cover various aspects of our investigational new treatment for Pompe disease, AT-GAA (ATB200/AT2221, an ERT/pharmacological chaperone combination) as well as foreign counterparts to the issued patents, most of which are still pending. Issued U.S. patents cover ATB200 compositions-of-matter, formulations, methods of manufacturing and methods of treatment and will expire in 2033, 2035 or 2037. We also have pending U.S. patent applications covering compositions, methods of treatment, methods of manufacture, and formulations with anticipated expiry in 2033, 2035, 2036, 2037, 2038, 2040, or 2042.

- From the Celenex acquisition, we acquired an exclusive license to composition-of-matter and intrathecal method of treatment patent applications covering the gene therapy for treating Batten disease that are pending in the U.S., Europe, Japan, and other jurisdictions. Any patents issued from these applications will expire in 2033 or 2040. The patent covering an intrathecal method of treatment, which expires in 2033, has issued in Europe and Japan.
- From our agreement with Penn, we have license to Penn's patent portfolio pertaining to vector and other platform technologies for treating Pompe disease, Fabry disease, CDD, CLN1, MPS IIIB, as well as a next generation program in MPS IIIA. Any patents issued from these applications will expire in 2039.

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

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

- Gene therapy protein engineering technology;
- Gene therapy (e.g., Pompe, Fabry, CDLK5, MPS IIIB and next generation MPS IIIA) and ERT (e.g., CDKL5) programs and the use to treat specified diseases.

We cannot be certain, however, that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents.

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

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

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

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

Collaboration and License Agreements

We have acquired rights to develop and commercialize our product candidates through licenses granted by various parties. The following summarizes our material rights and obligations under those licenses:

Nationwide Children's Hospital

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

University of Pennsylvania

In October 2018, as amended, we entered into a collaboration agreement with Penn to pursue research and development of novel gene therapies. Our gene therapy portfolio pipeline expanded to include Pompe disease, Fabry disease, CDD, CLN1, MPS IIIB, as well as a next generation program in MPS IIIA. This expanded collaboration with Penn also provides us with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies.

Under the expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in each indication, up to an aggregate of \$88.0 million per indication. Royalty payments are based on net sales of licensed products on a licensed product-by-licensed product and country- by-country basis. We will provide \$10.0 million each year during the five-year agreement to fund the discovery research program. In connection with the collaboration agreement, in 2018, we made an upfront payment of \$7 million in cash to Penn that was expensed to research and development expense in the Consolidated Statements of Operations.

GlaxoSmithKline

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

Manufacturing

We continue to rely on contract manufacturers to supply the active biopharmaceutical ingredients and 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. Although we rely on contract manufacturers, we have personnel with extensive manufacturing and quality experience to oversee our contract manufacturers. We have implemented appropriate controls for assuring the quality of both active biopharmaceutical ingredients and final drug products. Product specifications will be established in concurrence with regulatory bodies at the time of product registration.

While our third-party manufacturers have met our current manufacturing requirements, we anticipate taking steps to increase our manufacturing capabilities for our gene therapy platform. Our current arrangement with third-party manufacturers provide sufficient quantities of our program materials to meet anticipated clinical trial demands.

Competition

Overview

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

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

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

Major Competitors

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

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

Competitor ⁽¹⁾	Indication	Product	Class of Product	Status	2020 Sales (in millions)
Sanofi Aventis	Fabry Disease	Fabrazyme [®]	ERT	Marketed	€817
	Pompe Disease	Myozyme [®] / Lumizyme [®]	ERT	Marketed	€948
	Fabry Disease	GZ402671	Oral GCS Inhibitor	Phase 2	N/A
	Pompe Disease	GZ402666 ("neo GAA")	ERT	Regulatory Review	N/A
Takeda	Fabry Disease	Replagal [®]	ERT	Marketed	N/A
Idorsia	Fabry Disease	Lucerastat	Oral Therapy	Phase 3	N/A
Protalix Biotherapeutics	Fabry Disease	PRX-102	ERT	Phase 2/3	N/A
AvroBio	Fabry Disease	AVR-RD-01	Gene Therapy	Phase 1/2	N/A
Freeline	Fabry Disease	FLT190	Gene Therapy	Phase 1/2	N/A
Sangamo	Fabry Disease	ST-920	Gene Therapy	Phase 1/2	N/A
AskBio (Bayer)	Pompe Disease	ACTUS-101	Gene Therapy	Phase 1/2	N/A
Audentes (Astellas)	Pompe Disease	AT845	Gene Therapy	Phase 1/2	N/A
Roche (Spark)	Pompe Disease	SPK3006	Gene Therapy	Phase 1/2	N/A

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

Government Regulation

FDA Approval Process

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

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

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

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

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

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

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

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

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

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

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

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

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

The Hatch-Waxman Act

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

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

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

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

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

Other Regulatory Requirements

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

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

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

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

Orphan Drugs

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

Pediatric Information

Under the Pediatric Research Equity Act of 2007 ("PREA"), NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Fast Track Designation

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

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

Breakthrough Therapy Designation

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

Priority Review

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

Accelerated Approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. This approval mechanism is provided for under 21CFR314 Subpart H and Subpart E. In this case, clinical trials are conducted in which a surrogate endpoint is used as the primary outcome for approval. A surrogate endpoint is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. This surrogate endpoint substitutes for a direct measurement of how a patient feels, functions, or survives and is considered reasonably likely to predict clinical benefit. Such surrogate endpoints may be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. When the Phase 4 commitment is successfully completed, the biomarker is deemed to be a surrogate endpoint. Failure to conduct required post-approval studies or confirm a clinical benefit during post-marketing studies, could lead the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Section 505(b) (2) New Drug Applications

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

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

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

Biologics Price Competition and Innovation Act

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

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

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

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

Physician Drug Samples

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

Regulation Outside the U.S.

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

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

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

The draft decision is then sent to the Standing Committee on Medicinal Products for Human Use, (Member States have one representative each in both of these committees) for their opinions. The Centralized Procedure provides for the grant of a single marketing authorization that is valid for all E.U. member states. The Decentralized Procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

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

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

In March 2016, the EMA launched an initiative, the Priority Medicines ("PRIME") scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. In September 2020, AT-GTX-501 was granted PRIME designation.

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

The U.K. left the E.U. on January 31, 2020 following which, existing E.U. medicinal product legislation continued to apply in the U.K. during the transition period under the terms of the E.U.-U.K. Withdrawal Agreement. A transition period, which ended on December 31, 2020, maintained access to the E.U. single market and to the global trade deals negotiated by the E.U. on behalf of its members. The transition period provided time for the U.K. and E.U. to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("TCA") and became effective on January 1, 2021.

From January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") will be the U.K.'s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales and Scotland (together Great Britain, "GB"); broadly, Northern Ireland will continue to follow the E.U. regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a draft guidance on how various aspects of the U.K. regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, marketing authorizations, importing, exporting and pharmacovigilance and is relevant to any business involved in the research, development or commercialization of medicines in the U.K. The new guidance will be given effect via the Human Medicines Regulations ("Amendment etc.") ("E.U. Exit") Regulations 2019 (the "Exit Regulations"). The U.K. regulatory regime largely mirrors that of the E.U.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing E.U. MAs for centrally authorized products will automatically be converted ("grandfathered") into U.K. MAs free-of-charge on January 1, 2021. Galafold[®] now has a U.K. MA and we will have until January 1, 2022 to submit essential baseline data in order to support the conversion process.

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

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

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

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

U.S. Foreign Corrupt Practices Act

The 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.

Healthcare Reform

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

In recent years, Congress has considered reductions in Medicare reimbursement levels for drugs administered by physicians. CMS, the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payers.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act is intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers, and impose additional health policy reforms. Among other things, the Affordable Care Act expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum Medicaid rebate for both branded and generic drugs, expanded the 340B program, and revised the definition of AMP, which could increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also extended Medicaid drug rebates, previously due only on fee-for-service Medicaid utilization, to include the utilization of Medicaid managed care organizations as well and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the amount of rebates due on those drugs. On February 1, 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate program under the Affordable Care Act. These regulations became effective on April 1, 2016. Since that time, there have been significant ongoing efforts to modify or eliminate the Affordable Care Act.

On January 20, 2017, President Trump signed an executive order directing federal agencies to exercise existing authorities to reduce burdens associated with the Affordable Care Act pending further action by Congress. In October 2017, he signed an Executive Order which directed federal agencies to modify how the Affordable Care Act is implemented. The Tax Act, enacted on December 22, 2017, repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, as amended, or the Code, commonly referred to as the individual mandate.

Other legislative changes have been proposed and adopted since passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than \$1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further legislative and regulatory changes under the Affordable Care Act remain possible, although the new Administration under President Biden has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. President Biden indicated that he intends to use executive orders to undo changes to the Affordable Care Act made by the former administration and would advocate for legislation to build on the Affordable Care Act. It is unknown what form any such changes or any law would take, and how or whether it may affect our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the

federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

The Affordable Care Act has been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court which heard oral arguments in the case on November 10, 2020. A ruling is expected in 2021.

The Affordable Care Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each individual pharmaceutical manufacturer pays a prorated share of the branded prescription drug fee, based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. Furthermore, the law requires manufacturers to provide a 50% discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the “donut hole.” The Bipartisan Budget Act of 2018 (the “BBA”), among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole,” by increasing from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

The Affordable Care Act also expanded the Public Health Service’s 340B drug pricing program. The 340B drug pricing program requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B “ceiling price” for the manufacturer’s covered outpatient drugs. The Affordable Care Act expanded the 340B program to include additional types of covered entities: certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, each as defined by the Affordable Care Act. Because the 340B ceiling price is determined based on AMP and Medicaid drug rebate data, revisions to the Medicaid rebate formula and AMP definition could cause the required 340B discounts to increase.

Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives as well. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for pharmaceutical products.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional federal, state and foreign healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

Human Capital

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

We also believe that diversity of experience and thought is essential. At Amicus, we are committed to the advancement of diversity and inclusion in the workplace. Diversity is the representation of all our varied identities and differences (race, ethnicity, gender, disability, sexual orientation, gender identity, national origin, tribe, socio-economic status, thinking and communication styles, etc.), collectively and as individuals. Equity seeks to ensure fair treatment, equality of opportunity, and

fairness in access to information and resources for all. Inclusion means that all individuals feel respected, accepted, and valued. Inclusion builds a culture of belonging, by actively inviting the contribution and participation of all people. Combined, Diversity, Equity and Inclusion ("DEI") creates a work environment where every voice is heard and valued, resulting in a dimensional way of thinking that is used when meeting company goals. DEI at Amicus is about creating an environment that supports bringing the authentic employee to the workplace. Our unique experiences, cultures, and backgrounds are what make us so great at putting patients at the forefront of what we do and pushing ideas as far and fast as possible. As of December 31, 2020, we had 483 full-time employees. Currently, 50% of our executive management team are women and 20% of our board of directors are women.

We believe it is critical that our employees are informed and engaged. We communicate frequently and transparently with our employees through a variety of communication methods, including video and written communications, town hall meetings, round tables, employee pulse surveys, company intranet, and acknowledge individual contributions through a number of reward and recognition programs. We believe these engagement efforts keep employees informed about our strategy, culture and purpose and motivated to do their best work. As a result of the COVID-19 pandemic, we also further strengthened our digital communication and social networking platforms. Our communications during the pandemic have kept our employees informed on critical priorities, important actions being taken by management in response to the pandemic, and continued efforts to protect employee's health, safety and well-being.

We support and develop our employees through global training and development programs that build and strengthen employees' leadership and professional skills. These are further emphasized through our engagement on employee career paths through the annual goal process, a tuition reimbursement program, providing the ability to attend industry conferences and trainings, and holding patient-mission focused Lunch and Learns. Additionally, we strive to attract and retain the most talented employees in the industry and across the globe by offering competitive compensation and benefits that support their health, financial and emotional well-being. Our compensation philosophy is based on rewarding each employee's individual contributions and striving to achieve equal pay for equal work regardless of gender, race or ethnicity. We use a combination of fixed and variable pay including base salary, bonuses, and share based compensation.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. On February 1, 2021, we changed our global headquarters from 1 Cedar Brook Drive, Cranbury, NJ 08512 to 3675 Market Street, Philadelphia, PA 19104 and our telephone number is 215-921-7600. Our website address is www.amicusrx.com. We make available free of charge on our website our annual, quarterly, and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the U.S. Securities and Exchange Commission.

Information relating to our corporate governance, including our Code of Business Conduct for Employees, Executive Officers and Directors, 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 under the "Investors — Corporate Governance" caption and in print to any stockholder upon request. Any waivers or material amendments to the Code will be posted promptly on our website.

ITEM 1A. RISK FACTORS

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

Risks Related to our Ability to Generate and Sustain Revenue

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

We have invested a significant portion of our efforts and financial resources in the development of Galafold[®] for the treatment of Fabry disease and rely upon sales of Galafold[®] primarily in Europe and growing sales in the U.S. and Japan. Our ability to generate material product revenues will depend heavily on the successful development, regulatory approval, and commercialization of Galafold[®]. We began the commercial launch of Galafold[®] in the E.U. and U.K. in May 2016, in Japan in June 2018 and in the U.S. in August 2018 and continue to seek commercial approval in additional foreign jurisdictions. Approvals have been granted in over 40 countries around the world. We will continue to study Galafold[®] in a confirmatory Phase 4 program and other supportive Phase 4 studies. If the results of the Phase 4 studies negatively change the benefit/risk profile of Galafold[®], the commercial success of Galafold[®] may be substantially diminished. Any adverse market event with respect to Galafold[®], including failure to obtain sufficient market acceptance, could have a material adverse effect on our business, financial condition and results of operations. If our sales of Galafold[®] were to decrease, or such sales were substantially or completely displaced in the market, or if we are unable to achieve sufficient market acceptance of Galafold[®] by physicians, patients, third-party payors and others in the medical community, or if we fail to receive commercial approval in any additional jurisdictions, it could have a material adverse effect on our business, financial condition and results of operations. In addition, if Galafold[®] or similar products from our competitors were to become the subject of litigation and/or an adverse governmental action requiring us or such competitors, as applicable, to cease sales of Galafold[®], such an event could have a material adverse effect on our business, financial condition and results of operations. In addition, the entry into the market of competitors with new or generic treatments, including oral, ERT and gene therapies, may erode the market for Galafold[®] and have a material impact on our business.

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

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

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

- effectively competing with other therapies, including potential generics and potential gene therapies;
- a continued acceptable safety profile of Galafold®;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting and enforcing our rights in our intellectual property portfolio;
- obtaining and maintaining a commercially viable price for our products; and
- continuing to successfully mitigate the impact of the COVID-19 pandemic.

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

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

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

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

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

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

- the applicable regulatory authority may determine that we did not properly oversee our clinical trials or follow the regulatory authority's advice or recommendations in designing and conducting our clinical trials;
- an advisory committee, if convened by the applicable regulatory authority, may recommend against approval of our application or may recommend that the applicable regulatory authority require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, or even if an advisory committee, if convened, makes a favorable recommendation, the respective regulatory authority may still not approve the product candidate;
- the applicable regulatory authority may only approve a limited label for less than the full indicated population, as a second line or rescue therapy, or impose other label restrictions; and
- the applicable regulatory authority may identify deficiencies in the chemistry, manufacturing, and control sections of our application, our manufacturing processes, facilities, or analytical methods or those of our third-party contract manufacturers, 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.

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

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

Factors that may inhibit our efforts to successfully commercialize Galafold®, or our product candidates, if and when they are approved by regulatory authorities, including the FDA, PMDA and EMA, on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- efforts by our competitors to commercialize products at or about the time when our product candidates would be coming to market.

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

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

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

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

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

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

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

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

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

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

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

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product, Galafold[®], and product candidates, including AT-GAA, and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology and gene therapy companies worldwide. For example, several large pharmaceutical and biotechnology companies currently market and sell products for the treatment of lysosomal storage disorders, including Fabry disease. These products include Sanofi Aventis' Fabrazyme[®] and Takeda's Replagal[®], as well as other Fabry treatment products in development. In addition, Sanofi markets and sells Myozyme[®] and Lumizyme[®] for the treatment of Pompe disease and has another product for Pompe in development, Neo-GAA. We are also aware of other enzyme replacement and substrate reduction therapies in development by third parties for Pompe, as well as potential gene therapies for both Fabry and Pompe and our other product candidates.

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

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

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

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

- different regulatory requirements for maintaining approval of drugs in foreign countries;
- reduced protection for contractual and intellectual property rights in some countries;
- unexpected changes in 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;
- the impact of BREXIT on regulatory standards and operations; and
- business interruptions resulting from geopolitical actions (including war and terrorism), pandemic diseases (such as the recent spread of COVID-19 “coronavirus”), or natural disasters (including earthquakes, typhoons, floods and fires).

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

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

In a referendum held in the U.K. on June 23, 2016, a majority of those voting voted for the U.K. to leave E.U., commonly referred to as "Brexit". On March 29, 2017, the U.K. government delivered to the European Council notice of its intention to leave the E.U. The negotiation period (under Article 50 of the Treaty on European Union) had been extended repeatedly; however, on January 24, 2020, the U.K. and the E.U. entered into a withdrawal agreement pursuant to which the U.K. formally left the E.U. on January 31, 2020. A transition period which ended on December 31, 2020, maintained access to the E.U. single market and to the global trade deals negotiated by the E.U. on behalf of its members and remain subject to E.U. law.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") is the U.K.'s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales and Scotland (together Great Britain, "GB"); broadly, Northern Ireland will continue to follow the E.U. regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published guidance on how various aspects of the U.K. regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period. The guidance covers clinical trials, marketing authorizations, importing, exporting and pharmacovigilance and is relevant to any business involved in the research, development or commercialization of medicines in the U.K. The new guidance was given effect via the Human Medicines Regulations ("Amendment etc.") ("E.U. Exit") Regulations 2019 (the "Exit Regulations"). The U.K. regulatory regime largely mirrors that of the E.U. but the MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing E.U. marketing authorizations for centrally authorized products were automatically converted ("grand fathered") into U.K. MAs free-of-charge on January 1, 2021. The ultimate impact of the "leave" vote is not clear as there are still some legal and practical uncertainties surrounding the regulation of medicines in the U.K. and a risk of potential disruption in the movement of goods, services and people between the U.K. and the E.U. Such uncertainties and disruptions could result in higher costs of conducting business in the U.K. and the E.U. and negatively affect our business, operations and financial condition.

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

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

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

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

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that may affect our ability to profitably sell our product and product candidates, if approved. The United States government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. The Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

There have been significant ongoing judicial, administrative, executive and legislative efforts to modify or eliminate the Affordable Care Act. For example, the Tax 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. The Trump administration issued executive orders which sought to reduce burdens associated with the Affordable Care Act and modified how it was implemented. Other legislative changes have been proposed and adopted since passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than \$1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, the 2% Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The Affordable Care Act has also been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court which heard oral arguments in the case on November 10, 2020. A ruling is expected in 2021.

Further changes to and under the Affordable Care Act remain possible, although the new Biden administration has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. President Biden indicated that he intends to undo changes to the Affordable Care Act made by the Trump administration and would advocate for legislation to build on the Affordable Care Act. It is unknown precisely what form any such changes or any law would take, and how or whether it may affect our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

We expect that the Affordable Care Act, as well as other healthcare reform measures that have and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for our product and product candidates, if approved, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain and maintain profitability of our product and product candidates, if approved.

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

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

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk when we commercially sell any products that we develop, including those which may arise from misuse or malfunction of, or design flaws in, such products, whether or not such problems directly relate to the products and services we have provided. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We have increased our insurance coverage for the commercialization of Galafold[®] and may increase insurance coverage when, and if, we begin commercializing any other product candidate that receives marketing approval. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. On occasion, large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or a series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our available cash and adversely affect our business.

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

In the U.S., after an NDA is approved, such as Galafold[®], the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA, or ANDA. The Federal Food, Drug, and Cosmetic Act, or the FD&C Act, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredients, dosage form, strength, route of administration, and conditions of use, or product labeling, as our product or product candidate and that the generic product is absorbed in the body at the same rate and to the same extent as, or is bioequivalent to, our product or product candidate. These generic equivalents would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to our product or product candidates, including Galafold[®], would substantially limit our ability to generate revenues and therefore to obtain a return on the investments we have made in our product or product candidates.

The Biologics Price Competition and Innovation Act, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act of 2010, or the ACA, Pub. L. No. 111-148 (2010). The BPCIA authorizes the FDA to approve "abbreviated" BLAs for products whose sponsors demonstrate they are "biosimilar" to reference products previously approved under BLAs, including AT-GAA, if approved. The FDA may also separately determine whether "biosimilar" products are "interchangeable" with their reference products. However, the FDA may not approve an "abbreviated" BLA for a biosimilar product until at least twelve years after the date on which the BLA for the reference product was approved. FDA approval of abbreviated BLAs could be further delayed if the reference products are subject to unexpired and otherwise valid patents.

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

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

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

We have historically been focused on the development and commercialization of Galafold[®], a small molecule for Fabry disease and in a next generation ERT treatment for Pompe disease, AT-GAA. In 2018, we also made a significant investment in potential gene therapies for Fabry, Pompe, CDD, Batten's disease and other LDs. Notwithstanding our large investment in gene therapies and Pompe ERT to date and anticipated future expenditures in related proprietary technologies, we have not yet developed, and may never successfully develop, any marketed drugs using ERT and gene therapy approaches. As a result of pursuing the development and commercialization of our product and product candidates using our proprietary and licensed technologies, we may fail to develop products or product candidates, or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates yet fail to yield product candidates for clinical development.

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

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

Undesirable side effects caused by our product, Galafold[®] or product candidates including AT-GAA, CLN6 and CLN3, could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA, EMA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product or product candidates and generating revenues from their sale. In addition, if we or others identify undesirable side effects caused by our products or product candidates after receipt of marketing approval:

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

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or product candidate or could substantially increase the costs and expenses of commercializing the product or product candidate, which in turn could delay or prevent us from generating significant revenues from its sale or adversely affect our reputation.

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

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

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

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

Non-compliance with E.U. and U.K. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the E.U.'s and U.K.'s requirements regarding the protection of personal information, which are effective as of May 25, 2018, can also lead to significant penalties and sanctions and business restrictions.

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

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

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

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

- The U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute to defraud any healthcare benefit program or specific intent to violate it in order to have committed a violation. This statute also may impose monetary penalties on any offers or transfers of remuneration to Medicare or Medicaid beneficiaries (patients) which is likely to influence the beneficiary's selection of particular supplier of government payable items. States, such as California have enacted their own privacy regulations and others may enact similar legislation. Similarly, the collection and use of personal health data in the E.U. is governed by the E.U. General Data Protection Regulation (the "GDPR"), with many requirements mandated by the GDPR for the consent of the individuals to whom the personal data relates, the information provided to the individuals, transfer of personal data within and outside of the E.U. and the security and confidentiality of the personal data. Enforcement of the GDPR began on May 25, 2018, and failure to comply with the requirements of the GDPR may result in substantial fines and other administrative penalties. The GDPR increases our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms ensuring compliance with the GDPR. This may be onerous and adversely affect our business, financial condition, results of operations and prospects;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- U.S. federal laws requiring drug manufacturers to report annually information related to certain payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, commonly known as the Sunshine Act, as well as other state and foreign laws regulating marketing activities and requiring manufacturers to report marketing expenditures, payments and other transfers of value to physicians and other healthcare providers. Similarly, payments made to physicians in certain E.U. member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual E.U. member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the E.U. member states. In addition, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the E.U. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment;
- U.S. federal government price reporting laws, which require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our marketed drugs. Participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, potential liability for the failure to report such prices in an accurate and timely manner, and potentially limit our ability to offer certain marketplace discounts;
- U.S. Foreign Corrupt Practices Act, which prohibit us and third parties working on our behalf from making payments to foreign government officials to assist in obtaining or retaining business. Specifically, the anti-bribery provisions of the FCPA prohibit the willful use of the mails or any means of instrumentality of interstate commerce corruptly in furtherance of any offer, payment, promise to pay, or authorization of the payment of money or anything of value to any person, while knowing that all or a portion of such money or thing of value will be offered, given or promised, directly or indirectly, to a foreign official to influence the foreign official in his or her official capacity, induce the foreign official to do or omit to do an act in violation of his or her lawful duty, or to secure any improper advantage in order to assist in obtaining or retaining business for or with, or directing business to, any person; and

- state and foreign equivalents of each of the above laws, including foreign anti-bribery and corruption laws and state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers; state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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

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

In addition, the regulatory pathways for gene therapies are evolving. In some cases, the FDA will approve gene therapies based on Phase 2 clinical trial data. If, however, the FDA decides we need to complete Phase 3 clinical trial(s), we may need to expend significantly more capital to pursue FDA approval of gene therapies. If we are required to conduct additional clinical trials or other testing of our product candidates, including AT-GAA, CLN6, CLN3 and other gene therapies, that we develop beyond those tests and trials that we contemplate; if we are unable to successfully complete our clinical trials or other testing; if the results of these trials or tests are not positive or are only modestly positive; or if there are safety concerns, we may:

- choose not to seek regulatory approval in the U.S., E.U., U.K. or other key jurisdictions;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements, safety strategies or restrictions, such as a requirement of a risk evaluation and mitigation strategy, or REMS; or
- have the product removed from the market after obtaining regulatory approval.

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

We may experience numerous unforeseen events during, or as a result of, clinical trials including ongoing clinical trials of AT-GAA, CLN6 and CLN3 that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including:

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

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

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

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

Patient enrollment is affected by other factors including:

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

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

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

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

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Our product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials. For some of our product candidates, we have no safety or efficacy data in humans. There can be no assurance that the results seen in preclinical studies for any product candidates, including CLN6 and CLN3 will result in success in clinical trials. When administered in humans, the product candidates may perform differently than in preclinical studies. Product candidates may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies or animal studies, and may interact with human biological systems in unforeseen, ineffective or harmful ways. We may be unable to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials.

Initial results from a clinical trial do not necessarily predict final results. We cannot be assured that these trials will ultimately be successful. In addition, patients may not be compliant with their dosing regimen or trial protocols or they may withdraw from the clinical trial at any time for any reason. For example, we have reported data from a Phase 1/2 clinical trial of AT-GAA in Pompe disease. The data is based on a small patient sample and therefore may not be predictive of future results. The Phase 3 PROPEL study results may not support further development, or 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-3 trial. Results from these initial patients may not be predictive of results of the full data set, we may not be able to demonstrate safety and efficacy and the FDA, EMA and other regulatory authorities may not accept this data as sufficient for approval. In addition, while the clinical trials of our product candidates are designed based on the available relevant information, in view of the uncertainties inherent in drug development, such clinical trials may not be designed with focus on indications, patient populations, dosing regimens, safety or efficacy parameters or other variables that will provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting product candidates. This is particularly the case for emerging gene therapies where we do not yet have a defined regulatory pathway and there can be no assurance that regulators in the U.S., E.U., U.K., Japan or other jurisdictions will accept the existing CLN-6, CLN-3 or other gene therapy clinical data sets for approval and without additional clinical trials or that future trials will support approvals. In addition, individual patient responses to the dose administered of a product candidate may vary in a manner that is difficult to predict. Also, the methods we select to assess particular safety or efficacy parameters may not yield statistical precision in estimating our product candidates' effects on study participants. Even if we believe the data collected from clinical trials of our product candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us or our partners, which could delay, limit or prevent regulatory approval.

In addition, certain of our product candidates are based on gene therapy technology. The product candidates in our gene therapy program are being developed for the treatment of diseases in which there is little clinical experience, which increases the difficulty in selecting appropriate endpoints and the risk that regulatory authorities may not consider the endpoints of clinical trials to provide clinically meaningful results. As a result, if the FDA requires different endpoints than the endpoints we anticipate using or have used in our clinical trials, or a different analysis of those endpoints, it may be more difficult for us to obtain, or we may be delayed in obtaining, FDA approval of our product candidates. If we are not successful in commercializing any of our products or product candidates, or are significantly delayed in doing so, our business will be materially harmed.

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

Regulatory authorities in some jurisdictions, including the E.U., U.K., and the U.S., may designate drugs for relatively small patient populations as orphan drugs. We obtained orphan drug designations from the FDA for Galafold[®] for the treatment of Fabry disease in February 2004. We also obtained orphan medicinal product designation in the E.U. and U.K. for Galafold[®] in May 2006. AT-GAA has also received this designation from the FDA, EMA, and, in 2020, from PMDA. Our competitors have also received orphan designation. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which, subject to certain exceptions, precludes the EMA from approving another marketing application for a similar medicinal product or the FDA from approving another marketing application for the same drug for the same indication for that time period. The FDA defines "same drug" as a drug or biologic that contains the same active moiety and is intended for the same use. The applicable market exclusivity period for orphan drugs is ten years in the E.U. and U.K. and seven years in the U.S. The E.U. and U.K. exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified.

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

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

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

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

In order to market and sell our products in Europe and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, some countries outside the U.S. require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We may not obtain marketing, pricing or reimbursement approvals outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Regulatory approvals in countries outside the U.S. do not ensure pricing approvals in those countries or in any other countries, and regulatory approvals and pricing approvals do not ensure that reimbursement will be obtained.

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

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

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

In February 2021, we announced topline data results from the AT-GAA Phase 3 Propel Study and our intention to both complete the rolling BLA submission to the FDA and seek additional approvals worldwide. While we believe the results of the trial will permit successful regulatory submissions, and labels to support broad use and favorable pricing and reimbursement, there is no guarantee that the FDA or any other regulatory authority will accept our filings, or if accepted, subsequently grant AT-GAA marketing approval, or if approved will receive favorable pricing or reimbursement.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Regulatory authorities may determine that AT-GAA is 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. If AT-GAA fails to receive marketing approval, is significantly delayed in receiving marketing approval or if the approved labeling is not as expected, AT-GAA may fail to receive market acceptance, receive reimbursement or be able to generate material revenue, any of which could substantially harm our future business.

Risks Related to our Preclinical Product Candidates

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

Only a few gene therapy products have been approved in the U.S., E.U., and U.K. We have acquired the rights to many potential gene therapies and are focusing a substantial effort in our research and development efforts on these gene therapy platforms, and our future success depends on the successful development of these therapeutic approaches. There can be no assurance that any development problems we experience in the future related to our gene therapies will not cause significant delays or unanticipated costs, or that such development problems can be solved. In addition, the clinical study requirements of the FDA, the EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as our gene therapies can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. The number of gene therapy products approved in the Western world is rapidly increasing. Approved products include Spark's gene therapy product, which received approval from the FDA in 2017, GlaxoSmithKline's Strimvelis, and Novartis's and Gilead's CAR-T therapies, which received approval from the FDA in 2017, Avexis's Zolgensma which received FDA approval in 2019, Bluebird Bio's Zynteglo which received E.U. and U.K. approval in 2019, and Juno Therapeutic's CAR-T therapy, Breyanzi, which received approval in 2021. Given the few precedents of approved gene therapy products, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the U.S., the E.U., the U.K. or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval. Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In addition, the FDA can put an investigational new drug application, or IND, on clinical hold if the information in an IND is not sufficient to assess the risks in patients or a safety issue emerges in preclinical or clinical studies. Before a clinical study can begin at any institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval studies, limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

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

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

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

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 and gene therapy products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. In particular, the manufacture of our biologic product candidate ATB200 for Pompe, is highly complex and we may encounter difficulties in production. These problems include difficulties with production costs and yields and quality control, including stability of the product or product candidate. Further, our gene therapies may require new or specialized manufacturing with limited third-party manufacturers available to provide these services. The occurrence of any of these problems could significantly delay our clinical trials or the commercial availability of our product or product candidates.

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

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

- reliance on the third party for regulatory compliance and quality assurance;
- limitations on supply availability resulting from capacity and scheduling constraints of the third parties;
- inability to manufacture product that meets the regulatory requirements for product approval;
- inability to manufacture batches that meet specifications and quality standards;
- inability to hire and retain the skilled workers necessary to manufacture our products;
- impact on our reputation in the marketplace if manufacturers of our products, once commercialized, fail to meet the demands of our customers;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

The FDA and regulatory authorities in other jurisdictions require our contract manufacturers to comply with cGMP regulations. These regulations cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our product candidates and any products that we may commercialize, including Galafold[®], AT-GAA, and our gene therapy product candidates.

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

If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

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

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

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

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

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

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

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

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

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product or product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

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

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

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

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

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

We currently rely on WuXi App Tec Biopharmaceuticals, a company based in the People's Republic of China (the "PRC"), as the sole supplier of our biologic product, ATB200. Accordingly, there is a risk that supplies of our product may be significantly delayed by or may become unavailable as a result of manufacturing, equipment, process, or business-related issues affecting that company. We may also face additional manufacturing and supply-chain risks due to the regulatory and political structure of the PRC, or as a result of the international relationship between the PRC and the U.S. or any of the other countries in which our products are marketed. In addition, the recent out-breaks of SARS, COVID-19 "coronavirus" or other similar illnesses in PRC could impact operations at Wuxi. Although currently there has been no impact on operations and we and Wuxi have robust mitigation plans in place, there can be no assurance that operations would not be impacted in the future with a negative impact on supply of our product.

Risks Related to our Financial Position

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

To date, we have focused on developing and commercializing our first product, Galafold[®], and our pipeline product AT-GAA as well as our multiple gene therapies. Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. Although the European Commission, PMDA and FDA have granted approval for Galafold[®], for the treatment of adults with a confirmed diagnosis of Fabry disease and who have an amenable genetic variant, and we are generating product sales, we continue to incur significant research, development, commercialization and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. For the year ended December 31, 2020, we have a net loss of \$276.9 million, and we have an accumulated deficit of \$2.0 billion at December 31, 2020.

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, including Galafold[®] and AT-GAA in the U.S., the E.U., U.K., Japan and other foreign countries, as applicable;
- conduct additional clinical trials to support the full approval of Galafold[®] in the U.S. and post-approval commitments or trials;
- continue communicating with the EMA, as necessary, regarding post-marketing requirements and clinical trials for Galafold[®];
- continue to or initiate the regulatory submission process for marketing approval of Galafold[®] outside of the U.S. and E.U. and other foreign jurisdictions where approved, as applicable;
- build and maintain our commercial infrastructure so that it is capable of supporting product sales, marketing and distribution of Galafold[®] and our other product candidates in Europe, Japan and the U.S. or other territories in which we have received or may receive regulatory approval;
- prepare for launch of AT-GAA in the U.S., E.U., U.K. and other jurisdictions if approved by regulators;
- continue our preclinical studies and clinical trials on our gene therapies for Fabry, Pompe, Batten's, MPS and other LDs; and
- continue our preclinical studies of and potentially conduct clinical studies of ERT and gene therapy for CDD.

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

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

We began the commercial launch of our first product, Galafold[®], in May 2016, with the U.S. and Japan commercial launches in 2018 and are now approved in 40 countries. Our ability to generate material revenue and become profitable depends upon our ability to successfully commercialize our existing product and product candidates, or product candidates that we may in-license or acquire in the future. Even if we are able to successfully achieve regulatory approval for our product candidates, including AT-GAA, we do not know when any of these product candidates will generate revenue for us, if at all and we may not meet our current revenue and operating expense guidance. Our ability to generate revenue from our current or future product and product candidates depends on a number of factors, including our ability to:

- successfully complete development activities and obtain additional regulatory and pricing and reimbursement approvals for, and continue to successfully commercialize, Galafold[®];
- 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 Galafold[®] 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 our gene therapies;
- complete and submit regulatory submissions to the FDA, EMA, MHRA, PDMA and others and obtain regulatory approval for our product candidates including AT-GAA and our gene therapies; and
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities.

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

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

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

Our operations have consumed substantial amounts of cash. We expect to continue to spend substantial amounts to advance the preclinical and clinical development of our product candidates, and launch and commercialize our product and product candidates for which we may receive regulatory approval, including continuing to build our own commercial organization. We believe that our current cash position, including expected Galafold[®] revenues, is sufficient to fund ongoing Fabry and Pompe, and gene therapy program operations to achieve self-sustainability without the need for future dilutive financing. Potential future business development collaborations, restructurings, pipeline expansion, and investment in biologics or gene therapy manufacturing capabilities could impact our future capital requirements. However, we may require substantial additional capital for the development and commercialization of our product and further development and commercialization of our product candidates.

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

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

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

- the costs of commercialization activities, including maintaining sales, marketing, and distribution capabilities for Galafold[®] and any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own, including AT-GAA;
- the scope, progress, results, and costs of preclinical development, laboratory testing, and clinical trials for our product candidates and any other product candidates that we may in-license or acquire;
- the cost of manufacturing drug supply for our preclinical studies, clinical trials, and commercial supply, including the significant cost of manufacturing AT-GAA and our gene therapies;
- the 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 including AT-GAA;
- the cost of filing, prosecuting, defending, and enforcing any patent claims and other intellectual property rights;
- the cost and timing of completion of existing or expanded commercial-scale outsourced manufacturing activities;
- the cost of defending any claims asserted against us;
- the emergence of competing technologies and other adverse market developments;
- the extent to which we acquire or invest in additional businesses, products, and technologies.

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

We may seek additional capital through a combination of private and public equity offerings, debt financings, receivables or royalty financings, strategic collaborations and alliances, restructuring and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt, receivables, and royalty financings may be coupled with an equity component, such as warrants to purchase stock, which could also result in dilution of our existing stockholders' ownership. The incurrence of additional indebtedness beyond our existing indebtedness with the remaining convertible note holders and Senior Secured Term Loan due 2026 could also result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur further debt, limitations on our ability to acquire or license intellectual property rights, and other operating restrictions that could have a material adverse effect on our ability to conduct our business and may result in liens being placed on our assets and intellectual property. If we were to default on any of our indebtedness, we could lose such assets and intellectual property. If we raise additional funds through strategic collaborations and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to Galafold® 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% 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% 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 our common stock, par value \$0.01 per share, or a combination thereof and may be settled.

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

In July 2020, we entered into the Senior Secured Term Loan due 2026 for a \$400 million credit facility with Hayfin Capital Management, with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum that requires interest-only payments until mid-2024 and matures in six years in 2026. We received net proceeds of \$385.9 million in July 2020, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. The Senior Secured Term Loan due 2026 contains a minimum liquidity covenant of \$75 million, tested monthly and in effect at all times, and an incremental minimum consolidated revenue covenant, measured as of the previous four consecutive fiscal quarters. The minimum consolidated revenue covenant ranges from \$140 million, beginning March 31, 2021, and peaks at \$225 million by June 30, 2023, continuing at that level until the loan is repaid.

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

Foreign currency exchange rate fluctuations could harm our financial results.

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

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

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

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

As of December 31, 2020, we had federal and state net operating loss carry forwards ("NOLs") of approximately \$1,156 million and \$889.4 million respectively. The federal carry forward for losses generated prior to 2018 will expire in 2029 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the 2017 Tax Act. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2020 will expire in 2029 through 2040. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended (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.

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 35.5% of our common stock as of December 31, 2020. As a result, if these stockholders were to choose to act together, they would be able to exert significant influence and control over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could influence the election of directors and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization. This concentration of voting power could delay or prevent an acquisition of us on terms that other stockholders may desire. The interests of this group of stockholders may not always coincide with the interests of other stockholders, and they may act, whether by meeting or written consent of stockholders, in a manner that advances their best interests and not necessarily those of other stockholders, including obtaining a premium value for their common stock, and might affect the prevailing market price for our common stock.

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

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

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

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission. We believe that any disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations reflect the reality that judgments can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Risks Related to our Intellectual Property

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

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

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

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

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

In addition, we cannot be assured that any of our pending patent applications will result in issued patents. In particular, we have filed patent applications in the U.S., the European Patent Office and other countries outside the U.S. that have not been issued as patents. These pending applications include, among others, some of the patent applications for ATB200, Galafold[®], and our gene therapy platforms and product candidates. If patents are not issued in respect of our pending patent applications, we may not be able to stop competitors from marketing similar products in Europe and other countries in which we do not have issued patents.

The patents that we have licensed from Mt. Sinai School of Medicine relating to use of Galafold[®] to treat Fabry disease expired in 2018 in the U.S. and expired in 2019 in all other jurisdictions. In addition to patent protection outside of the U.S., we intend to seek orphan medicinal product designation of our product candidates and to rely on statutory data exclusivity provisions in jurisdictions outside the U.S. where such protections are available, including Europe. The patent rights that we own or have licensed relating to our product candidates are limited in ways that may affect our ability to exclude third parties from competing against us if we obtain regulatory approval to market these product candidates. In particular:

- We do not hold composition of matter patents covering Galafold[®] but we have several method of treatment patents issued and listed. We do have composition of matter patents, method of manufacture and other patents issued for ATB200. We also have several pending applications covering Galafold[®], ATB200 and gene therapy. There can be no assurance that these applications will be allowed or that allowed applications will be issued or that the scope of such patents, if they issue, will be sufficient to protect our product. Composition of matter patents can provide protection for pharmaceutical products to the extent that the specifically covered compositions are important. For our product candidates for which we do not hold composition of matter patents, competitors who obtain the requisite regulatory approval can offer products with the same composition as our products so long as the competitors do not infringe any method of use patents that we may hold.
- For some of our product candidates the principal patent protection that covers or those we expect will cover our product candidate is a method of use patent. This type of patent only protects the product when used or sold for the specified method. However, this type of patent does not limit a competitor from making and marketing a product that is identical to our product that is labeled for an indication that is outside of the patented method, or for which there is a substantial use in commerce outside the patented method.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

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

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

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

We are a party to license agreements with Nationwide Children's Hospital ("Nationwide Children's") and University of Pennsylvania ("Penn") pursuant to which we license key intellectual property relating to our gene therapy product candidates. We expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will impose, various diligences, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

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

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

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

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

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

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

Risks Related to the COVID-19 Pandemic

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

The COVID-19 pandemic has substantially burdened healthcare systems worldwide which may impact progression of our clinical trials, development and manufacturing of our product and product candidates and continued commercialization of Galafold®. Required inspections and reviews by regulatory agencies may also be delayed due to the focus of resources on COVID-19 as well as travel and other restrictions. Significant delays in the timing of our clinical trials and in regulatory reviews could adversely affect our ability to commercialize some assets in our product pipeline. Lack of normal access by patients to the healthcare system, along with concern about the continued supply of medications, may result in changes in buying patterns throughout the supply chain, including by patients, which could increase or decrease demand for our products. Similarly, we have temporarily halted in-person interactions by our employees with healthcare providers, which may decrease demand for our products. COVID-19 could also have an adverse impact on our supply chain and distribution systems, which could impact our ability to distribute our products and the ability of third parties on which we rely to fulfill their obligations to us, increase our expenses and have a material adverse effect on our ability to generate revenue. In addition, the conditions created by the pandemic may intensify other risks inherent in our business, including, among other things, risks related to drug pricing and access, intellectual property protection, product safety and efficacy concerns, product liability and other litigation, and the impact of adverse global and local economic conditions.

As a result, while the financial impact on us has not been material to date, given the rapid and evolving nature of the virus, COVID-19 could negatively affect our results of operations, financial condition, liquidity and cash flows in future periods, perhaps materially. The degree to which COVID-19 affects us will depend on developments that are highly uncertain and beyond our knowledge or control, including, but not limited to, the duration and severity of the pandemic, the actions taken to

reduce its transmission, and the speed with which, and extent to which, more stable economic and operating conditions resume. Should the COVID-19 pandemic and any associated mitigation measures, recession or depression continue for a prolonged period, our results of operations, financial condition, liquidity, and cash flows could be materially impacted by lower revenues and profitability and a lower likelihood of effectively and efficiently developing and launching new products.

Risks Related to Employment, Environmental, Social and Governance Matters

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

We are highly dependent on John F. Crowley, our Chairman and Chief Executive Officer, Bradley L. Campbell, our President and Chief Operating Officer, and Daphne Quimi, our Chief Financial Officer. These executives each have significant pharmaceutical industry experience. The loss of the services of any of these executives might impede the achievement of our research, development and commercialization objectives and materially adversely affect our business and we may not be able to replace these executives with candidates with similar background and experience in the event of the loss of their services. We do not maintain "key person" insurance on Mr. Crowley or on any of our other executive officers.

Recruiting and retaining qualified scientific, clinical and sales and marketing personnel will also be critical to our success, including our Research and Gene Therapy Center of Excellence in Philadelphia. In addition, maintaining a qualified finance and legal department is key to our ability to meet our regulatory obligations as a public company and important in any potential capital raising activities. Our industry has experienced a high rate of turnover in recent years. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, particularly in New Jersey and Philadelphia and their surrounding areas. Although we believe we offer competitive salaries and benefits, we may have to increase spending in order to retain personnel. If we fail to retain our remaining qualified personnel or replace them when they leave, we may be unable to recruit replacements nor continue our development and commercialization activities.

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

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

As of December 31, 2020, we had 483 full-time employees. As our development and commercialization strategies develop, we will need additional managerial, operational, sales, marketing, financial, technical operations and other resources. Our management, personnel and systems currently in place may not be adequate to support this future growth. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our existing or future product candidates and we may not be able to replace key personnel in the event of turnover. Future growth would impose significant added responsibilities on members of management, including:

- managing the development and commercialization of any product candidates approved for marketing;
- overseeing our ongoing preclinical studies and clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees, including any sales and marketing personnel engaged in connection with the commercialization of any approved product;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- managing our collaboration partners and associated joint steering committees;
- managing any clinical or commercial collaborations with third parties;
- improving our managerial, development, operational and financial systems and procedures;

- monitoring and improving diversity, inclusion and pay-equity initiatives;
- developing our compliance infrastructure and processes to ensure compliance with regulations applicable to public companies;
- developing biologics and gene therapy manufacturing expertise; and
- expanding our facilities.

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

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

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

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

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

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

Our ability to identify, manage and respond to the various risks related to our business is largely dependent on our established and maintained compliance, risk, audit and reporting systems and procedures. The Board of Directors has ultimate responsibility for risk oversight of the Company and carries out this duty through its Committees. Our Audit and Compliance Committee, Nominating and Corporate Governance Committee, Compensation and Leadership Development Committee and Science and Technology Committee have each been delegated oversight authority by the Board of Directors with respect to

issues in their applicable areas of expertise. These committees are responsible for identifying, monitoring and reporting areas of concern to the full Board of Directors. At the Company level, our senior management team similarly monitors risk through the Global Risk Committee, which is co-chaired by our Chief Compliance Officer and President and Chief Operating Officer. Membership of the Global Risk Committee consists primarily of key department heads who are asked to bring to such committee relevant items for discussion that they or their teams have identified at the numerous sub-committees these individuals chair or attend. The Global Risk Committee then uses this information to develop an Enterprise Risk Management Program, which identifies key risks and mitigation strategies and which is reported directly to the Audit and Compliance Committee on a quarterly basis, and to the full Board of Directors on a yearly basis. Our international business segment also has its own companion committee which operates in substantially the same way as the Global Risk Committee and reports key risks to the Global Risk Committee for inclusion in the Enterprise Risk Management Program.

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

General Risk Factors

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

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

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

As part of our business strategy, we may continue to pursue acquisitions or licenses of assets or businesses, or strategic alliances and collaborations, to expand our existing technologies and operations, such as our acquisition of Celenex in 2018 and the research collaboration with Penn to develop gene therapies in 2018 and expanded in 2019. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any such transaction, any of which could have a detrimental effect on our financial condition, results of operations, and cash flows. We may not be able to find suitable acquisition or licensing candidates, and if we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business and we may incur additional debt or assume unknown or contingent liabilities in connection therewith. Integration of an acquired company or assets may also disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, especially the acquisition of commercial assets, and require management resources that would otherwise focus on developing our existing business. We may not be able to find suitable collaboration partners or identify other investment opportunities, and we may experience losses related to any such investments.

To finance any acquisitions, licenses or collaborations, we may choose to issue debt or shares of our common stock as consideration. Any such issuance of shares would dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may not be able to acquire other assets or companies or fund a transaction using our stock as consideration.

Alternatively, it may be necessary for us to raise additional funds for acquisitions through public or private financings. Additional funds may not be available on terms that are favorable to us, or at all.

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

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

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

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

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

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

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

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

In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks stated above could have a material adverse effect on the market price of our common stock.

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

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Certain holders of our common stock have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered on a Form S-8 registration statement all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. In addition, certain of our employees, executive officers and directors have entered into, or may enter into, Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

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

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

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

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

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

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

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

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

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

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

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

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

As we continue to increase the size of our workforce, the risk of potential employment-related claims will also increase. As such, we may be subject to claims, allegations or legal proceedings related to employment matters including, but not limited to, discrimination, harassment (sexual or otherwise), wrongful termination or retaliation, local, state or federal labor law violations, injury, and wage violations. In the event we are subject to one or more employment-related claims, allegations or legal proceedings, we may incur substantial costs, losses or other liabilities in the defense, investigation, settlement or other disposition of such claims. In addition to the economic impact, we may also suffer reputational harm as a result of such claims, allegations and legal proceedings and the investigation, defense and prosecution of such claims, allegations and legal proceedings could cause substantial disruption in our business and operations. While we do have policies and procedures in place to reduce our exposure to these risks, there can be no assurance that such policies and procedures will be effective or that we will not be exposed to such claims, allegations or legal proceedings.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

The following table contains information about our current significant leased properties as of December 31, 2020.

Location	Approximate Square Feet	Use	Lease expiry date ⁽¹⁾
Philadelphia, Pennsylvania, U.S. ⁽²⁾	50,816	Office and laboratory	September 2044
Cranbury, New Jersey, U.S. ⁽²⁾	90,000	Office and laboratory	March 2021
Marlow, United Kingdom	36,796	Office	August 2028
Princeton, New Jersey, U.S.	21,922	Office	January 2022

⁽¹⁾ Includes renewal options on leases which we are reasonably certain to exercise.

⁽²⁾ On February 1, 2021, we changed our global headquarters from Cranbury, NJ to Philadelphia, PA.

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

Item 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

Item 4. MINE SAFETY DISCLOSURES

None.

PART II

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

Market for Our Common Stock

Our common stock has been traded on the NASDAQ Global Market under the symbol "FOLD" since May 31, 2007. Prior to that time, there was no public market for our common stock. The closing price for our common stock as reported by the NASDAQ Global Market on February 19, 2021 was \$12.22 per share. As of February 19, 2021, there were 21 holders of record of our common stock.

Dividends

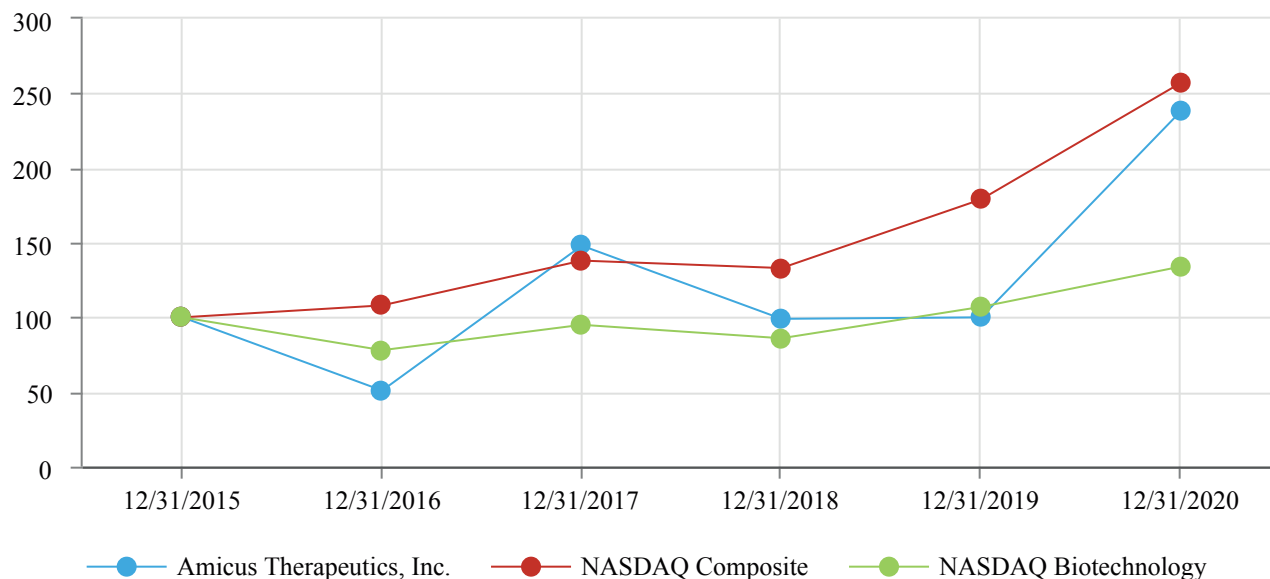
We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance the development and growth of our business. We do not intend to declare or pay cash dividends to our stockholders in the foreseeable future.

Recent Sales of Unregistered Securities

We did not sell any equity securities during the fiscal year ended December 31, 2020 in transactions that were not registered under the Securities Act.

Performance Graph

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



	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019	12/31/2020
Amicus Therapeutics, Inc.	\$100	\$51	\$148	\$99	\$100	\$238
NASDAQ Composite	\$100	\$108	\$138	\$133	\$179	\$257
NASDAQ Biotechnology	\$100	\$78	\$95	\$86	\$107	\$134

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

Issuer Purchases of Equity Securities

The following table provides certain information with respect to purchase of our common stock during the three months ended December 31, 2020:

Period	Total Number of Shares Purchased ⁽¹⁾	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares That May Yet Be Purchased Under the Plans or Programs
October 1, 2020 through October 31, 2020	11,654	\$ 15.98	—	—
November 1, 2020 through November 30, 2020	3,632	\$ 21.75	—	—
December 1, 2020 through December 31, 2020	10,306	\$ 23.80	—	—
Total	25,592	\$ 19.95	—	—

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

Item 6. SELECTED FINANCIAL DATA

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

	Years Ended December 31,				
	2020	2019	2018	2017	2016
Net product sales	\$ 260,886	\$ 182,237	\$ 91,245	\$ 36,930	\$ 4,958
Cost of goods sold	31,044	21,963	14,404	6,236	833
Gross profit	229,842	160,274	76,841	30,694	4,125
Operating expenses:					
Research and development	308,443	286,378	270,902	149,310	104,793
Selling, general, and administrative	156,407	169,861	127,200	88,671	71,151
Changes in fair value of contingent consideration payable	3,144	3,297	3,300	(234,322)	6,760
Loss on impairment of assets	—	—	—	465,427	—
Restructuring charges	—	—	—	—	69
Depreciation and amortization	8,846	4,775	4,216	3,593	3,242
Total operating expenses	476,840	464,311	405,618	472,679	186,015
Loss from operations	(246,998)	(304,037)	(328,777)	(441,985)	(181,890)
Other income (expense):					
Interest income	3,226	10,249	10,461	4,096	1,602
Interest expense	(22,425)	(18,872)	(22,402)	(17,240)	(5,398)
Loss on exchange of convertible notes	—	(40,624)	—	—	—
Loss on extinguishment of debt	(7,276)	—	—	—	(13,302)
Change in fair value of derivatives	—	—	(2,739)	—	—
Other (expense) income	(781)	(2,626)	(5,632)	6,008	(4,793)
Loss before income tax	(274,254)	(355,910)	(349,089)	(449,121)	(203,781)
Income tax (expense) benefit	(2,598)	(478)	94	165,119	3,739
Net loss attributable to common stockholders	\$ (276,852)	\$ (356,388)	\$ (348,995)	\$ (284,002)	\$ (200,042)
Net loss attributable to common stockholders per common share — basic and diluted	\$ (1.07)	\$ (1.48)	\$ (1.88)	\$ (1.85)	\$ (1.49)
Weighted-average common shares outstanding — basic and diluted	258,867,380	240,421,001	185,790,021	153,355,144	134,401,588

Balance Sheet Data (in thousands)

	As of December 31,				
	2020	2019	2018	2017	2016
Cash, cash equivalents, and marketable securities	\$ 483,269	\$ 452,740	\$ 504,152	\$ 358,562	\$ 330,351
Working capital	449,793	391,261	464,971	321,925	229,105
Total assets	886,520	850,207	789,951	627,024	1,036,845
Total liabilities	600,140	373,782	447,039	274,174	676,694
Accumulated deficit	(2,045,462)	(1,768,610)	(1,412,222)	(1,063,610)	(779,608)
Total stockholders' equity	286,380	476,425	342,912	352,850	360,151

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

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We have a portfolio of product opportunities led by the first, oral monotherapy for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease, and an industry leading rare disease gene therapy portfolio.

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cripaglucoisidase alfa/miglustat), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the U.S. Food and Drug Administration ("FDA") granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. We initiated the rolling Biologic License Application ("BLA") submission to the FDA in the fourth quarter of 2020.

We initiated ATB200-03 (or "PROPEL"), a global Phase 3 clinical study of AT-GAA in adult patients with late onset Pompe disease in December 2018 and completed last patient, last visit in December 2020. In February 2021, we reported topline results from the Phase 3 PROPEL study.

Patients enrolled in PROPEL were randomized 2:1 so that for every two patients randomized to be treated with AT-GAA, one was randomized to be treated with alglucosidase alfa. Of the Pompe patients enrolled, 77% were being treated with alglucosidase alfa (n=95) immediately prior to enrollment ("Switch") and 23% had never been treated with any ERT (n=28) ("Naïve"). 117 patients completed the PROPEL study and all 117 voluntarily enrolled in the long-term extension study.

The primary endpoint of the study was the mean change in 6-minute walk distance as compared with baseline measurements at 52 weeks across the combined ERT Switch and ERT Naïve patient populations. In this combined population patients taking AT-GAA (n=85) walked on average 21 meters farther at 52 weeks compared to 7 meters with those treated with alglucosidase alfa (n=37). This primary endpoint in the combined population was assessed for superiority and while numerically greater, statistical significance for superiority on this combined population was not achieved for the AT-GAA arm as compared to the alglucosidase alfa arm (p=0.072).

Per the hierarchy of the statistical analysis plan, the first key secondary endpoint of the study was the mean change in percent-predicted Forced Vital Capacity ("FVC") at 52 weeks across the combined population. In this combined population patients taking AT-GAA demonstrated a nominally statistically significant and clinically meaningful difference for superiority over those treated with alglucosidase alfa. AT-GAA significantly slowed the rate of respiratory decline in patients after 52 weeks. Patients treated with AT-GAA showed a 0.9% absolute decline in percent-predicted FVC, compared to a 4.0% absolute decline in the alglucosidase alfa arm (p=0.023).

Patients within the combined study population demonstrated statistically significant improvements on the GSGC ("Gait, Stairs, Gower's Chair") key secondary endpoint, which captures strength, coordination and mobility, compared to a worsening for alglucosidase alfa treated patients in the overall population (p<0.05). Additionally, lower MMT (Manual Muscle Testing), Patient-Reported Outcomes Measurement Information System ("PROMIS") physical function and PROMIS fatigue secondary endpoints favored AT-GAA treated patients over alglucosidase alfa treated patients. Results also showed improvements in the two important biomarker endpoints of Pompe disease (Hex-4 and CK), which significantly favored AT-GAA compared to alglucosidase alfa (p<0.001). AT-GAA demonstrated a similar safety profile to alglucosidase alfa.

The PROPEL Switch patients entered the study having been treated with alglucosidase alfa for a minimum of two years. More than two thirds (67%+) of those patients had been on ERT treatment for more than five years prior to entering the PROPEL study (mean of 7.4 years). A pre-specified analysis of the patients switching from alglucosidase alfa on 6-minute walk

distance showed that after 52 weeks from switching, AT-GAA treated patients (n=65) walked 16.9 meters farther than their baseline, compared to 0.0 meters for those patients who were randomized to remain on alglucosidase alfa (n=30) (p=0.046).

A pre-specified analysis of the patients switching from alglucosidase alfa on percent-predicted FVC showed that AT-GAA treated patients stabilized and slightly improved their respiratory function on this important measure while those patients remaining on alglucosidase alfa continued to significantly decline in respiratory muscle function. AT-GAA patients showed a 0.1% absolute increase in percent-predicted FVC while the alglucosidase alfa patients showed a 4.0% absolute decline over the course of the year (p=0.006).

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

We have established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children's Hospital ("Nationwide Children's") and an expanded collaboration with the University of Pennsylvania ("Penn"). Our pipeline includes gene therapy programs in rare, neurologic lysosomal disorders ("LDs"), specifically: CLN6, CLN3, and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Mucopolysaccharidosis Type IIIB ("MPS IIIB"), as well as a next generation program in Mucopolysaccharidosis Type IIIA ("MPS IIIA"). Our expanded collaboration with Penn also provides us with exclusive disease-specific access and the option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. In the first quarter of 2020, the FDA granted Fast Track designation to the CLN3 Batten disease gene therapy, AT-GTX-502, for the treatment of pediatric patients less than 18 years of age. In September 2020 and February 2021, the European Medicines Agency granted Priority Medicines ("PRIME") designation and the FDA granted Fast Track Designation, respectively, to the CLN6 Batten disease gene therapy, AT-GTX-501, for the treatment of patients with variant late infantile neuronal ceroid lipofuscinosis 6 ("vLINCL6").

In July 2020, we entered into a definitive agreement for a \$400 million credit facility with Hayfin Capital Management ("Senior Secured Term Loan due 2026") with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum and requires interest-only payments until mid-2024 and matures in six years in 2026. This transaction resulted in net proceeds of \$385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. Additionally, we used \$156.3 million of the proceeds to voluntarily settle the principal amount, accrued interest, and early settlement premiums of the Senior Secured Term Loan with BioPharma Credit PLC that was due in 2023 ("Senior Secured Term Loan due 2023").

Our operations have not been significantly impacted from the novel coronavirus ("COVID-19") pandemic in 2020; however, we observed increased lag times between patient identification and Galafold[®] initiation due to the resurgence of COVID-19 in the fourth quarter. We have maintained operations in all geographies, secured our global supply chain for our commercial and clinical products, as well as maintained the operational integrity of our clinical trials, with minimum disruptions. Our ability to continue to operate without any significant disruptions will depend on the continued health of our employees, the ongoing demand for Galafold[®] and the continued operation of our global supply chain. We have continued to provide uninterrupted access to medicines for those in need of treatment, while prioritizing the health and safety of our global workforce. However, our results of operations in future periods may be negatively impacted by unknown future impacts from the COVID-19 pandemic.

Consolidated Results of Operations

The following section generally discusses 2020 and 2019 items and year-to-year comparisons between 2020 and 2019. Discussions of 2018 items and year-to-year comparisons between 2019 and 2018 that are not included in this Form 10-K can be found in Part II, Item 7 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which comparisons are hereby incorporated by reference.

Year Ended December 31, 2020 Compared to Year Ended December 31, 2019

The following table provides selected financial information for the Company:

(in thousands)	Years Ended December 31,		
	2020	2019	Change
Net product sales	\$ 260,886	\$ 182,237	\$ 78,649
Cost of goods sold	31,044	21,963	9,081
Cost of goods sold as a percentage of net product sales	11.9 %	12.1 %	(0.2)%
Operating expenses:			
Research and development	308,443	286,378	22,065
Selling, general, and administrative	156,407	169,861	(13,454)
Changes in fair value of contingent consideration payable	3,144	3,297	(153)
Depreciation and amortization	8,846	4,775	4,071
Other income (expense):			
Interest income	3,226	10,249	(7,023)
Interest expense	(22,425)	(18,872)	(3,553)
Loss on exchange of convertible notes	—	(40,624)	40,624
Loss on extinguishment of debt	(7,276)	—	(7,276)
Other expense	(781)	(2,626)	1,845
Income tax expense	(2,598)	(478)	(2,120)
Net loss attributable to common stockholders	<u>\$ (276,852)</u>	<u>\$ (356,388)</u>	<u>\$ 79,536</u>

Net Product Sales. Net product sales increased \$78.6 million during the year ended December 31, 2020 compared to the same period in the prior year. The increase was primarily due to continued growth in the Europe, U.S. and Japan markets.

Cost of Goods Sold. Cost of goods sold includes manufacturing costs as well as royalties associated with sales of our product. Cost of goods sold as a percentage of net product sales was 11.9% during the year ended December 31, 2020 compared to 12.1% during the same period in the prior year primarily due to the proportion of sales in countries subject to a higher royalty burden.

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

(in thousands)	Years Ended December 31,	
Projects	2020	2019
Third-party direct project expenses		
Galafold [®] (Fabry Disease)	\$ 12,399	\$ 19,598
AT-GAA (Pompe Disease)	112,733	103,884
Gene therapy programs	64,834	39,836
Pre-clinical and other programs	2,381	1,915
Total third-party direct project expenses	192,347	165,233
Other project costs		
Personnel costs	84,607	81,496
Other costs	31,489	39,649
Total other project costs	116,096	121,145
Total research and development costs	<u>\$ 308,443</u>	<u>\$ 286,378</u>

The \$22.1 million increase in research and development costs was primarily due to increases in gene therapy programs driven by the pipeline growth, and clinical research and manufacturing costs with the advancement and enrollment of clinical studies in the Pompe program, and an increase in personnel costs primarily due to realignment with strategic priorities. These increases were partially offset by a decrease in expense associated with the ongoing regulatory requirements, approval in new geographies, and pediatric and other studies to support label expansion of Galafold[®] and a decrease in other costs, primarily driven by reduced employee travel and professional fees.

Selling, General, and Administrative Expense. Selling, general, and administrative expense decreased \$13.5 million, mainly driven by reduction in third-party professional fees and travel.

Depreciation and Amortization. Depreciation and Amortization increased \$4.1 million during the year ended December 31, 2020. The increase was primarily due to the increase in fixed assets put in service in the fourth quarter of 2019 for the Philadelphia office.

Interest Income. Interest income decreased \$7.0 million during the year ended December 31, 2020. The decrease was primarily due to a lower average overall cash and investment balance on December 31, 2020 as compared to December 31, 2019 and reduced interest rates.

Interest Expense. Interest expense increased \$3.6 million during the year ended December 31, 2020. The increase was driven by the \$400 million Senior Secured Loan due 2026 in July 2020.

Loss on Exchange of Convertible Notes. During the first and second quarters of 2019, the Company entered into separate, privately negotiated Exchange Agreements with a limited number of holders of the Convertible Notes. As a result of this exchange, the Company recognized a loss on exchange of debt of \$40.6 million in the Consolidated Statements of Operations.

Loss on Extinguishment of Debt. In July 2020, the Company voluntarily settled the principal amount, accrued interest, and early settlement premiums of the Senior Secured Term Loan due 2023. As a result of this early extinguishment, a loss on extinguishment of debt of \$7.3 million was recognized in the Consolidated Statements of Operations.

Income Tax Expense. The income tax expense for the year ended December 31, 2020 was \$2.6 million. We are subject to income taxes in various jurisdictions. Our tax liabilities are largely dependent on the distributions of pre-tax earnings among the many jurisdictions in which we operate.

Critical Accounting Policies and Significant Judgments and Estimates

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

Revenue Recognition

Our net product sales consist of sales of Galafold[®] for the treatment of Fabry disease. We have 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.

We recognize revenue when our performance obligation with our customers have been satisfied, which occurs at a point in time when the pharmacies or distributors obtain control of Galafold[®]. The transaction price is determined based on fixed consideration in our customer contracts and is recorded net of estimates for variable consideration, which are third-party discounts and rebates. The identified variable consideration is recorded as a reduction of revenue at the time revenue from sale of Galafold[®] is recognized. We recognize revenue to the extent that it is probable that a significant revenue reversal will not occur in a future period. These estimates may differ from actual consideration received. We evaluate these estimates each reporting period to reflect known changes.

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

Leases

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

ROU assets represent the Company's right to control the use of an explicitly or implicitly identified fixed asset for a period of time and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Control of an underlying asset is conveyed to the Company if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments.

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

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

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

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

Research and Development Expenses

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

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

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

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

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

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

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

Share-based Compensation

Stock Option Grants

In accordance with the applicable accounting guidance, we estimate the fair value of each equity award granted. We chose the "straight-line" attribution method for allocating compensation costs and recognized the fair value of each stock option on a straight-line basis over the vesting period of the related awards.

We use the Black-Scholes option pricing model when estimating the grant date fair value for stock-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was based on our historical volatility since our initial public offering in May 2007. We determine the average expected life using our actual historical data. The risk-free interest rate is based on U.S. Treasury, zero-coupon issues with a remaining term equal to the expected life assumed at the date of grant. Forfeitures are estimated based on historical analysis of actual option forfeitures.

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

RSUs awarded under the plan are generally subject to graded vesting and are contingent on an employee's continued service on such date. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. We expense the cost of the RSUs, which is determined to be the fair market value of the shares of common stock underlying the RSUs at the date of grant, ratably over the period during which the vesting restrictions lapse. In addition, certain of our share-based awards are market- and performance-based and dependent upon achieving certain goals. The related share-based compensation expense is determined based on the estimated fair value of the underlying shares on the date of grant and is recognized on a straight-line basis over the vesting term. With respect to performance-based awards, we estimate the probability that the performance conditions will be achieved.

Business Combinations

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

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

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

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

Intangible Assets and Goodwill

We record goodwill in a business combination when the total consideration exceeds the fair value of the net tangible and identifiable intangible assets acquired. Purchased in-process research and development is accounted for as an indefinite lived intangible asset until the underlying project is completed, at which point the intangible asset will be accounted for as a definite lived intangible asset, or abandoned, at which point the intangible asset will be written off or partially impaired. Goodwill and indefinite lived intangible assets are assessed annually for impairment on October 1 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. No indicators of impairment were noted during the years ended December 31, 2020 and December 31, 2019.

Valuation of Contingent Consideration Payable

Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved and the consideration is paid or becomes payable. This does not apply in circumstances when the contingent consideration meets the definition of a derivative, in which case the amount becomes part of the basis in the asset acquired. Upon recognition of the contingent consideration payment, the amount is included in the cost of the acquired asset or group of assets. Each period we reassess the fair value of the contingent acquisition consideration payable associated with certain acquisitions and record changes in the fair value as contingent consideration expense. Increases or decreases in the fair value of the contingent acquisition consideration payable can result from changes in estimated probability adjustments with respect to regulatory approval, changes in the assumed timing of when milestones are likely to be achieved and changes in assumed discount periods and rates. Significant judgment is employed in determining the appropriateness of these assumptions each period. Accordingly, future business and economic conditions, as well as changes in any of the assumptions described in the accounting for business combinations above can materially impact the amount of contingent consideration expense that we record in any given period.

Liquidity and Capital Resources

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

Sources of Liquidity

In July 2020, we entered into the Senior Secured Term Loan due 2026. This transaction resulted in net proceeds of \$385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. Additionally, we used \$156.3 million of the proceeds to voluntarily settle the principal amount, accrued interest, and early settlement premiums of the Senior Secured Term Loan due 2023.

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

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

Cash Flow Discussion

As of December 31, 2020, we had cash, cash equivalents, and marketable securities of \$483.3 million. We invest cash in excess of our immediate requirements in regard to liquidity and capital preservation in a variety of interest-bearing instruments, including obligations of U.S. government agencies and money market accounts. Wherever possible, we seek to minimize the potential effects of concentration and degrees of risk. Although we maintain cash balances with financial institutions in excess of insured limits, we do not anticipate any losses with respect to such cash balances. For more details on the cash, cash equivalents, and marketable securities, refer to "-Note 5. Cash, Cash Equivalents, Marketable Securities, and Restricted Cash," in our Notes to Consolidated Financial Statements.

Net Cash Used in Operating Activities

Net cash used in operations for the year ended December 31, 2020 was \$233.3 million. The components of net cash used in operations included the net loss for the year ended December 31, 2020 of \$276.9 million and the net change in operating assets and liabilities of \$32.1 million. The change in operating assets was primarily due to increases in accounts receivable by \$11.2 million due to increased commercial sales of Galafold[®], an increase in inventory of \$4.6 million, and increase in prepaid and other current assets of \$8.8 million to support commercial activities for Galafold[®] launch. The net cash used in operations was also impacted by a decrease in accounts payable and accrued expenses of \$10.6 million, mainly related to program expenses and support for the commercial launch of Galafold[®], and decrease in deferred reimbursement of \$1.3 million.

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

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities for the year ended December 31, 2020 was \$13.6 million. Our investing activities have consisted primarily of purchases, sales, and maturities of investments and capital expenditures. Net cash used in investing activities reflects \$365.2 million for the purchase of marketable securities and \$3.2 million for capital expenditures, partially offset by \$354.8 million for the sale and redemption of marketable securities.

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

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was \$262.9 million. Net cash provided by financing activities primarily reflects \$385.9 million in proceeds from the Senior Secured Term Loan due 2026, net of issuance costs, and \$42.3 million from the exercise of stock options. This was partially offset by \$155.2 million for the voluntary settlement of the Senior Secured Term Loan due 2023, and \$10.0 million from the purchase of vested restricted stock units.

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

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 scope, progress, results and costs of our clinical trials of our drug candidates and gene therapy candidates, including but not limited to AT-GAA, CLN6 and CLN3;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200" or "cipaglucosidase alfa") and gene therapies;
- the future results of on-going preclinical research and subsequent clinical trials for CDD, Pompe gene therapy, Fabry gene therapy, MPS IIIB, next generation MPS IIIA, and other pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates;
- 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") and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold[®], AT-GAA and our gene therapy candidates;
- our ability to obtain reimbursement for Galafold[®] and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold[®];
- our ability to obtain market acceptance of Galafold[®] and, if our regulatory filings are accepted and approved, AT-GAA;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- the extent to which we acquire or invest in businesses, products, and technologies;
- our ability to successfully integrate our acquired products and technologies into our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;
- our ability to adjust to changes in the European and U.K. markets in the wake of the U.K. leaving the E.U.;
- the extent to which our business could be adversely impacted by the effects of COVID-19 outbreak, including due to actions by us, governments, our customers or suppliers or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

While we continue to generate revenue from product sales, in the absence of additional funding, we expect our continuing operating losses to result in increases in our cash used in operations over the next several quarters and years. We may seek additional funding through public or private financings of debt or equity. Based on current operating models, we believe that the current cash position, which includes the net proceeds from the Senior Secured Term Loan due 2026 and expected revenues is sufficient to fund our operations and ongoing research programs to achieve self-sustainability. Potential impacts of the COVID-19 pandemic, 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 connection with our acquisition of Celenex in 2018, we agreed to pay up to an additional \$10 million in connection with the achievement of certain development milestones, \$220 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to \$75 million in tiered sales milestone payments.

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

Penn - Under our expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty, and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in each indication, up to an aggregate of \$88.0 million per indication. Royalty payments are based on net sales of licensed products on a licensed product-by-licensed product and country-by-country basis. We will provide \$10.0 million each year during the five-year agreement to fund the discovery research program.

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

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2020 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 ⁽²⁾	\$ 195,750	\$ 8,549	\$ 17,185	\$ 16,775	\$ 153,241
Debt obligations, including interest ⁽³⁾	543,670	30,502	63,825	311,500	137,843
Purchase obligations ⁽⁴⁾	\$ 41,154	\$ 41,154	\$ —	\$ —	\$ —
Total fixed contractual obligations ⁽¹⁾	<u>\$ 780,574</u>	<u>\$ 80,205</u>	<u>\$ 81,010</u>	<u>\$ 328,275</u>	<u>\$ 291,084</u>

⁽¹⁾ 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[®]. 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.

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

⁽³⁾ Represents the future payments of principal and interest to be made on our \$2.8 million 3% unsecured Convertible Notes due 2023 (the "Convertible Notes") and our \$400 million Secured Senior Term Loan due 2026 ("Senior Secured Term Loan due 2026"). The Convertible Notes bear interest at a fixed rate of 3% per year, payable semiannually on June 15 and December 15 of each year, and will mature on December 15, 2023. The Senior Secured Term Loan due 2026 bears interest at a rate equal to the 3-month LIBOR, subject to a 1% floor, plus 6.5% per year, payable quarterly and requires interest-only payments until mid-2024. The Senior Secured Term Loan due 2026 will be repaid in nine quarterly payments of \$44.4 million, starting on July 2024 with the final balance due on the maturity date in July 2026.

⁽⁴⁾ Represents minimum purchase commitments due to third parties. Contracts for which our commitment is variable, based on volumes, with no fixed minimum quantities, and contracts that can be canceled without payment penalties have been excluded. The purchase obligations included above are in addition to amounts included in total recorded on our December 31, 2020 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, 2020 and 2019.

Recent Accounting Pronouncements

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

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Market risk is the risk of change in fair value of a financial instrument due to changes in interest rates, equity prices, creditworthiness, financing, exchange rates or other factors. Our primary market risk exposure relates to changes in interest rates in our cash, cash equivalents, and marketable securities. We place our investments in high-quality financial instruments, primarily money market funds, corporate debt securities, asset backed securities, and U.S. government agency notes with maturities of less than one year, which we believe are subject to limited interest rate and credit risk. The securities in our investment portfolio are not leveraged, are classified as available-for-sale and, due to the short-term nature, are subject to minimal interest rate risk. We believe that a 1% (100 basis points) change in average interest rates would either increase or decrease the market value of our investment portfolio by \$0.9 million as of December 31, 2020. 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, 2020, we had a \$400 million Senior Secured Term Loan due 2026 that bears interest at a rate equal to the 3-month LIBOR, subject to a 1% floor, plus 6.5% per year. We do not currently hedge our variable interest rate debt. The annual average variable interest rate for our variable rate debt as of December 31, 2020 was 7.5%. A hypothetical 100 basis point increase or decrease in the average interest rate on our variable rate debt would result in \$1.0 million change in the interest expense as of December 31, 2020.

The Financial Conduct Authority has announced the intent to phase out the use of LIBOR by the end of 2021. If LIBOR is discontinued, we may need to renegotiate the terms of the Senior Secured Term Loan due 2026 in order to replace LIBOR with an alternative standard. As a result, we may incur incremental costs in transitioning to a new standard, and interest rates on our current or future indebtedness may be adversely affected by the new standard. The potential effect of any such event on our cost of capital cannot yet be determined, but we do not expect it to have a material impact on our consolidated financial condition, results of operations, or cash flows.

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

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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

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

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

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

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

We assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. 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, 2020, 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, 2020 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report. This report appears on the following page.

Dated March 1, 2021

/s/ JOHN F. CROWLEY

Chairman and Chief Executive Officer

/s/ DAPHNE QUIMI

Chief Financial Officer

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control Over Financial Reporting

We have audited Amicus Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Amicus Therapeutics, Inc. (the "Company") maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, 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, 2020 and 2019, 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, 2020, and the related notes and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

Iselin, New Jersey
March 1, 2021

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Amicus Therapeutics, Inc. (the "Company") as of December 31, 2020 and 2019, 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, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

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

Fair Value Measurement of the Contingent Consideration

Description of the Matter As described in Note 11 to the consolidated financial statements, the Company has a \$25.8 million contingent consideration liability recorded as of December 31, 2020 representing the fair value of additional amounts that management believes are likely to be paid to the former stockholders of Callidus Biopharma, Inc. The determination of the recorded amount of the contingent consideration liabilities requires the Company to make significant estimates and assumptions.

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

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

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

/s/ Ernst & Young LLP

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

Iselin, New Jersey
March 1, 2021

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

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 163,240	\$ 142,837
Investments in marketable securities	320,029	309,903
Accounts receivable	46,923	33,284
Inventories	19,556	14,041
Prepaid expenses and other current assets	29,721	20,008
Total current assets	579,469	520,073
Operating lease right-of-use assets, less accumulated amortization of \$7,574 and \$5,342 at December 31, 2020 and December 31, 2019, respectively	23,296	33,315
Property and equipment, less accumulated depreciation of \$14,487 and \$17,604 at December 31, 2020 and December 31, 2019, respectively	43,863	47,705
In-process research & development	23,000	23,000
Goodwill	197,797	197,797
Other non-current assets	19,095	28,317
Total Assets	\$ 886,520	\$ 850,207
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 17,063	\$ 21,722
Accrued expenses and other current liabilities	96,841	99,901
Contingent consideration payable	8,900	—
Operating lease liabilities	6,872	7,189
Total current liabilities	129,676	128,812
Deferred reimbursements	7,406	8,906
Long-term debt	389,254	149,505
Contingent consideration payable	16,925	22,681
Deferred income taxes	4,896	5,051
Operating lease liabilities	45,604	53,531
Other non-current liabilities	6,379	5,296
Total liabilities	600,140	373,782
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$0.01 par value, 500,000,000 shares authorized, 262,063,461 and 255,417,869 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	2,650	2,598
Additional paid-in capital	2,308,578	2,227,225
Accumulated other comprehensive loss:		
Foreign currency translation adjustment	8,412	2,785
Unrealized (loss) gain on available-for securities	(185)	40
Warrants	12,387	12,387
Accumulated deficit	(2,045,462)	(1,768,610)
Total stockholders' equity	286,380	476,425
Total Liabilities and Stockholders' Equity	\$ 886,520	\$ 850,207

See accompanying Notes to Consolidated Financial Statements

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

	Years Ended December 31,		
	2020	2019	2018
Net product sales	\$ 260,886	\$ 182,237	\$ 91,245
Cost of goods sold	31,044	21,963	14,404
Gross profit	229,842	160,274	76,841
Operating expenses:			
Research and development	308,443	286,378	270,902
Selling, general, and administrative	156,407	169,861	127,200
Changes in fair value of contingent consideration payable	3,144	3,297	3,300
Depreciation and amortization	8,846	4,775	4,216
Total operating expenses	476,840	464,311	405,618
Loss from operations	(246,998)	(304,037)	(328,777)
Other (expense) income:			
Interest income	3,226	10,249	10,461
Interest expense	(22,425)	(18,872)	(22,402)
Loss on exchange of convertible notes	—	(40,624)	—
Loss on extinguishment of debt	(7,276)	—	—
Change in fair value of derivatives	—	—	(2,739)
Other expense	(781)	(2,626)	(5,632)
Loss before income tax	(274,254)	(355,910)	(349,089)
Income tax (expense) benefit	(2,598)	(478)	94
Net loss attributable to common stockholders	\$ (276,852)	\$ (356,388)	\$ (348,995)
Net loss attributable to common stockholders per common share — basic and diluted	\$ (1.07)	\$ (1.48)	\$ (1.88)
Weighted-average common shares outstanding — basic and diluted	258,867,380	240,421,001	185,790,021

See accompanying Notes to Consolidated Financial Statements

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

	Years Ended December 31,		
	2020	2019	2018
Net loss	\$ (276,852)	\$ (356,388)	\$ (348,995)
Other comprehensive gain:			
Foreign currency translation adjustment gain, net of tax impact of \$1,552, \$889, and \$0, respectively	5,627	2,290	2,537
Unrealized (loss) gain on available-for-sale securities, net of tax impact of \$(50), \$182, and \$0, respectively	(225)	467	9
Other comprehensive income	5,402	2,757	2,546
Comprehensive loss	<u>\$ (271,450)</u>	<u>\$ (353,631)</u>	<u>\$ (346,449)</u>

See accompanying Notes to Consolidated Financial Statements

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

	Common Stock		Additional Paid-In Capital	Warrants	Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
Balance at December 31, 2017	166,989,790	\$ 1,721	\$ 1,400,758	\$ 16,076	\$ (2,095)	\$ (1,063,610)	\$ 352,850
Stock issued from exercise of stock options, net	1,397,908	14	9,130	—	—	—	9,144
Stock issued from equity financing	20,239,839	202	294,381	—	—	—	294,583
Restricted stock tax vesting	303,173	—	(2,832)	—	—	—	(2,832)
Stock-based compensation	—	—	29,260	—	—	—	29,260
Reclassification upon ASU 2018-02 adoption	—	—	—	—	(383)	383	—
Warrants exercised	453,214	5	6,625	(3,013)	—	—	3,617
Change in fair value of derivatives	—	—	2,739	—	—	—	2,739
Unrealized holding gain on available-for-sale securities	—	—	—	—	9	—	9
Foreign currency translation adjustment	—	—	—	—	2,537	—	2,537
Net loss	—	—	—	—	—	(348,995)	(348,995)
Balance at December 31, 2018	189,383,924	1,942	1,740,061	13,063	68	(1,412,222)	342,912
Stock issued from exercise of stock options, net	1,967,087	20	11,456	—	—	—	11,476
Stock issued from equity financing	18,720,930	187	188,807	—	—	—	188,994
Restricted stock tax vesting	477,198	—	(3,235)	—	—	—	(3,235)
Stock issued for contingent consideration	771,804	8	9,308	—	—	—	9,316
Stock-based compensation	—	—	44,430	—	—	—	44,430
Warrants exercised	101,787	1	1,487	(676)	—	—	812
Equity component of the convertible notes	43,995,139	440	215,036	—	—	—	215,476
Termination of capped call confirmations	—	—	19,875	—	—	—	19,875
Unrealized holding gain on available-for-sale securities	—	—	—	—	467	—	467
Foreign currency translation adjustment	—	—	—	—	2,290	—	2,290
Net loss	—	—	—	—	—	(356,388)	(356,388)
Balance at December 31, 2019	255,417,869	2,598	2,227,225	12,387	2,825	(1,768,610)	476,425
Stock issued from exercise of stock options, net	5,233,672	52	42,230	—	—	—	42,282
Restricted stock tax vesting	1,411,920	—	(10,028)	—	—	—	(10,028)
Stock-based compensation	—	—	49,151	—	—	—	49,151
Unrealized holding (loss) on available-for-sale securities	—	—	—	—	(225)	—	(225)
Foreign currency translation adjustment	—	—	—	—	5,627	—	5,627
Net loss	—	—	—	—	—	(276,852)	(276,852)
Balance at December 31, 2020	262,063,461	\$ 2,650	\$ 2,308,578	\$ 12,387	\$ 8,227	\$ (2,045,462)	\$ 286,380

See accompanying Notes to Consolidated Financial Statements

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

	Years Ended December 31,		
	2020	2019	2018
Operating activities			
Net loss	\$ (276,852)	\$ (356,388)	\$ (348,995)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of debt discount and deferred financing	1,794	2,546	10,976
Depreciation and amortization	8,846	4,775	4,216
Stock-based compensation	49,151	44,430	29,260
Loss on exchange of convertible notes	—	40,624	—
Loss on extinguishment of debt	7,276	—	—
Change in fair value of derivatives	—	—	2,739
Non-cash changes in the fair value of contingent consideration payable	3,144	3,297	3,300
Foreign currency remeasurement loss	5,471	254	3,217
Non-cash deferred taxes	(155)	(1,415)	—
Other	99	(149)	59
Changes in operating assets and liabilities:			
Accounts receivable	(11,219)	(11,114)	(13,294)
Inventories	(4,639)	(5,114)	(4,205)
Prepaid expenses and other current assets	(8,766)	(3,287)	2,488
Accounts payable, accrued expenses, and other current liabilities	(10,610)	46,742	17,115
Other non-current assets and liabilities	4,420	(10,117)	(581)
Deferred reimbursements	(1,250)	(5,500)	(6,250)
Net cash used in operating activities	\$ (233,290)	\$ (250,416)	\$ (299,955)
Investing activities			
Sale and redemption of marketable securities	354,826	499,047	463,502
Purchases of marketable securities	(365,178)	(383,882)	(578,394)
Capital expenditures	(3,227)	(20,012)	(6,308)
Net cash (used in) provided by investing activities	\$ (13,579)	\$ 95,153	\$ (121,200)
Financing activities			
Proceeds from issuance of common stock, net of issuance costs	—	188,994	294,584
Payment of long-term debt	(155,249)	—	—
Proceeds from long-term debt, net of issuance costs	385,929	—	146,596
Payment of finance leases	(76)	(420)	(334)
Purchase of vested restricted stock units	(10,028)	(3,235)	(2,832)
Proceeds from termination of capped call confirmations	—	19,875	—
Proceeds from exercise of stock options	42,282	11,476	9,144
Proceeds from exercise of warrants	—	812	3,617
Net cash provided by financing activities	\$ 262,858	\$ 217,502	\$ 450,775
Effect of exchange rate changes on cash, cash equivalents, and restricted cash	\$ 3,830	\$ 1,729	\$ 1,518
Net increase in cash, cash equivalents, and restricted cash	19,819	63,968	31,138
Cash, cash equivalents, and restricted cash at the beginning of the year	146,343	82,375	51,237
Cash, cash equivalents, and restricted cash at the end of the year	\$ 166,162	\$ 146,343	\$ 82,375

	Years Ended December 31,		
	2020	2019	2018
Supplemental disclosures of cash flow information			
Tenant improvements paid through lease incentive	\$ 470	\$ 19,388	\$ —
Cash paid during the period for interest	\$ 24,683	\$ 16,966	\$ 7,500
Contingent consideration paid in shares	\$ —	\$ 9,316	\$ —
Capital expenditures unpaid at the end of period	\$ 985	\$ 1,865	\$ 106
Cash paid for taxes	\$ 10,371	\$ 691	\$ 1,062

See accompanying Notes to Consolidated Financial Statements

Amicus Therapeutics, Inc.**Notes To Consolidated Financial Statements****1. Description of Business**

Amicus Therapeutics, Inc. (the "Company") is a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. The Company has a portfolio of product opportunities led by the first, oral monotherapy for Fabry disease that has achieved widespread global approval, a differentiated biologic for Pompe disease, and an industry leading rare disease gene therapy portfolio.

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

The lead biologics program of the Company's pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. The Company initiated the rolling Biologic License Application ("BLA") submission to the FDA in the fourth quarter of 2020.

The Company has established an industry leading gene therapy portfolio of potential therapies for people living with rare metabolic diseases, through a license with Nationwide Children's Hospital ("Nationwide Children's") and an expanded collaboration with the University of Pennsylvania ("Penn"). The Company's pipeline includes gene therapy programs in rare, neurologic lysosomal disorders ("LDs"), specifically: CLN6, CLN3, and CLN1 Batten disease, Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Mucopolysaccharidosis Type IIIB ("MPS IIIB"), as well as a next generation program in Mucopolysaccharidosis Type IIIA ("MPS IIIA"). This expanded collaboration with Penn also provides the Company with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of more prevalent rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies. In the first quarter of 2020, the FDA granted Fast Track designation to the CLN3 Batten disease gene therapy, AT-GTX-502, for the treatment of pediatric patients less than 18 years of age. In September 2020 and February 2021, the European Medicines Agency granted Priority Medicines designation and the FDA granted Fast Track Designation, respectively, to the CLN6 Batten disease gene therapy, AT-GTX-501, for the treatment of patients with variant late infantile neuronal ceroid lipofuscinosis 6 ("vLINCL6").

The Company's operations have not been significantly impacted from the novel coronavirus ("COVID-19") pandemic in 2020; however, the Company observed increased lag times between patient identification and Galafold[®] initiation due to the resurgence of COVID-19 in the fourth quarter. The Company has maintained operations in all geographies, secured its global supply chain for its commercial and clinical products, and maintained the operational integrity of its clinical trials, with minimal disruption. The Company believes its ability to continue to operate without any significant disruptions will depend on the continued health of its employees, the ongoing demand for Galafold[®] and the continued operation of its global supply chain. The Company has continued to provide uninterrupted access to medicines for those in need of treatment, while prioritizing the health and safety of its global workforce. However, the Company's results of operations in future periods may be negatively impacted by unknown future impacts from the COVID-19 pandemic.

In July 2020, the Company entered into a definitive agreement for a \$400 million credit facility with Hayfin Capital Management ("Senior Secured Term Loan due 2026") with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum and requires interest-only payments until mid-2024 and matures in six years in 2026. This transaction resulted in net proceeds of \$385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. Additionally, the Company used \$156.3 million of the proceeds to voluntarily settle the principal amount, accrued interest, and early settlement premiums of the Senior Secured Term Loan with BioPharma Credit PLC that was due in 2023 ("Senior Secured Term Loan due 2023").

The Company had an accumulated deficit of \$2.0 billion as of December 31, 2020 and anticipates incurring losses through the fiscal year ending December 31, 2021 and beyond. The Company has historically funded its operations through stock offerings, debt issuances, Galafold[®] revenues, collaborations, and other financing arrangements.

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

Based on current operating models, the Company believes that the current cash position, which includes the net proceeds from the Senior Secured Term Loan due 2026 and expected revenues, is sufficient to fund the Company's operations and ongoing research programs to achieve self-sustainability. Potential impacts of the COVID-19 pandemic, business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact the Company's future capital requirements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company has prepared the accompanying Consolidated Financial Statements in accordance with U.S. generally accepted accounting principles ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Consolidation

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

Foreign Currency Transactions

The functional currency for most of the Company's foreign subsidiaries is their local currency. For non-U.S. subsidiaries that transact in a functional currency other than the U.S. dollar, assets and liabilities are translated at current rates of exchange at the balance sheet date. Income and expense items are translated at the average foreign exchange rates for the period. Adjustments resulting from the translation of the financial statements of the Company's foreign operations into U.S. dollars are excluded from the determination of net income and are recorded in accumulated other comprehensive income, a separate component of stockholders' equity.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

Additionally, the Company assessed the impact COVID-19 pandemic has had on its operations and financial results as of December 31, 2020 and through the issuance of this report. The Company's analysis was informed by the facts and circumstances as they were known to the Company. This assessment considered the impact COVID-19 may have on financial estimates and assumptions that affect the reported amounts of assets and liabilities and revenue and expenses.

Cash, Cash Equivalents, Marketable Securities, and Restricted Cash

The Company considers all highly liquid investments purchased with a maturity of three months or less at the date of acquisition to be cash equivalents. Marketable securities consist of fixed income investments with a maturity of greater than three months and other highly liquid investments that can be readily purchased or sold using established markets. These investments are classified as available-for-sale and are reported at fair value on the Company's Consolidated Balance Sheets. Unrealized holding gains and losses are reported within 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 other current assets and other non-current assets on the Company's Consolidated Balance Sheets.

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

The Company is subject to credit risk from its accounts receivable related to its product sales of Galafold[®]. The Company's accounts receivable at December 31, 2020 have arisen from product sales primarily in Europe and the U.S. The Company will periodically assess the financial strength of its customers to establish allowances for anticipated losses, if any. For accounts receivable that have arisen from named patient sales, the payment terms are predetermined, and the Company evaluates the creditworthiness of each customer on a regular basis. As of December 31, 2020, the Company recorded an allowance for doubtful accounts of \$0.1 million.

Property and Equipment

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

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

Revenue Recognition

The Company's net product sales consist of sales of Galafold[®] for the treatment of Fabry disease. The Company has recorded revenue on sales where Galafold[®] is available either on a commercial basis or through a reimbursed early access program ("EAP"). Orders for Galafold[®] are generally received from distributors and pharmacies, with the ultimate payor often a government authority. In 2020, one customer accounted for 25% of net product sales and 12% of accounts receivable from product sales. In 2019, one customer accounted for 22% of net product sales and 11% of accounts receivable from product sales.

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

The following table summarizes the Company's net product sales from Galafold[®] disaggregated by geographic area:

(in thousands)	For the Year		
	2020	2019	2018
U.S.	\$ 80,046	\$ 52,478	\$ 7,223
Ex-U.S.	180,840	129,759	84,022
Total net product sales	\$ 260,886	\$ 182,237	\$ 91,245

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

Inventories and Cost of Goods Sold

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

Cost of goods sold includes the cost of inventory sold, manufacturing and supply chain costs, product shipping and handling costs, provisions for excess and obsolete inventory, as well as royalties payable.

Fair Value Measurements

The Company records certain asset and liability balances under the fair value measurements as defined by the 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.

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

Research and Development Costs

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

Interest Income and Interest Expense

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

Income Taxes

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

Other Comprehensive Income (Loss)

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

Leases

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

ROU assets represent the Company's right to control the use of an explicitly or implicitly identified fixed asset for a period of time and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Control of an underlying asset is conveyed to the Company if the Company obtains the rights to direct the use of and to obtain substantially all of the economic benefits from using the underlying asset. ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments.

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

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

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

The information presented for the periods prior to January 1, 2019 has not been restated and is reported under the accounting standard in effect for those periods. For additional information, see " -Note 13. Leases".

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

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, 2020, the Company had one equity-based employee compensation plan, which is described more fully in "— Note 9. Stockholders' Equity." The Company applies the fair value method of measuring equity-based compensation, which requires a public entity to measure the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award.

Loss per Common Share

The Company calculates net loss per share as a measurement of the Company's performance while giving effect to all dilutive potential common shares that were outstanding during the reporting period. The Company had a net loss for all periods presented; accordingly, the inclusion of common stock options, unvested RSUs, and warrants would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same. See "— Note 17. Basic and Diluted Net Loss per Common Share" for further discussion on net loss per share.

Segment Information

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

Business Combinations

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

Contingent Consideration Payable

Contingent consideration payments in asset acquisitions are recognized when the contingency is resolved and the consideration is paid or becomes payable. This does not apply in circumstances when the contingent consideration meets the definition of a derivative, in which case the amount becomes part of the basis in the asset acquired. Upon recognition of the contingent consideration payment, the amount is included in the cost of the acquired asset or group of assets. The Company determines the fair value of contingent acquisition consideration payable on the acquisition date using a probability-based income approach utilizing an appropriate discount rate. The short term and long term portions of the contingent consideration payable is shown on the Company's Consolidated Balance Sheets. The fair value of the contingent consideration payable will be determined each period end and the resulting change will be recorded on the Consolidated Statements of Operations.

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

Intangible Assets and Goodwill

The Company records goodwill in a business combination when the total consideration exceeds the fair value of the net tangible and identifiable intangible assets acquired. Purchased IPR&D is accounted for as an indefinite lived intangible asset until the underlying project is completed, at which point the intangible asset will be accounted for as a definite lived intangible asset, or abandoned, at which point the intangible asset will be written off or partially impaired. Goodwill and indefinite lived intangible assets are assessed annually for impairment and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. No indicators of impairment were noted during the years ended December 31, 2020 and December 31, 2019.

Recent Accounting Developments - Guidance Adopted in 2020

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

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

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

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

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

Recent Accounting Developments - Guidance Not Yet Adopted

ASU 2019-12 - In December 2019, the FASB issued ASU 2019-15, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes ("ASU 2019-12"). This new guidance removes specific exceptions to the general principles in Topic 740. It eliminates the need for an organization to analyze whether the following apply in a given period: (i) exception to the incremental approach for intraperiod tax allocation; (ii) exceptions to accounting for basis differences when there are ownership changes in foreign investments; and (iii) exception in interim period income tax accounting for year-to-date losses that exceed anticipated losses. ASU 2019-12 also improves financial statement preparers' application of income tax-related guidance and simplifies the following: (i) franchise taxes that are partially based on income; (ii) transactions with a government that result in a step up in the tax basis of goodwill; (iii) separate financial statements of legal entities that are not subject to tax; and (iv) enacted changes in tax laws in interim periods. ASU 2019 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. Early adoption is permitted for public business entities for periods for which financial statements have not yet been issued. The Company will adopt this guidance prospectively on January 1, 2021, and it believes the adoption of this guidance will not have a material impact on its Consolidated Financial Statements or related disclosures.

3. Acquisitions

Acquisition of Celenex

In September 2018, the Company expanded its pipeline by acquiring the rights and related intellectual property of ten gene therapy programs through its acquisition of Celenex, Inc., ("Celenex"). Celenex is a private, clinical stage gene therapy company whose lead programs are ten gene therapy programs including CLN6 and CLN3, which are in clinical stage, and several programs in pre-clinical stage. Pursuant to the terms of the agreement, the Company agreed to pay up to an additional \$10 million in connection with the achievement of certain development milestones, \$220 million in connection with the achievement of certain regulatory approval milestones across multiple programs and up to \$75 million in tiered sales milestone payments. Celenex has an exclusive license agreement with Nationwide Children's Hospital ("Nationwide Children's"). Under this license agreement, Nationwide Children's is eligible to receive development and sales-based milestones of up to \$7.8 million for each product.

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 million upfront payment was expensed to research and development expense in the Consolidated Statements of Operations for the year ended December 31, 2018.

4. Goodwill and Intangible Assets

As of December 31, 2020, in connection with the acquisitions, the Company had goodwill of \$197.8 million and IPR&D of \$23.0 million, which are reported at fair value on the Company's Consolidated Balance Sheets. Intangible assets related to IPR&D assets are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. During the period the assets are considered indefinite-lived, they will not be amortized but will be tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D assets below their respective carrying amounts.

Goodwill and intangible assets are assessed annually for impairment on October 1 and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. 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.

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

The following table represents the changes in IPR&D for the years ended December 31, 2020 and 2019, respectively:

	(in millions)
Balance at December 31, 2018	\$ 23.0
Change in IPR&D	—
Balance at December 31, 2019	\$ 23.0
Change in IPR&D	—
Balance at December 31, 2020	<u>\$ 23.0</u>

The following table represents the changes in Goodwill for the years ended December 31, 2020 and 2019, respectively:

	(in millions)
Balance at December 31, 2018	\$ 197.8
Change in goodwill	—
Balance at December 31, 2019	\$ 197.8
Change in goodwill	—
Balance at December 31, 2020	<u>\$ 197.8</u>

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

As of December 31, 2020, the Company held \$163.2 million in cash and cash equivalents and \$320.0 million of marketable securities which are reported at fair value on the Company's Consolidated Balance Sheets. Unrealized holding gains and losses are generally reported within 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 or if an available-for-sale debt security's fair value is determined to be less than the amortized cost and the Company intends or is more than likely to sell the security before recovery and it is not considered a credit loss, such security is written down to its estimated fair value as a new cost basis and the amount of the write-down is included in earnings as an impairment charge. If the unrealized loss of an available-for-sale debt security is determined to be a result of credit loss the Company would recognize an allowance and the corresponding credit loss would be included in earnings.

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

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, 2020			
	Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Cash and cash equivalents	\$ 163,240	\$ —	\$ —	\$ 163,240
Corporate debt securities	39,525	4	(16)	39,513
Commercial paper	217,087	14	(6)	217,095
Asset-backed securities	9,420	18	—	9,438
U.S. government agency bonds	53,583	3	(4)	53,582
Money market	350	—	—	350
Certificates of deposit	51	—	—	51
	<u>\$ 483,256</u>	<u>\$ 39</u>	<u>\$ (26)</u>	<u>\$ 483,269</u>
Included in cash and cash equivalents	\$ 163,240	\$ —	\$ —	\$ 163,240
Included in marketable securities	320,016	39	(26)	320,029
Total cash, cash equivalents, and marketable securities	<u>\$ 483,256</u>	<u>\$ 39</u>	<u>\$ (26)</u>	<u>\$ 483,269</u>

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

⁽¹⁾ As of December 31, 2019, \$9.5 million of marketable securities had maturity dates greater than 12 months and were available to convert into cash, if needed.

For the year ended December 31, 2020 there were nominal realized gains. For the fiscal year ended December 31, 2019, there were no realized gains or losses. The cost of securities sold is based on the specific identification method.

Unrealized loss positions in the marketable securities as of December 31, 2020 and 2019 reflect temporary impairments and are not a result of credit loss. Additionally, as these positions have been in a loss position for less than twelve months and the Company does not intend to sell these securities before recovery, the losses are recognized in other comprehensive gain (loss). The fair value of these marketable securities in unrealized loss positions was \$124.9 million and \$42.6 million as of December 31, 2020 and December 31, 2019, respectively.

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

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

(in thousands)	December 31, 2020	December 31, 2019	December 31, 2018
Cash and cash equivalents	\$ 163,240	\$ 142,837	\$ 79,749
Restricted cash	2,922	3,506	2,626
Cash, cash equivalents, and restricted cash shown in the Consolidated Statements of Cash Flows	<u>\$ 166,162</u>	<u>\$ 146,343</u>	<u>\$ 82,375</u>

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, 2020	December 31, 2019
Raw materials	\$ 5,547	\$ 6,544
Work-in-process	7,693	3,660
Finished goods	6,316	3,837
Total inventories	<u>\$ 19,556</u>	<u>\$ 14,041</u>

The Company recorded a reserve for inventory of \$0.1 million and \$0.2 million as of December 31, 2020 and December 31, 2019, respectively.

7. Property and Equipment

Property and equipment consist of the following:

(in thousands)	December 31,	
	2020	2019
Property and equipment consist of the following:		
Computer equipment	\$ 5,546	\$ 6,185
Computer software	1,207	1,607
Research equipment	15,387	14,568
Furniture and fixtures	2,880	5,157
Leasehold improvements	24,146	30,294
Vehicles	124	124
Land	3,190	3,190
Construction in progress	5,870	4,184
Gross property and equipment	58,350	65,309
Less accumulated depreciation	(14,487)	(17,604)
Net property and equipment	<u>\$ 43,863</u>	<u>\$ 47,705</u>

Depreciation expense was \$8.4 million and \$4.5 million for the years ended December 31, 2020 and December 31, 2019, respectively.

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

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

(in thousands)	December 31,	
	2020	2019
Accrued professional fees	\$ 3,700	\$ 7,832
Accrued contract manufacturing & contract research costs	19,617	17,800
Accrued compensation and benefits	23,025	27,156
Accrued program fees	16,599	17,016
Accrued royalties	6,550	5,196
Accrued interest	—	3,679
Accrued milestones	—	4,000
Accrued sales rebates and discounts	12,079	5,900
Accrued taxes	11,177	7,300
Deferred reimbursements	1,500	1,250
Other	2,594	2,772
	\$ 96,841	\$ 99,901

9. Stockholders' Equity

Common Stock and Warrants

As of December 31, 2020, the Company was authorized to issue 500 million shares of common stock. Dividends on common stock will be paid when, and if, declared by the board of directors. Each holder of common stock is entitled to vote on all matters that are appropriate for stockholder voting and is entitled to one vote for each share held.

In February 2021, 1,050,000 warrants were exercised at \$7.06 per share of common stock resulting in gross cash proceeds of \$7.4 million.

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

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

As discussed in "— Note 11. Assets and Liabilities Measured at Fair Value", during the fourth quarter of 2018, the Company reached a clinical milestone, which was the dosing of the first patient in a Phase 3 study, related to the contingent consideration from the acquisition of Callidus Biopharma, Inc. ("Callidus"). The milestone for this event was \$9.0 million, which was paid in Company common stock in the first quarter of 2019 and resulted in a \$9.3 million impact on stockholder's equity.

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

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

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

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

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

Nonqualified Cash Plan

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

The Company had a deferred compensation investment balance of \$4.1 million and \$4.4 million as of December 31, 2020 and December 31, 2019, 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 Plan

The Company's Amended and Restated 2007 Equity Incentive Plan (the "Plan") provides for the granting of restricted stock units and options to purchase common stock in the Company to employees, directors, advisors, and consultants at a price to be determined by the Company's Board of Directors. The Plan is intended to encourage ownership of stock by employees and consultants of the Company and to provide additional incentives for them to promote the success of the Company's business. Under the provisions of the Plan, no option will have a term in excess of 10 years. The Board of Directors, or its committee, is responsible for determining the individuals to be granted options, the number of options each individual will receive, the option price per share, and the exercise period of each option. Options granted pursuant to the Plan generally vest 25% on the first year anniversary date of grant plus an additional 1/48th for each month thereafter and may be exercised in whole or in part for 100% of the shares vested at any time after the date of grant. As of December 31, 2020, the Company has reserved up to 15,018,368 shares for issuance under the Plan.

10. Share based Compensation

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

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

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 PRSUs.

Stock Option Grants

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

The Company uses the Black-Scholes option pricing model when estimating the grant date fair value for stock-based awards. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was based on our historical volatility since our initial public offering in May 2007. The average expected life is determined using our actual historical data. The risk-free interest rate is based on U.S. Treasury, zero-coupon issues with a remaining term equal to the expected life assumed at the date of grant. Forfeitures are estimated based on 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,		
	2020	2019	2018
Expected stock price volatility	75.1 %	74.1 %	78.6 %
Risk free interest rate	1.6 %	2.4 %	2.4 %
Expected life of options (years)	5.67	5.68	5.62
Expected annual dividend per share	\$ 0.00	\$ 0.00	\$ 0.00

The weighted average grant-date fair value per share of options granted during 2020, 2019, and 2018 were \$6.40, \$6.67, and \$10.19, respectively.

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

A summary of the Company's stock options for the year ended December 31, 2020 were as follows:

	Number of Shares <u>(in thousands)</u>	Weighted Average Exercise Price	Weighted Average Remaining Years	Aggregate Intrinsic Value <u>(in millions)</u>
Options outstanding, December 31, 2017	15,181	\$ 7.48		
Granted	2,348	\$ 14.96		
Exercised	(1,398)	\$ 6.54		
Forfeited	(313)	\$ 9.55		
Expired	(8)	\$ 10.76		
Options outstanding, December 31, 2018	15,810	\$ 8.63		
Granted	4,091	\$ 10.29		
Exercised	(1,967)	\$ 5.83		
Forfeited	(879)	\$ 11.07		
Expired	(331)	\$ 13.38		
Options outstanding, December 31, 2019	16,724	\$ 9.15		
Granted	4,362	\$ 9.98		
Exercised	(5,243)	\$ 8.11		
Forfeited	(1,376)	\$ 10.42		
Expired	(435)	\$ 13.33		
Options outstanding, December 31, 2020	<u>14,032</u>	\$ 9.54	6.5	\$ 190.1
Vested and unvested expected to vest, December 31, 2020	13,267	\$ 9.49	6.4	\$ 180.5
Exercisable at December 31, 2020	8,130	\$ 8.86	5.1	\$ 115.7

The aggregate intrinsic value of options exercised during the years ended December 31, 2020, 2019 and 2018 was \$40.9 million, \$11.8 million, and \$11.9 million respectively. Cash proceeds from stock options exercised during the years ended December 31, 2020, 2019, and 2018 were \$42.3 million, \$11.5 million, and \$9.1 million, respectively. As of December 31, 2020, the total unrecognized compensation cost related to non-vested stock options granted was \$29.4 million and is expected to be recognized over a weighted average period of three years.

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

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

RSUs awarded under the Plan are generally subject to graded vesting and are contingent on an employee's continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. The Company expenses the cost of the RSUs, which is determined to be the fair market value of the shares of common stock underlying the RSUs at the date of grant, ratably over the period during which the vesting restrictions lapse. A summary of non-vested RSU activity under the Plan for the year ended December 31, 2020 is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value	Weighted Average Remaining Years	Aggregate Intrinsic Value
	(in thousands)			(in millions)
Non-vested units as of December 31, 2017	2,575	\$ 5.85		
Granted	1,812	\$ 16.11		
Vested	(530)	\$ 6.01		
Forfeited	(145)	\$ 9.65		
Non-vested units as of December 31, 2018	3,712	\$ 10.59		
Granted	3,526	\$ 10.92		
Vested	(921)	\$ 8.49		
Forfeited	(525)	\$ 10.52		
Non-vested units as of December 31, 2019	5,792	\$ 11.18		
Granted	4,692	\$ 11.29		
Vested	(2,164)	\$ 10.70		
Forfeited	(1,240)	\$ 11.14		
Non-vested units as of December 31, 2020	<u>7,080</u>	\$ 11.35	2.3	\$ 158.0

For the year ended December 31, 2020, 2,163,732 RSUs have vested and all non-vested units are expected to vest over their normal term. As of December 31, 2020, there was \$59.4 million of total unrecognized compensation cost related to unvested RSUs with service-based vesting conditions. These costs are expected to be recognized over a weighted average period of two years.

Compensation Expense Related to Equity Awards

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

(in thousands)	Years Ended December 31,		
	2020	2019	2018
Equity compensation expense recognized in:			
Research and development expense	\$ 20,817	\$ 17,575	\$ 11,740
Selling, general, and administrative expense	28,334	26,855	17,520
Total equity compensation expense	<u>\$ 49,151</u>	<u>\$ 44,430</u>	<u>\$ 29,260</u>

Amicus Therapeutics, Inc.
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, 2020 are identified in the following tables:

(in thousands)	Level 2	Total
Assets:		
Commercial paper	\$ 217,095	\$ 217,095
Asset-backed securities	9,438	9,438
Corporate debt securities	39,513	39,513
U.S. government agency bonds	53,582	53,582
Money market funds	4,427	4,427
	<u>\$ 324,055</u>	<u>\$ 324,055</u>

(in thousands)	Level 2	Level 3	Total
Liabilities:			
Contingent consideration payable	\$ —	\$ 25,825	\$ 25,825
Deferred compensation plan liability	4,078	—	4,078
	<u>\$ 4,078</u>	<u>\$ 25,825</u>	<u>\$ 29,903</u>

A summary of the fair value of the Company's recurring assets and liabilities aggregated by the level in the fair value hierarchy within which those measurements fall as of December 31, 2019 are identified in the following tables:

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

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

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

The Company's Convertible Notes fall into the Level 2 category within the fair value level hierarchy. The fair value was determined using broker quotes in a non-active market for valuation. The fair value of the Convertible Notes at December 31, 2020 was \$10.9 million.

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

The Company did not have any Level 3 assets as of December 31, 2020 or December 31, 2019.

Cash, Money Market Funds and Marketable Securities

The Company classifies its cash within the fair value hierarchy as Level 1 as these assets are valued using quoted prices in an active market for identical assets at the measurement date. The Company considers its investments in marketable securities as available-for-sale and classifies these assets and the money market funds within the fair value hierarchy as Level 2 primarily utilizing broker quotes in a non-active market for valuation of these securities. No changes in valuation techniques or inputs occurred during the year ended December 31, 2020. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the year ended December 31, 2020.

Contingent Consideration Payable

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

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

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

Contingent Consideration Liability	Fair Value as of December 31, 2020 (in thousands)	Valuation Technique	Unobservable Input	Range
Clinical and regulatory milestones	\$ 25,101	Probability weighted discounted cash flow	Discount rate	7.5%
			Probability of achievement of milestones	75%-78%
			Projected year of payments	2021-2022

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

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.

During the fourth quarter of 2018, the Company reached a clinical milestone, which was the dosing of the first patient in a Phase 3 study, related to the contingent consideration from the acquisition of Callidus. The milestone for this event was \$9.0 million, which was paid in Company common stock in the first quarter of 2019 and resulted in a \$9.3 million impact on stockholder's equity.

The following table shows the change in the balance of contingent consideration payable for the year ended December 31, 2020 and December 31, 2019, respectively:

(in thousands)	Years ended December 31,	
	2020	2019
Balance, beginning of the period	\$ 22,681	\$ 19,700
Changes in fair value during the period, included in the Consolidated Statements of Operations	3,144	3,297
Adjustment for contingent consideration paid in stock	—	(316)
Balance, end of the period	\$ 25,825	\$ 22,681

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

12. Debt

The Company's debt consists of the following:

(in thousands)	December 31, 2020	December 31, 2019
Senior Secured Term Loan due 2026:		
Principal	\$ 400,000	\$ —
Less: debt discount ⁽¹⁾	(7,434)	—
Less: deferred financing ⁽¹⁾	(5,592)	—
Net carrying value of the Senior Secured Term Loan	<u>\$ 386,974</u>	<u>\$ —</u>
Senior Secured Term Loan due 2023 ⁽²⁾:		
Principal	\$ —	\$ 150,000
Less: debt discount ⁽¹⁾	—	(2,315)
Less: deferred financing ⁽¹⁾	—	(311)
Net carrying value of the Senior Secured Term Loan	<u>\$ —</u>	<u>\$ 147,374</u>
Convertible Notes ⁽³⁾:		
Principal	\$ 2,825	\$ 2,825
Less: debt discount ⁽¹⁾	(518)	(659)
Less: deferred financing ⁽¹⁾	(27)	(35)
Net carrying value of the Convertible Notes	<u>\$ 2,280</u>	<u>\$ 2,131</u>
Net carrying value of Long-term debt	<u><u>\$ 389,254</u></u>	<u><u>\$ 149,505</u></u>

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

⁽²⁾ The principle, accrued interest and early settlement premiums associated with the Senior Secured Term Loan due 2023 were fully paid and settled in July 2020.

⁽³⁾ The Convertible Notes are currently convertible as the last reported sale price of the Company's common stock was equal to or more than 130% of the conversion price for at least 20 trading days of the 30 consecutive trading days ending on the last day of the quarter.

Senior Secured Term Loan due 2026

In July 2020, the Company entered into a definitive agreement for a \$400 million credit facility with Hayfin Capital Management (“Senior Secured Term Loan due 2026”) with an interest rate equal to 3-month LIBOR, subject to a 1% floor, plus 6.5% per annum and requires interest-only payments until mid-2024. The Senior Secured Term Loan due 2026 will be repaid in nine quarterly payments of \$44.4 million, starting on July 2024 with the final balance due on the maturity date in July 2026. This transaction resulted in net proceeds of \$385.9 million, after deducting fees and expenses. There were no warrants or equity conversion features associated with the Senior Secured Term Loan due 2026. The Company used the proceeds to voluntarily settle the Senior Secured Term Loan with BioPharma Credit PLC that was due in 2023 (“Senior Secured Term Loan due 2023”).

The Senior Secured Term Loan due 2026 is subject to mandatory prepayment provisions that require prepayment upon a change of control, the incurrence of certain additional indebtedness, asset sale, or an event of loss, subject to certain conditions set forth in the Senior Secured Term Loan due 2026. The Company may prepay the Senior Secured Term Loan due 2026 in whole, at its option at any time. Any prepayment of the Senior Secured Term Loan due 2026 is subject to certain make-whole premiums and prepayment premiums, the latter of which decrease until the fourth anniversary of the transaction date at which point no prepayment penalty shall exist. The obligations under the Senior Secured Term Loan due 2026 are secured by a first lien security interest in certain assets of the Company. The Senior Secured Term Loan due 2026 contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to the Company. The Senior Secured Term Loan due 2026 also contains a minimum liquidity covenant of \$75 million, and an incremental minimum consolidated revenue covenant, measured as of the previous four consecutive fiscal quarters. The minimum consolidated

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

revenue covenant ranges from \$140 million, beginning March 31, 2021, and peaks at \$225 million by June 30, 2023, continuing at that level until the Senior Secured Term Loan due 2026 is repaid. If an event of default occurs and is continuing, Hayfin Capital Management may declare all amounts outstanding under the Senior Secured Term Loan due 2026 to be immediately due and payable.

Senior Secured Term Loan due 2023

In September 2018, the Company entered into a loan agreement with BioPharma Credit PLC ("Senior Secured Term Loan due 2023") as the lender. The loan agreement provided for a \$150 million senior secured term loan with an interest rate equal to the 3-month LIBOR plus 7.5% per annum and would mature in 5 years from the maturity date. The Senior Secured Term Loan due 2023 would be repaid in four quarterly payments equal to 12.5% 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 was payable quarterly in arrears. The Senior Secured Term Loan due 2023 contained certain customary representations and warranties, affirmative and negative covenants, and events of default applicable to the Company and certain of its subsidiaries but did not include any financial covenants relating to the achievement or maintenance of revenue or cash flow. If an event of default occurred and was continuing, the lender could declare all amounts outstanding under the Senior Secured Term Loan due 2023 to be immediately due and payable. The Company received net proceeds of \$146.6 million in September 2018, after deducting fees and expenses.

In July 2020, the Company used \$156.3 million of the proceeds from the Senior Secured Term Loan due 2026 to voluntarily settle the principal amount, \$1.1 million accrued interest, and \$5.2 million in early settlement premiums. As a result of this early extinguishment, the Company recognized a loss on extinguishment of debt of \$7.3 million in the Consolidated Statements of Operations.

Convertible Notes

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

- during any fiscal quarter commencing after March 31, 2017, if the last reported sale price of the Company's common stock for at least 20 trading days in the period of 30 consecutive trading days ending on the last trading day of the immediately preceding fiscal quarter is equal to or more than 130% of the conversion price of the Convertible Notes on the last day of such preceding fiscal quarter;
- a holder submits its Convertible Notes for conversion during the five business day period following any five consecutive trading day period in which the trading price for the Convertible Notes, per \$1,000 principal amount of the Convertible Notes, for each such trading day was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate of the Convertible Notes on such date;

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

- 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.

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

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

Interest Expense

The following table sets forth interest expense recognized related to the Company's debt for the years ended December 31, 2020 and 2019 respectively:

(in thousands)	December 31, 2020	December 31, 2019
Contractual interest expense	\$ 20,933	\$ 16,483
Amortization of debt discount	\$ 1,267	\$ 2,381
Amortization of deferred financing	\$ 527	\$ 165
Effective interest rate of the liability component, Convertible debt	10.6 %	10.6 %
Effective interest rate of the liability component, Senior Secured Term Loan due 2026	8.4 %	— %
Effective interest rate of the liability component, Senior Secured Term Loan due 2023	— %	10.2 %

13. Leases

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

For the years ended December 31, 2020, and 2019, the operating lease expense was \$11.1 million and \$10.8 million, respectively. For the years ended December 31, 2020, and 2019, the Company paid \$9.6 million and \$4.9 million, respectively,

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

for amounts included in the measurement of operating lease liabilities and recorded \$1.7 million and \$21.8 million, respectively, of right-of-use assets and \$0.5 million and \$19.4 million, respectively of tenant improvements paid through lease incentives in exchange for new operating lease liabilities.

Commitments under finance leases are not significant for the years ended December 31, 2020, and 2019.

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

(in thousands, except year and discount rate amounts)	December 31, 2020	December 31, 2019
Operating lease ROU asset	\$ 23,296	\$ 33,315
Current portion of the operating lease liabilities	\$ 6,872	\$ 7,189
Non-current portion of the operating lease liabilities	45,604	53,531
Total operating lease liability	<u>\$ 52,476</u>	<u>\$ 60,720</u>
Weighted-average remaining lease terms (years)	19.8	18.2
Weighted-average discount rate	13.0 %	13.1 %

At December 31, 2020, the future minimum operating lease payments were as follows:

(in thousands)	Operating Lease
2021	\$ 8,549
2022	8,494
2023	8,691
2024	8,404
2025	8,371
Thereafter	153,241
Total lease payments	195,750
Less lease incentives	(28,939)
Less imputed interest	(114,335)
Total operating lease liability	<u>\$ 52,476</u>

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

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

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

Rent expense, including fees for utilities and common area maintenances under ASC 840 for the year ended December 31, 2018 was \$5.7 million.

14. Income Taxes

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

(in thousands)	Years Ended December 31,		
	2020	2019	2018
United States	\$ (365,332)	\$ (393,955)	\$ (309,183)
Foreign	91,078	38,045	(39,906)
Total	\$ (274,254)	\$ (355,910)	\$ (349,089)

Following were the components of income tax expense (benefit) for the years ended December 31, 2020, 2019, and 2018:

(in thousands)	2020	2019	2018
Current			
Federal	\$ —	\$ —	\$ —
State	—	—	6
Foreign	4,163	2,877	(100)
Deferred			
Federal	(1,410)	(984)	—
State	(155)	(1,415)	—
Foreign	—	—	—
Total	\$ 2,598	\$ 478	\$ (94)

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2020, 2019, and 2018 are as follows:

	Years Ended December 31,		
	2020	2019	2018
Statutory rate	(21)%	(21)%	(21)%
State taxes, net of federal benefit	—	—	(4)
Nondeductible IPR&D	—	—	6
Contingent consideration	—	—	1
Tax credits	(7)	(16)	(10)
Impact of foreign operations	4	9	2
Nondeductible executive compensation	2	1	—
Nondeductible debt conversion	—	(1)	—
Other	—	(1)	—
Valuation allowance	23	29	26
Net	1 %	— %	— %

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

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

The Company recorded an income tax expense of \$4.2 million in 2020 for taxes in foreign jurisdictions and a \$1.6 million tax benefit in 2020 for taxes in U.S. federal and state jurisdictions.

The Company did not recognize interest or penalties related to income tax during the period ended December 31, 2020 and did not accrue for interest or penalties as of December 31, 2020. The Company does not have an accrual for uncertain tax positions as of December 31, 2020. Tax returns for years 2015 through 2019 are open to examination by tax authorities. The Company is also subject to examination in any period for which it has net operating losses.

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

(in thousands)	Years Ended December 31,	
	2020	2019
Deferred tax assets		
Intellectual property	\$ 68,209	\$ 46,521
Amortization/depreciation	489	2,329
Research tax credit	182,651	141,669
Net operating loss carry forwards	305,876	286,850
Deferred reimbursements	1,912	2,230
Non-cash stock issue	17,553	19,058
Interest carry forward limitation	5,655	2,224
Lease liability	9,235	6,983
Other	10,855	13,921
Gross deferred tax assets	602,435	521,785
Deferred tax liabilities		
Business acquisition	(4,937)	(5,051)
Royalty payable	(68,209)	(46,521)
Convertible notes	(94)	(653)
Advanced R&D payments	(1,776)	(2,611)
Right of use asset	(3,420)	(5,643)
Total net deferred tax assets	523,999	461,306
Less: valuation allowance	(528,895)	(466,357)
Net deferred tax liability	\$ (4,896)	\$ (5,051)

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, 2020 and 2019, the Company recorded valuation allowances of \$528.9 million and \$466.4 million, respectively, representing an increase in the valuation allowance of \$62.5 million in 2020, 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.

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

As of December 31, 2020, the Company had federal and state net operating loss carry forwards ("NOLs") of approximately \$1,156 million and \$889.4 million, respectively. The federal carry forward for losses generated prior to 2018 will expire in 2029 through 2037. Federal net operating losses incurred in 2018 and onward have an indefinite expiration under the 2017 Tax Act. Most of the state carry forwards generated prior to 2009 have expired through 2016. The remaining state carry forwards including those generated in 2009 through 2020 will expire in 2029 through 2040. Utilization of NOLs may be subject to a substantial limitation pursuant to Section 382 of the Internal Revenue Code of 1986, as amended (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. The Company may experience ownership changes in the future as a result of shifts in the stock ownership some of which are outside the Company's control. The Company completed a detailed study of the NOLs and determined that there was not an ownership change in excess of 50%. Ownership changes in future periods may place additional limits on the Company's ability to utilize net operating loss and tax credit carry forwards. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently decrease the amount of state attributes and increase state taxes owed.

The Company also has research and experimentation and orphan drug credit carryforwards of approximately \$30.4 million and \$141.8 million, respectively, which will expire in the years 2021 through 2040. Deferred tax assets for these carryforwards are subject to a full valuation allowance.

15. Collaborative Agreements

University of Pennsylvania

In October 2018, as amended, the Company entered into a collaboration agreement with Penn to pursue research and development of novel gene therapies. The Company's gene therapy portfolio pipeline expanded to include Pompe disease, Fabry disease, CDD, CLN1, MPS IIIB, as well as a next generation program in MPS IIIA. This expanded collaboration with Penn also provides the Company with exclusive disease-specific access and option rights to develop potentially disruptive new gene therapy platform technologies and programs for most LDs and a broader portfolio of rare diseases, including Rett Syndrome, Angelman Syndrome, Myotonic Dystrophy, and select other muscular dystrophies.

Under the expanded collaboration agreement with Penn, Penn is eligible to receive certain milestone, royalty and discovery research payments with respect to licensed products for each indication. Milestone payments are payable following the achievement of certain development and commercial milestone events in each indication, up to an aggregate of \$88.0 million per indication. Royalty payments are based on net sales of licensed products on a licensed product-by-licensed product and country- by-country basis. The Company will provide \$10.0 million each year during the five-year agreement to fund the discovery research program. In connection with the collaboration agreement, the Company made an upfront payment of \$7 million in cash to Penn in 2018 that was expensed to research and development expense in the Consolidated Statements of Operations.

GlaxoSmithKline

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

The contingent milestone payments due to GSK are recorded within the short term and long term deferred reimbursements accounts on the Consolidated Balance Sheets. Sales based tiered royalties due to GSK are recorded within the cost of goods sold within the Consolidated Statements of Operations.

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

For the year ended December 31, 2020, under the GSK collaboration agreements, the Company paid \$1.3 million in sales-based milestones and the Company incurred approximately \$21.7 million of royalty expenses. As of December 31, 2020, \$8.9 million was recorded as deferred reimbursements and the Company recognized a liability of \$6.6 million related to royalties payable to GSK in accounts payable and accrued expenses in the Consolidated Balance Sheets.

16. Basic and Diluted Net Loss per Common Share

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

(in thousands, except per share amounts)	Years Ended December 31,		
	2020	2019	2018
Numerator:			
Net loss attributable to common stockholders	\$ (276,852)	\$ (356,388)	\$ (348,995)
Denominator:			
Weighted average common shares outstanding — basic and diluted	258,867,380	240,421,001	185,790,021

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.

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

(in thousands)	Years ended December 31,		
	2020	2019	2018
Options to purchase common stock	14,032	16,724	15,810
Convertible notes	462	462	40,850
Outstanding warrants, convertible to common stock	2,555	2,555	2,657
Unvested restricted stock units	7,080	5,792	3,712
Total number of potentially issuable shares	24,129	25,533	63,029

17. Selected Quarterly Financial Data (Unaudited)

(in thousands except per share data)	Quarters Ended			
	March 31	June 30	September 30	December 31
2020				
Net product sales	\$ 60,525	\$ 62,353	\$ 67,437	\$ 70,571
Net loss	\$ (88,948)	\$ (52,492)	\$ (64,011)	\$ (71,401)
Basic and diluted net loss per common share ⁽¹⁾	\$ (0.35)	\$ (0.20)	\$ (0.25)	\$ (0.27)
2019				
Net product sales	\$ 34,046	\$ 44,130	\$ 48,768	\$ 55,293
Net loss	\$ (120,299)	\$ (84,551)	\$ (61,809)	\$ (89,729)
Basic and diluted net loss per common share ⁽¹⁾	\$ (0.56)	\$ (0.36)	\$ (0.24)	\$ (0.35)

⁽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.

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, 2020. 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, 2020, 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, 2020 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Management's Report on Internal Control Over Financial Reporting

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

Item 9B. *OTHER INFORMATION.*

None.

PART 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 2021 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 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.

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULE

1. Consolidated Financial Statements

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

2. Consolidated Financial Statement Schedules

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

3. Exhibits

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
2.1	Agreement and Plan of Merger, dated November 19, 2013, by and among Amicus Therapeutics, Inc., CB Acquisition Corp., Callidus BioPharma, Inc., and Cuong Do	Form 8-K	2/12/2014	2.1	
2.2	Amendment to Agreement and Plan of Merger, dated September 30, 2015, by and among the Registrant, Titan Merger Sub Corp. and Scioderm, Inc.	Form 8-K	9/30/2015	2.2	
+2.3	Agreement and Plan of Merger, dated July 5, 2016, by and among MiaMed, Inc., the Registrant and Minervas Merger Sub, Inc.	Form 8-K	7/6/2016	2.1	
+2.4	Agreement and Plan of Merger, dated as of September 19, 2018, by and among Amicus Therapeutics, Inc., Columbus Merger Sub Corp., Celenex, Inc. and Shareholder Representative Services LLC, solely in its capacity as the Shareholders' Representative	Form 8-K	9/25/2018	2.1	
3.1	Restated Certificate of Incorporation of the Registrant.	Form 10-K	2/28/2012	3.1	
3.2	Restated By-laws of the Registrant.	S-1/A (333-141700)	4/27/2007	3.4	
3.3	Certificate of Amendment to the Registrant's Restated Certificate of Incorporation, as amended.	Form 8-K	6/10/2015	3.1	
3.4	Certificate of Amendment to the Restated Certificate of Incorporation	Form 8-K	6/8/2018	3.1	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1 (333-141700)	3/30/2007	4.1	
4.2	Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended	S-1 (333-141700)	3/30/2007	4.2	
4.3	Form of Warrant to Purchase Common Stock	Form 8-K	2/22/2016	4.1	
4.4	Form of Warrant to Purchase Common Stock	Form 8-K	7/1/2016	4.1	
4.5	Indenture, dated December 21, 2016, by and between the Registrant and Wilmington Trust, National Association	Form 8-K	12/21/2016	4.1	
4.6	Form of Indenture	Form S-3ASR	4/24/2016	4.7	
4.7	Description of the Registrant's securities	Form 10-K	3/2/2020	4.8	
*10.1	2002 Equity Incentive Plan, as amended, and forms of option agreements thereunder	S-1/A (333-141700)	4/27/2007	10.1	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
10.2	Form of Director and Officer Indemnification Agreement	S-1 (333-141700)	3/30/2007	10.17	
*10.3	Amended and Restated 2007 Director Option Plan and form of option agreement	Form 8-K	6/18/2010	10.2	
10.4	Lease Agreement dated August 16, 2011 between the Registrant and Cedar Brook 3 Corporate Center, L.P.	Form 8-K	8/16/2011	10.1	
10.5	Securities Purchase Agreement, dated November 20, 2013 by and among the Company and the purchasers identified therein	Form 8-K	11/20/2013	10.1	
+10.6	Second Restated Agreement, dated November 19, 2013 by and between the Registrant and Glaxo Group Limited	Form 10-K	3/3/2014	10.46	
*10.7	Amicus Amicus Therapeutics, Inc. Amended and Restated Restricted Stock Unit Deferral Plan	Form 8-K	12/28/2017	10.1	
*10.8	Employment Agreement dated April 23, 2014, between the Registrant and John F. Crowley	Form 8-K	4/25/2014	10.1	
*10.9	Amended and Restated 2007 Equity Incentive Plan	DEF 14A	4/24/2020	A	
*10.10	Amicus Therapeutics, Inc. Cash Deferral Plan	Form 8-K	10/28/2016	10.1	
10.11	First Amendment to Lease, dated September 9, 2015, by and between Cedar Brook 3 Corporate Center, L.P. and the Registrant	Form 8-K	9/14/2015	10.1	
10.12	Note and Warrant Purchase Agreement by and among the Registrant and the purchasers identified on the signature pages thereto, dated February 19, 2016.	Form 8-K	2/22/2016	10.1	
10.13	Joinder to and Amendment of Note and Warrant Purchase Agreement by and among Amicus Therapeutics, Inc., Amicus Therapeutics UK Limited, Amicus Therapeutics International Holding LTD and the purchasers identified on the signature pages thereto, dated as of June 30, 2016	Form 8-K	7/1/2016	10.2	
10.14	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and P Redmile Ltd.	Form 8-K	12/21/2016	10.7	
10.15	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund, Ltd.	Form 8-K	12/21/2016	10.8	
10.16	Note Purchase Agreement, dated December 15, 2016, by among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Offshore Fund II, Ltd.	Form 8-K	12/21/2016	10.9	
10.17	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Special Opportunities Fund, Ltd.	Form 8-K	12/21/2016	10.10	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
10.18	Note Purchase Agreement, dated December 15, 2016, by and among the Registrant, Amicus Therapeutics International Holding LTD and Redmile Capital Fund, LP	Form 8-K	12/21/2016	10.11	
10.19	Note Purchase Agreement, dated December 15, 2016, by and between Amicus Therapeutics International Holding LTD and GCM Grosvenor Special Opportunities Master Fund, Ltd.	Form 8-K	12/21/2016	10.12	
10.20	Form of Performance-Based Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan	Form 8-K	12/30/2016	10.1	
10.21	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	1/24/2019	10.1	
10.22	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	2/8/2019	10.1	
10.23	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	3/13/2019	10.1	
10.24	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	5/22/2019	10.1	
10.25	Form of Exchange Agreements Relating to Company's 3.00% Convertible Senior Notes due 2023	Form 8-K	6/19/2019	10.1	
**10.26	Amended and Restated Research, Collaboration & License Agreement, dated May 28, 2019, by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania	Form 10-Q	8/8/2019	10.2	
10.27	Amendment #1 to the Amicus Therapeutics, Inc. Cash Deferral Plan.	Form 8-K	10/26/2014	10.1	
10.28	Amendment #2 to the Amicus Therapeutics, Inc. Cash Deferral Plan.	Form 8-K	12/19/2019	10.1	
*10.29	Amendment No. 1 to Employment Agreement dated April 23, 2014 between the Registrant and John F. Crowley	Form 10-K	3/2/2020	10.44	
*10.30	Employment Agreement dated February 18, 2020 between the Registrant and Ellen S. Rosenberg	Form 10-K	3/2/2020	10.45	
*10.31	Employment Agreement dated February 18, 2020, between the Registrant and Bradley L. Campbell	Form 10-K	3/2/2020	10.46	
*10.32	Employment Agreement dated February 18, 2020, between the Registrant and Jay Barth, M.D.	Form 10-K	3/2/2020	10.47	

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
*10.33	Employment Agreement dated February 18, 2020, between the Registrant and Daphne Quimi	Form 10-K	3/2/2020	10.48	
*10.34	Employment Agreement dated February 18, 2020 between the Registrant and Hung Do	Form 10-K	3/2/2020	10.49	
10.35	First Amendment to the Amended and Restated Research, Collaboration & License Agreement dated December 20, 2019 by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania.	Form 10-Q	5/7/2020	10.1	
10.36	Second Amendment to the Amended and Restated Research, Collaboration & License Agreement dated March 26, 2020 by and between Amicus Therapeutics, Inc. and the Trustees of the University of Pennsylvania.	Form 10-Q	5/7/2020	10.2	
10.37	Notice of Non-Renewal of Lease Agreement dated August 16, 2011 between the Registrant and Cedar Brook 3 Corporate Center, L.P.	Form 10-Q	8/10/2020	10.1	
10.38	Loan Agreement, dated as of July 17, 2020, by and among Amicus Therapeutics International Holding Ltd, as Borrower, Amicus Therapeutics, Inc. as Parent and a Guarantor, certain subsidiaries of Parent as additional Guarantors, and Hayfin Services LLP as Agent for certain lenders	Form 10-Q	8/10/2020	10.2	
*10.39	Form of Board Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan				X
*10.40	Form of Restricted Stock Unit Award Agreement under the Amended and Restated 2007 Equity Incentive Plan				X
*10.41	Form of Board Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan				X
*10.42	Form of Stock Option Award Agreement under the Amended and Restated 2007 Equity Incentive Plan				X
21	List of Subsidiaries				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
31.1	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				X
31.2	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				X
32.1	Certificate of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				X

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing			Filed with this Form 10-K
		Form	Date	Exhibit No.	
32.2	Certificate of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				X
101	The following financial information from this Annual Report on Form 10-K for the year ended December 31, 2020, formatted in Inline XBRL (Extensible Business Reporting Language) and filed electronically herewith: (i) the Consolidated Balance Sheets; (ii) the Consolidated Statements of Operations; (iii) the Consolidated Statements of Comprehensive Loss; (iv) the Consolidated Statements of Cash Flows; (v) and the Notes to the Consolidated Financial Statements.				X
104	The cover page from the Annual Report on Form 10-K for the year ended December 31, 2020 formatted in Inline XBRL (included in Exhibit 101).				X

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

++ Subject to confidential treatment request.

* Indicates management contract or compensatory plan.

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

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

Item 16. *FORM 10-K SUMMARY.*

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

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on March 1, 2021.

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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ John F. Crowley</u> (John F. Crowley)	Chairman and Chief Executive Officer (Principal Executive Officer)	March 1, 2021
<u>/s/ Bradley L. Campbell</u> (Bradley L. Campbell)	President and Chief Operating Officer (President)	March 1, 2021
<u>/s/ Daphne Quimi</u> (Daphne Quimi)	Chief Financial Officer (Principal Financial Officer)	March 1, 2021
<u>/s/ Samantha Prout</u> (Samantha Prout)	Global Controller (Principal Accounting Officer)	March 1, 2021
<u>/s/ Robert Essner</u> (Robert Essner)	Director	March 1, 2021
<u>/s/ Margaret G. McGlynn, R.Ph.</u> (Margaret G. McGlynn, R.Ph.)	Director	March 1, 2021
<u>/s/ Michael G. Raab</u> (Michael G. Raab)	Director	March 1, 2021
<u>/s/ Glenn Sblendorio</u> (Glenn Sblendorio)	Director	March 1, 2021

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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Craig Wheeler</u> (Craig Wheeler)	Director	March 1, 2021
<u>/s/ Lynn Bleil</u> (Lynn Bleil)	Director	March 1, 2021
<u>/s/ Burke Whitman</u> (Burke Whitman)	Director	March 1, 2021
<u>/s/ Michael A. Kelly</u> (Michael A. Kelly)	Director	March 1, 2021

COMPANY INFORMATION

HEADQUARTERS

Amicus Therapeutics, Inc.
3675 Market Street
Philadelphia, PA 19104

TRANSFER AGENT

**American Stock Transfer
& Trust Company, LLC**

6201 15th Avenue
Brooklyn, NY 11219
718 921 8200

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Ernst & Young LLP

STOCKHOLDER INQUIRIES

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

Amicus Therapeutics Inc.
Investor Relations
ir@amicusrx.com

COMMON STOCK

NASDAQ Symbol: FOLD

SEC FORM 10-K

A copy of the Company's annual report to the Securities and Exchange Commission on Form 10-K will be available without charge upon written request to Amicus Therapeutics, Inc., 3675 Market Street, Philadelphia, PA 19104 or via the Company's website at www.amicusrx.com.

ANNUAL MEETING

Amicus will hold its Annual General Meeting of Shareholders virtually on June 10, 2021 at 9:00 a.m. ET.

SAFE HARBOR

This annual report contains certain forward-looking statements. For a discussion of forward-looking statements, please see Part 1, Item 1 of our annual report on Form 10-K for 2020.

EXECUTIVE OFFICERS

JOHN F. CROWLEY

Chairman and
Chief Executive Officer

BRADLEY L. CAMPBELL

President and
Chief Operating Officer

DAPHNE QUIMI

Chief Financial Officer

ELLEN S. ROSENBERG

Chief Legal Officer and
Corporate Secretary

DAVID CLARK

Chief People Officer

HUNG DO PH.D.

Chief Science Officer

SAMANTHA PROUT

Global Controller and
Principal Accounting Officer

BOARD OF DIRECTORS

JOHN F. CROWLEY

Chairman and
Chief Executive Officer

MICHAEL G. RAAB

Lead Independent Director
Nominating and Governance
(Chair)
Audit and Compliance
Science and Technology

LYNN D. BLEIL

Compensation and
Leadership Development
Nominating and Governance
Science and Technology

ROBERT ESSNER

Audit and Compliance

MICHAEL A. KELLY

Audit and Compliance
Science and Technology

BRADLEY L. CAMPBELL

President and
Chief Operating Officer

MARGARET G. MCGLYNN

Compensation and Leadership
Development (Chair)
Nominating and Governance

GLENN P. SBLENDORIO

Audit and Compliance (Chair)

CRAIG A. WHEELER

Science and Technology (Chair)
Compensation and
Leadership Development

BURKE W. WHITMAN

Audit and Compliance
Nominating and Governance

AMICUS THERAPEUTICS, INC.

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Hiroki, Age 26
Nagoya, Japan
Living with Pompe Disease



Natalie, Age 31
Los Angeles, CA
Living with Fabry Disease



Hudson, Age 11
Columbus, OH
Living with Batten Disease