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CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common stock, par value $0.01 per share	18,720,930	$10.75	$201,249,998	$24,391.50

(1) Includes an additional 2,441,860 shares of common stock that the underwriters have an option to purchase.

(2) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended. This "Calculation of Registration Fee" table shall be deemed to update the "Calculation of Registration Fee" table in the registrant's Registration Statement on Form S-3 (File No. 333-211005) in accordance with Rules 456(b) and 457(r) under the Securities Act of 1933, as amended.

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Filed pursuant to Rule 424(b)(5)
Registration No.: 333-231017

Prospectus Supplement
(to prospectus dated April 24, 2019)

AMICUS THERAPEUTICS, INC.

16,279,070 shares

We are offering 16,279,070 shares of our common stock, par value $0.01 per share, at a public offering price of $10.75 per share.

Our common stock is listed on The NASDAQ Global Market under the symbol "FOLD." On May 30, 2019, the last reported sale price of our common stock on The NASDAQ Global Market was $10.96 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page S-11 of this prospectus supplement, page 3 of the accompanying prospectus and under similar headings in the other documents that are incorporated by reference in this prospectus supplement and the accompanying prospectus.

	Per share	Total
Public offering price	$ 10.75	$ 175,000,000
Underwriting discounts and commissions	$ 0.645	$ 10,500,000
Proceeds to us before expenses	$ 10.105	$ 164,500,000

The underwriters may also purchase up to an additional 2,441,860 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, within 30 days of the date of this prospectus supplement. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be approximately $12,075,000, and our total proceeds before expenses, will be approximately $189,175,000.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of our common stock on or about June 4, 2019.

J.P. Morgan **Goldman Sachs & Co. LLC** **SVB Leerink**

The date of this prospectus supplement is May 30, 2019.

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Prospectus supplement

Prospectus

About this prospectus supplement

This prospectus supplement and the accompanying prospectus are part of a universal shelf registration statement on Form S-3 (File No. 333-231017) that we filed with the U.S. Securities and Exchange Commission (the "SEC") on April 24, 2019, which became effective automatically upon the filing thereof. This document is in two parts. The first part is this prospectus supplement which describes the terms of this offering of our common stock and adds to and updates the information contained in the accompanying prospectus. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or in any document incorporated by reference into this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, you should rely on the information in this prospectus supplement.

This prospectus supplement and the accompanying prospectus relate to the offering of shares of our common stock. Before buying any of the shares of common stock offered hereby, we urge you to read carefully this prospectus supplement and the accompanying prospectus, together with the information incorporated herein by reference as described below under the heading "Incorporation of Certain Information by Reference." This prospectus supplement contains information about the common stock offered hereby and may add to, update or change information in the accompanying prospectus.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different or additional information.

We are not making offers to sell or solicitations to buy our common stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. Persons outside the United States who come into possession of this prospectus supplement and accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of our securities and the distribution of this prospectus supplement and accompanying prospectus outside the United States. You should assume that the information in this prospectus supplement and the accompanying prospectus is accurate only as of the date on the front of the respective document and that any information that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or the accompanying prospectus or the time of any sale of a security.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated herein by reference as exhibits to the registration statement, and you may obtain copies of those documents as described below under the section entitled "Incorporation of Certain Information by Reference."

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when

made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement and the accompanying prospectus contain and incorporate by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly-available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information.

Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus supplement, accompanying prospectus or the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors. Accordingly, investors should not place undue reliance on this information.

Unless the context otherwise requires, in this prospectus supplement the "Company," "we," "us," "our" and similar names refer to Amicus Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

This prospectus supplement and the accompanying prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. We have registrations and/or filed applications to register certain trademarks in the U.S. 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. All other trademarks or trade names referred to in this prospectus supplement are the property of their respective owners.

Prospectus supplement summary

This summary highlights selected information about us and this offering and does not contain all of the information that you should consider in making your investment decision. You should carefully read this entire prospectus supplement and the accompanying prospectus, including the risks and uncertainties discussed under the heading "Risk Factors" beginning on page S-11 of this prospectus supplement, and the information incorporated by reference in this prospectus supplement, including our financial statements, before making an investment decision. If you invest in our securities, you are assuming a high degree of risk.

Our company

Overview

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

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. Our Chaperone-Advanced Replacement Therapy platform technology is leveraged to combine our novel Pompe biologic ATB200 with a pharmacological chaperone AT2221.

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

In October 2018, we further expanded our gene therapy portfolio through a collaboration agreement with the Gene Therapy Program in the Perelman School of Medicine at the University of Pennsylvania ("Penn") to pursue the research and development of novel gene therapies for four additional indications, including Pompe disease, Fabry disease, cyclin-dependent kinase-like 5 ("CDKL5") deficiency disorder and one additional undisclosed rare metabolic disorder. On May 29, 2019, we announced an expansion of the Penn

collaboration to include 1) exclusive worldwide rights to a majority of lysosomal disorders to next generation Penn gene technologies; 2) expansion from 3 to 6 immediate programs for rare genetic diseases; and 3) exclusive worldwide rights to 12 additional specified rare diseases. This relationship will combine our protein engineering and glycobiology expertise with Penn's adeno associated virus ("AAV") gene transfer technologies to develop gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability.

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

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

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 make current treatments obsolete, provide significant benefits to patients, and be first- or best-in-class. In addition to our lead programs in Fabry and Pompe, we have begun to leverage our global capabilities to develop and expand our robust pipeline through our recent entry into genomic medicine. Since the beginning of 2017, we have made significant progress toward fulfilling our vision to build a leading global biotechnology company focused on rare metabolic diseases.

Highlights of our progress in 2018 and 2019 include:

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

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

- *Pipeline Growth:* With 14 new gene therapy programs for LDs, we have established a leading portfolio of medicines for people living with rare metabolic disorders. Through our license with NCH, we acquired worldwide development and commercial rights for ten gene therapy programs in rare, neurologic LDs with lead programs in CLN6, CLN3, and CLN8 Batten disease. An additional six programs were added to the pipeline through the collaboration with Penn to pursue research and development of novel gene therapies for Pompe disease, Fabry disease, CDKL5 deficiency disorder ("CDD"), Niemann Pick Type C, Mucopolysaccharidosis Type IIIA and Mucopolysaccharidosis Type IIIB. In addition, we have rights to

initiate additional programs for the treatment of certain lysosomal diseases and other rare metabolic disorders yet to be identified.

- *Manufacturing.* We successfully scaled up manufacturing of our Pompe biologic to commercial scale (1,000L) for our pivotal PROPEL study and commercial supply. Our supply agreement with WuXi Biologics and current capacity are expected to produce sufficient quantities to serve the entire Pompe population as quickly as possible after receipt of applicable regulatory approvals. Through our collaborations with NCH and Penn, we also gain access to their preclinical manufacturing capabilities, clinical supply and CMO relationships for those gene therapy programs.

- *Financial strength.* Total cash, cash equivalents and marketable securities of $504.2 million at December 31, 2018 compared to $358.6 million at December 31, 2017. The current cash position, including expected Galafold® revenues, is sufficient to fund ongoing Fabry, Pompe and gene therapy program operations into at least mid-2021. Potential future business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

Our commercial product and product candidates

Galafold® (Migalastat HCl) for fabry disease

Fabry disease is an X-linked disease caused by mutations in the GLA gene, which encodes the alpha-Gal A enzyme. 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. 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.

Our oral precision medicine Galafold® was granted accelerated approval by the FDA in August 2018 under the brand name Galafold® for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene ("GLA") variant based on in vitro assay data. The FDA approved Galafold® for 348 amenable GLA variants. Galafold® was approved in the EU in May 2016 as a first-line therapy for long-term treatment of adults and adolescents, aged 16 years and older, with a confirmed diagnosis of Fabry disease and who have an amenable variant. The approved EU label includes 367 Fabry-causing variants, which represent up to half of all patients with Fabry disease. Approvals have also been granted in Australia, Canada, Israel, Japan, South Korea, and Switzerland, with additional applications pending in other geographies. We have been granted pricing and reimbursement in 24 countries. We plan to continue to launch Galafold® in additional countries during 2019.

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

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. Through our collaboration agreement with Penn we are pursuing research and development of novel gene therapies for Fabry disease.

Novel ERT for pompe disease

We are leveraging our biologics capabilities and CHART® platform to develop AT-GAA, a novel treatment paradigm for Pompe disease. AT-GAA consists of a uniquely engineered rhGAA enzyme, ATB200, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with a pharmacological chaperone, AT2221, to improve activity and stability. We initiated a global phase 3 clinical study (ATB200-03, or PROPEL) of AT-GAA in adult patients with late onset Pompe disease in 2018, with the first patient dosed in December 2018.

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

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

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

On February 5, 2019 we reported additional interim data from our clinical study ATB200-02 at the 15th Annual WORLDSymposium™. Highlights included safety and tolerability data in patients as well as pharmacodynamic "PD" data (muscle damage biomarker and disease substrate biomarker). To date, adverse events have been generally mild and transient. AT-GAA has resulted in a low rate of infusion-associated reactions ("IARs") following 1,110+ infusions (16 events of IARs in six patients). The clinical pharmacokinetic profile has been consistent with previously reported preclinical data. Treatment with AT-GAA resulted in persistent and durable reductions in creatine kinase and urine hexose tetrasaccharide across all patient cohorts up to month 24.

With regard to efficacy, muscle function improved in 16 out of 17 patients who have available data for up to 21 or 24 months. Mean 6MWT improved in both ERT-naïve and ERT-switch patients with continued benefit observed out to month 24. All 5 ERT-naive patients showed increases in 6MWT distance at all time points out to month 21. The ERT-naïve patients showed mean increases of 42 meters at month 6 (n=5), 63 meters at month 12 (n=5), and 55 meters at month 21 (n=5). 6MWT increased in 7/10, 9/10, and 8/8 ERT-switch patients at Months 6, 12, and 24 respectively. The ERT-switch patients showed mean increases of 24 meters at month 6 (n=10), 42 meters at month 12 (n=10), and 54 meters at month 24 (n=8). Other motor function tests generally showed mean improvements consistent with 6MWT distance out to month 21 or 24 in both ambulatory cohorts. Non-ambulatory ERT-switch patients showed improvements in upper extremity strength (which includes elbow and shoulder) from baseline to month 24, as measured by quantitative muscle testing and manual muscle testing. Pulmonary function improved in ERT-naïve

patients and was generally stable in ERT-switch patients. In ERT-naïve patients, mean absolute change in forced vital capacity (FVC), one of the main measures of pulmonary function in Pompe disease, was +4.2% at month 6 (n=5), +4.5% at month 12 (n=5), and +6.1% at month 21 (n=5). In ERT-switch patients mean absolute change in FVC was –1.2% at month 6 (n=9), –3.0% at month 12 (n=9), and –0.6% at month 24 (n=7). Overall, other pulmonary tests of maximal inspiratory pressure (MIP), a measure of inhalation, and maximal expiratory pressure (MEP), a measure of exhalation, were stable or increased in both ERT-naïve and ERT-switch patients.

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. Through our collaboration agreement with Penn we are pursuing research and development of novel gene therapies for Pompe disease.

In April 2019, we presented initial preclinical data from our investigational adeno-associated viral ("AAV") gene therapy program for Pompe disease in mice. This initial preclinical study used a single high dose of AAV in the acid alpha-glucosidase ("GAA") knockout mice with either natural unmodified hGAA ("natural hGAA") or an Amicus/Penn engineered hGAA transgene with a Lysosomal-Targeting Cell receptor binding motif ("engineered hGAA"). The Amicus/Penn engineered hGAA AAV gene therapy demonstrated more uniform cellular uptake and lysosomal targeting compared to natural hGAA AAV gene therapy, as well as, robust glycogen reduction in all key tissues in Pompe disease that were assessed. In the central nervous system, the engineered hGAA AAV gene therapy showed robust glycogen reduction in neuronal cells, suggesting this may be an effective way to address neuronal aspects of Pompe disease. Natural hGAA AAV gene therapy did not show glycogen reduction in neuronal cells. This initial preclinical study provides initial validation for combining Amicus-engineered transgenes with Penn's AAV gene therapy technologies.

CDKL5 Deficiency Disorder ("CDD")

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

Batten disease product candidates

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

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

CLN6 Batten disease Phase 1/2 study in 2019. In the CLN3 Batten disease study, a total of three patients were dosed in the low dose group with no serious adverse events after up to 5 months following a single administration of AAV9-CLN3 gene therapy.

Strategic alliances and arrangements

We will continue to evaluate other 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 pharmacological chaperone therapeutics, ERTs, gene therapies and other technologies or products. 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.

Corporate information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our principal executive offices are located at 1 Cedar Brook Drive, Cranbury, NJ 08512 and our telephone number is (609) 662-2000. Our website address is *www.amicusrx.com*. 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 SEC. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus, and you should not consider information contained on our website as part of this prospectus supplement or the accompanying prospectus.

The offering

Common stock offered by us pursuant to this prospectus supplement	16,279,070 shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to an additional 2,441,860 shares of our common stock at the public offering price less the underwriting discounts and commissions.
Common stock to be outstanding immediately after this offering	246,459,784 shares (248,901,644 shares assuming the underwriters exercise in full their option to purchase additional shares).
Use of Proceeds	We currently intend to use the net proceeds of this offering for investment in the development of the expanded gene therapy pipeline, manufacturing capabilities for Pompe biologic AT-GAA and gene therapy product candidates, including contract manufacturing partnerships, completion of the design and build of the Amicus Process Science and Gene Therapy Manufacturing facility and for other general corporate and product development purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses. See "Use of Proceeds" on page S-16 of this prospectus supplement.
Risk Factors	An investment in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under "Risk Factors" on page S-11 of this prospectus supplement, page 3 of the accompanying prospectus, page 25 of our Annual Report on Form 10-K for the year ended December 31, 2018, and under similar headings in the other documents that are incorporated by reference herein, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus.
Market for the common stock	Our common stock is quoted and traded on The NASDAQ Global Market under the symbol "FOLD."

The number of shares of our common stock to be outstanding immediately after this offering is based on 230,180,714 shares of common stock outstanding as of March 31, 2019. Unless specifically stated otherwise, the information in this prospectus supplement is as of March 31, 2019 and excludes:

- 18,331,000 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted average exercise price of $8.94 per share, of which options to purchase 10,538,000 shares of our common stock were then exercisable;

- 2,555,000 shares of our common stock issuable upon the exercise of warrants to purchase common stock, at a weighted-average exercise price of $7.53 per share;
- 6,010,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2019;
- an aggregate of 3,403,781 shares of our common stock reserved for future grants of stock options (or other similar equity instruments) under the Amended and Restated Equity Incentive Plan;
- 13,039,635 shares of our common stock, which represents the maximum number of shares of common stock issuable upon conversion of our 3.00% Convertible Senior Notes due 2023 (the "Notes");
- 4,790,046 shares of our common stock issued since March 31, 2019 upon the conversion of the Notes; and
- 537,521 shares of our common stock issued since March 31, 2019 upon the exercise of outstanding stock options or vesting of restricted stock units.

On May 21, 2019, we entered into separate, privately negotiated exchange agreements with a limited number of holders of the Notes. As a result of these transactions, we issued an aggregate of approximately 4.8 million shares in exchange for approximately $27 million of the aggregate principal amount of the Notes. Following these transactions, $3,734,000 of the aggregate principal amount of the Notes remains outstanding.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares of common stock.

Risk factors

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the risks described below, together with all of the other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference herein and therein, including from our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q. Some of these factors relate principally to our business and the industry in which we operate. Other factors relate principally to your investment in our securities. The risks and uncertainties described therein and below are not the only risks facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also materially and adversely affect our business and operations.

If any of the matters included in the following risks were to occur, our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected. In such case, you may lose all or part of your investment.

Risks related to this offering

The exercise of options and warrants and other issuances of shares of common stock or securities convertible into or exercisable for shares of common stock following this offering will dilute your ownership interests and may adversely affect the future market price of our common stock.

Sales of our common stock in the public market, either by us or by our current stockholders, or the perception that these sales could occur, could cause a decline in the market price of our securities. All of the shares of our common stock held by those of our current stockholders who have not entered into lock-up agreements with the underwriters may be immediately eligible for resale in the open market either in compliance with an exemption under Rule 144 promulgated under the Securities Act of 1933, as amended (the "Securities Act"), or pursuant to an effective resale registration statement that we have previously filed with the SEC. Such sales, along with any other market transactions, could adversely affect the market price of our common stock.

In addition, as of March 31, 2019, there were outstanding options to purchase an aggregate of 18,331,000 shares of our common stock at a weighted average exercise price of $8.94 per share, of which options to purchase 10,538,000 shares of our common stock were then exercisable and 6,010,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2019. As of March 31, 2019, there were warrants outstanding to purchase 2,555,000 shares of our common stock, with a weighted-average exercise price of $7.53 per share, and a maximum of 13,039,635 shares of common stock issuable upon conversion of the Notes. On May 21, 2019, we entered into separate, privately negotiated exchange agreements with a limited number of holders of the Notes. Following these transactions, 4,790,046 shares were issued in exchange for approximately $27 million aggregate principal of the Notes.

The exercise of options and warrants or conversion of notes at prices below the market price of our common stock could adversely affect the price of shares of our common stock. Additional dilution may result from the issuance of shares of our common stock in connection with collaborations or manufacturing arrangements or in connection with other financing efforts.

Any issuance of our common stock that is not made solely to then-existing stockholders proportionate to their interests, such as in the case of a stock dividend or stock split, will result in dilution to each stockholder by reducing his, her or its percentage ownership of the total outstanding shares. Moreover, if

we issue options or warrants to purchase our common stock or notes convertible into our common stock in the future and those options or warrants are exercised or convertible notes are converted, you may experience further dilution. Holders of shares of our common stock have no preemptive rights that entitle them to purchase their pro rata share of any offering of shares of any class or series.

You will suffer immediate and substantial dilution in the securities you purchase.

The public offering price of $10.75 per share of our common stock is substantially higher than the pro forma net tangible book value per share of our outstanding shares immediately after this offering. As a result, investors purchasing securities in this offering will incur immediate and substantial dilution of approximately $9.15 per share of common stock, or approximately 85.1% of the public offering price. Accordingly, existing stockholders will benefit disproportionately from this offering. If we raise additional capital through the sale of equity, including convertible securities, or if our convertible securities are exchanged for equity, your percentage of ownership will be diluted. You may also experience additional dilution if stock options or warrants to purchase our shares are exercised or convertible notes are converted at less than the offering price. As of March 31, 2019, we had reserved 3,403,781 shares of our common stock for issuance under our Amended and Restated Equity Incentive Plan, 13,039,635 shares of our common stock for issuance upon conversion of the Notes and 2,555,000 shares of our common stock for issuance upon exercise of outstanding warrants. On May 21, 2019, we entered into separate, privately negotiated exchange agreements with a limited number of holders of the Notes. Following these transactions, 4,790,046 shares were issued in exchange for approximately $27 million aggregate principal of the Notes.

We have broad discretion in the use of the net proceeds of this offering and, despite our efforts, we may use the proceeds in a manner that does not increase the value of your investment.

We currently anticipate that the net proceeds from the sale of our common stock will be used for investment in the United States and international commercial infrastructure for migalastat HCl, manufacturing for ATB200 and our gene therapy product candidates in the clinical stage, the continued clinical development of our product candidates, research and development expenditures, clinical and preclinical trial expenditures, commercialization expenditures and for other general corporate purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses. However, we have not determined the specific allocation of the net proceeds among these potential uses. Our management will have broad discretion over the use and investment of the net proceeds of this offering, and, accordingly, investors in this offering will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning our specific intentions. These proceeds could be applied in ways that do not improve our operating results or increase the value of your investment. Please see the section entitled "Use of Proceeds" on page S-16 of this prospectus supplement for further information.

Risks related to our business

We depend heavily on sales of our first product, Galafold®, in the EU, the U.S. and Japan.

We rely upon sales of our lead product, Galafold®, for the treatment of Fabry disease, which is the only product for which we have received commercial approval. We began the commercial launch of Galafold® in the EU in May 2016, in Japan in June 2018 and in the U.S. in August 2018, and have received and continue to seek commercial approval in additional foreign jurisdictions. Accordingly, we have only generated limited

revenue from product sales. 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, 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 to cease sales of Galafold®, such an event could have a material adverse effect on our business, financial condition and results of operations.

Special note regarding forward-looking statements

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements that involve substantial risks, uncertainties and assumptions. All statements, other than statements of historical facts, included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. 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, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein include, among other things, statements about:

- our expectations related to the use of proceeds, if any, from this offering;
- the progress and results of our clinical trials of our drug candidates;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT") and gene therapies;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of lysosomal disorders and gene therapies for the treatment of rare genetic metabolic diseases;
- the future results of on-going preclinical research and subsequent clinical trials for cyclin-dependent kinase-like 5 ("CDKL5") deficiency, including our ability to obtain regulatory approvals and commercialize CDKL5 therapies and obtain market acceptance for such therapies;
- the costs, timing and outcome of regulatory review of our product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the emergence of competing technologies and other adverse market developments;
- our ability to successfully commercialize Galafold® ("migalastat HCl")
- our ability to manufacture or supply sufficient clinical or commercial products;
- our ability to obtain reimbursement for Galafold®;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®;
- our ability to obtain market acceptance of Galafold®;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;

- the extent to which we acquire or invest in businesses, products and technologies;
- our ability to successfully integrate our acquired products and technologies into our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish collaborations and obtain milestone, royalty or other payments from any such collaborators;
- our ability to adjust to changes in European and United Kingdom markets as the United Kingdom leaves the European Union; and
- fluctuations in foreign currency exchange rates; and changes in accounting standards.

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 prospectus supplement, particularly under "Risk Factors", that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. 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 prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. You should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to purchase our securities, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus supplement and the accompanying prospectus and in the registration statement of which this prospectus supplement and the accompanying prospectus form a part.

Use of proceeds

We expect to receive net proceeds of approximately $164.0 million from the sale of 16,279,070 shares of our common stock in this offering, or approximately $188.7 million if the underwriters exercise in full their option to purchase additional shares of common stock, based on a public offering price of $10.75 per share after deducting the estimated expenses related to this offering and the underwriting discounts and commissions payable by us.

We currently intend to use the net proceeds from the sale of the shares of common stock offered by us hereunder for, without limitation:

- investment in the development of the expanded gene therapy pipeline;
- manufacturing capabilities for Pompe biologic AT-GAA and gene therapy product candidates, including contract manufacturing partnerships;
- completion of the design and build of the Amicus Process Science and Gene Therapy Manufacturing facility; and
- for other general corporate and product development purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the shares of common stock offered by us hereunder. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

Dilution

Purchasers of common stock in this offering will experience immediate dilution to the extent of the difference between the public offering price per share of common stock, and the net tangible book value per share of common stock immediately after this offering.

Our net tangible book value as of March 31, 2019 was approximately $231 million, or $1.00 per share of common stock. Net tangible book value per share is determined by dividing total tangible assets less total liabilities by the aggregate number of shares of common stock outstanding as of March 31, 2019. After giving effect to the sale by us of 16,279,070 shares of common stock at the public offering price of $10.75 per share of common stock and after deducting the underwriting discounts and commissions and estimated offering expenses, our net tangible book value as of March 31, 2019 would have been approximately $395 million, or $1.60 per share of common stock. This represents an immediate increase in net tangible book value of $0.60 per share to our existing stockholders and an immediate dilution of $9.15 per share of common stock issued to the new investors purchasing securities in this offering.

The following table illustrates this per share dilution:

Public offering price per share of common stock		$ 10.75
Net tangible book value per share as of March 31, 2019	$ 1.00	
Increase per share attributable to new investors	$ 0.60	
Net tangible book value per share after this offering		$ 1.60
Dilution per share to new investors		$ 9.15

If the underwriters exercise their option in full to purchase 2,441,860 additional shares of common stock in this offering at the public offering price of $10.75 per share, the net tangible book value per share after the offering would be $1.69 per share, the increase in the net tangible book value per share to existing stockholders would be $0.69 per share and the dilution to new investors purchasing securities in this offering would be $9.06 per share.

The number of shares of our common stock to be outstanding immediately after this offering is based on 230,180,714 shares of common stock outstanding as of March 31, 2019. Unless specifically stated otherwise, the information in this prospectus supplement is as of March 31, 2019 and excludes:

- 18,331,000 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted average exercise price of $8.94 per share, of which options to purchase 10,538,000 shares of our common stock were then exercisable;
- 2,555,000 shares of our common stock issuable upon the exercise of warrants to purchase common stock, at a weighted-average exercise price of $7.53 per share;
- 6,010,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2019;
- an aggregate of 3,403,781 shares of our common stock reserved for future grants of stock options (or other similar equity instruments) under the Amended and Restated Equity Incentive Plan;
- 13,039,635 shares of our common stock, which represents the maximum number of shares of common stock issuable upon conversion of our 3.00% Convertible Senior Notes due 2023 (the "Notes");

- 4,790,046 shares of our common stock issued since March 31, 2019 upon the conversion of the Notes; and
- 537,521 shares of our common stock issued since March 31, 2019 upon the exercise of outstanding stock options or vesting of restricted stock units.

On May 21, 2019, we entered into separate, privately negotiated exchange agreements with a limited number of holders of the Notes. As a result of these transactions, we issued an aggregate of approximately 4.8 million shares in exchange for approximately $27 million of the aggregate principal amount of the Notes. Following these transactions, $3,734,000 of the aggregate principal amount of the Notes remains outstanding.

To the extent that options or warrants are exercised, new options are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there may be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Underwriting

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC and SVB Leerink LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities LLC	6,104,651
Goldman Sachs & Co. LLC	5,697,675
SVB Leerink LLC	4,476,744
Total	16,279,070

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated. The offering of the shares by the underwriters is subject to receipt and acceptance of orders and subject to the underwriters' right to reject any order in whole or in part.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $0.3870 per share. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters.

The underwriters have an option to buy up to 2,441,860 additional shares of common stock from us. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $0.645 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without exercise	With full exercise
Per Share	$ 0.645	$ 0.645
Total	$ 10,500,000	$ 12,075,000

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $489,000.

A prospectus supplement in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of the representatives for a period of 60 days after the date of this prospectus supplement, other than (A) the shares of our common stock to be sold hereunder; (B) any shares of our common stock issued upon the exercise or conversion of any options, warrants, rights or convertible securities granted under our existing stock-based compensation plans; or (C) (x) the aggregate number of securities issued in connection with any acquisition or strategic investment (including any joint venture, collaboration, partnership, alliance or other strategic or commercial relationship) existing on or following the date of the underwriting agreement; provided, however, that in the case of this clause (C), (x) the aggregate number of our securities issued does not exceed 10% of the number of shares of our common stock outstanding immediately after the issuance and sale of the shares and (y) any recipient of such securities agrees to be bound in writing by the restrictions on the resale of securities consistent with the lock-up letters described below for the lock-up period.

Our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, including permitting sales of shares of common stock pursuant to existing trading plans established pursuant to Rule 10b5-1 of the Exchange Act and the establishment of trading plans under Rule 10b5-1 of the Exchange Act (provided that no sales are made thereunder during the lock-up period), for a period of 60 days after the date of this prospectus supplement, may not, without the prior written consent of the representatives, (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares

of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on The NASDAQ Global Market under the symbol "FOLD".

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through their option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Stock Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The NASDAQ Stock Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ Stock Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling with Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Notice to prospective investors in the United Kingdom

This prospectus is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a "relevant person"). The ADSs are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such ADSs will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common shares to be offered so as to enable an investor to decide to purchase our common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU, and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

Notice to prospective investors in Hong Kong, Singapore and Japan

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any

person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to prospective investors in Canada

The shares offered in this prospectus supplement may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor. Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Legal matters

The validity of the securities we are offering will be passed upon by Pepper Hamilton LLP, Philadelphia, Pennsylvania. In connection with this offering, Dechert LLP, Philadelphia, Pennsylvania advised the underwriters with respect to certain U.S. securities law matters.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018, and the effectiveness of our internal control over financial reporting as of December 31, 2018, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Where you can find more information

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement and the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated herein by reference for a copy of such contract, agreement or other document.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov.

We also maintain a website at amicusrx.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus supplement, and you should not consider such information contained on, or accessed through, our website as part of this prospectus supplement.

In addition, you may request copies of these filings at no cost, by writing or telephoning us at the following address or telephone number:

Office of the Corporate Secretary
Amicus Therapeutics, Inc.
1 Cedar Brook Drive
Cranbury, NJ 08512
(609) 662-2000

Incorporation of certain information by reference

The SEC allows us to "incorporate by reference" information into this prospectus supplement. This means that we can disclose important information to you by referring you to other documents we have filed separately with the SEC, without actually including the specific information in this prospectus supplement. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC (and that is deemed to be "filed" with the SEC) will automatically update, and may supersede, information in this prospectus supplement.

- Our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on February 28, 2019;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2018 from our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 29, 2019;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed with the SEC on May 9, 2019;
- Our Current Reports on Form 8-K filed with the SEC on January 3, 2019, January 7, 2019, January 18, 2019, January 24, 2019, February 5, 2019, February 8, 2019, February 25, 2019, February 26, 2019, February 28, 2019 (Film No. 19645014), March 13, 2019, March 20, 2019, April 30, 2019, May 13, 2019, May 14, 2019, May 21, 2019, May 22, 2019, and May 29, 2019; and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed on May 23, 2007, under the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference any future filings (except as specifically enumerated above, other than any filings or portions of such reports that are not deemed "filed" under the Exchange Act in accordance with the Exchange Act and applicable SEC rules, including current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus supplement forms a part, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus supplement and will become a part of this prospectus supplement from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see "Where You Can Find More Information" on page S-25 of this prospectus supplement.

PROSPECTUS

AMICUS THERAPEUTICS, INC.

Common Stock
Preferred Stock
Warrants
Debt Securities
Units
Subscription Rights

We may offer to the public from time to time in one or more series or issuances:

- shares of our common stock;
- shares of preferred stock;
- warrants to purchase shares of our common stock, preferred stock and/or debt securities;
- debt securities consisting of debentures, notes or other evidences of indebtedness;
- units consisting of a combination of the foregoing securities;
- subscription rights to purchase any of the foregoing securities; or
- any combination of these securities.

This prospectus provides a general description of the securities that we may offer. Each time that we offer securities under this prospectus, we will provide the specific terms of the securities offered, including the public offering price, in a supplement to this prospectus. Any prospectus supplement may add to, update or change information contained in this prospectus. You should read this prospectus and any applicable prospectus supplement together with additional information described under the heading "Where You Can Find More Information" before you make your investment decision.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and the comparable section of any applicable prospectus supplement. If any underwriters are involved in the sale of the securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in the applicable prospectus supplement.

Our common stock is traded on the NASDAQ Global Market under the symbol "FOLD." On April 23, 2019, the closing price of our common stock was $13.29.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. RISKS ASSOCIATED WITH AN INVESTMENT IN OUR SECURITIES WILL BE DESCRIBED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND CERTAIN OF OUR FILINGS WITH THE SECURITIES AND EXCHANGE COMMISSION INCORPORATED BY REFERENCE INTO THIS PROSPECTUS, AS DESCRIBED UNDER "RISK FACTORS" ON PAGE 3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is April 24, 2019.

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Prospectus

ABOUT THIS PROSPECTUS

This prospectus is part of a universal shelf registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission, or the SEC, under the Securities Act of 1933, as amended, or the Securities Act. To the extent required for any offer and sale, a prospectus supplement will set forth the type and number of securities being offered, the offering price, the names of any underwriters, dealers, brokers or agents and the applicable sales commission or discount. We may offer and sell any combination of the securities described in this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read carefully the entire prospectus and any prospectus supplement, as well as the documents incorporated by reference into this prospectus and/or any prospectus supplement, before making an investment decision.

This prospectus provides you only with a general description of the securities that we may offer and sell. Each time securities are offered and sold under the shelf registration statement, we will provide a prospectus supplement that will contain specific information about the terms of those securities and the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement, including all documents incorporated herein by reference herein and therein, together with the additional information described under "Where You Can Find More Information" below.

The information contained in this prospectus is not complete and may be changed. You should rely only on the information provided in or incorporated by reference in this prospectus or in any prospectus supplement, or documents to which we otherwise refer you. We have not authorized anyone else to provide you with different information.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement, if any, is accurate on any date subsequent to the date set forth on the front of such document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

References in this prospectus to the terms "the Company," "Amicus," "we," "our" and "us" or other similar terms mean Amicus Therapeutics, Inc. and our wholly owned subsidiary, unless we state otherwise or the context indicates otherwise.

THE COMPANY

Overview

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

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221), a novel, clinical-stage, potential best-in-class treatment paradigm for Pompe disease. Our Chaperone-Advanced Replacement Therapy platform technology is leveraged to combine our novel Pompe biologic ATB200 with a pharmacological chaperone AT2221.

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

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

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

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

Corporate information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our global headquarters are located at 1 Cedar Brook Drive, Cranbury, NJ 08512 and our telephone number is (609) 662-2000. Our website address is www.amicusrx.com. 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 SEC. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider information contained on our website as part of this prospectus.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 filed on February 28, 2019, with the SEC, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

FORWARD-LOOKING STATEMENTS

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

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

- the progress and results of our preclinical and clinical trials of our drug candidates;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT") and gene therapies;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of lysosomal storage disorders and gene therapies for the treatment of rare genetic metabolic diseases;

- the future results of on-going preclinical research and subsequent clinical trials for CDKL5 deficiency, including our ability to obtain regulatory approvals and commercialize CDKL5 therapies and obtain market acceptance for such therapies;
- the costs, timing and outcome of regulatory review of our product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the emergence of competing technologies and other adverse market developments;
- our ability to successfully commercialize Galafold®;
- our ability to manufacture or supply sufficient clinical or commercial products;
- our ability to obtain reimbursement for Galafold®;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®;
- our ability to obtain market acceptance of Galafold®;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the extent to which we acquire or invest in businesses, products and technologies;
- our ability to successfully integrate our acquired products and technologies into our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish collaborations and obtain milestone, royalty or other payments from any such collaborators;
- our ability to adjust to changes in European and United Kingdom markets as the United Kingdom leaves the European Union; and
- fluctuations in foreign currency exchange rates; and changes in accounting standards.

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 prospectus, particularly under "Risk Factors" that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Those factors and the other risk factors described herein are not necessarily all of the important factors that could cause actual results or developments to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors also could harm our results. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make. Consequently, there can be no assurance that actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, us. Given these uncertainties, investors are cautioned not to place undue reliance on such forward-looking statements.

You should read this prospectus and the documents that we incorporate by reference herein and therein 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 prospectus. 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. Before deciding to purchase our securities, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus and in the registration statement of which this prospectus is a part.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement relating to a specific offering, we intend to use the net proceeds from the sale of securities by us under this prospectus for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, manufacturing expenditures, clinical trial expenditures, commercial expenditures, repayment and refinancing of debt, acquisitions of new technologies or businesses, and investments. Additional information on the use of net proceeds from the sale of securities by us under this prospectus shall be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

We may sell the offered securities in any of the ways described below or in any combination or any other way set forth in an applicable prospectus supplement from time to time:

- to or through underwriters or dealers;
- through one or more agents; or
- directly to purchasers or to a single purchaser.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

In connection with each offering, a prospectus supplement will describe the method of distribution of the securities and any applicable restrictions. The prospectus supplement will also describe the specific terms of the offering of the securities, including the following:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallowed or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Any offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

In compliance with the guidelines of the Financial Industry Regulatory Authority, the maximum compensation to the underwriters or dealers in connection with the sale by the Company of its securities pursuant to this prospectus and the accompanying supplement to this prospectus may not exceed 8% of the aggregate offering price of the securities as set forth on the cover page of any prospectus supplement.

Only the agents or underwriters named in each prospectus supplement are agents or underwriters in connection with the securities being offered thereby.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution from us with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale.

The securities we offer may be new issues of securities and may have no established trading market. The securities may or may not be listed on a securities exchange. Underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making

at any time without notice. We can make no assurance as to the liquidity of, or the existence of trading markets for, any of the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

We also may sell any of the securities through agents designated by us from time to time. We will name any agent involved in the offer or sale of these securities and will list commissions payable by us to these agents in the applicable prospectus supplement. These agents will be acting on a best efforts basis to solicit purchases for the period of its appointment, unless stated otherwise in the applicable prospectuses.

We may sell any of the securities directly to purchasers. In this case, we will not engage underwriters or agents in the offer and sale of these securities.

GENERAL DESCRIPTION OF SECURITIES

We may offer and sell, at any time and from time to time:

- shares of our common stock;
- shares of preferred stock;
- warrants to purchase shares of our common stock, preferred stock and/or debt securities;
- debt securities consisting of debentures, notes or other evidences of indebtedness;
- units consisting of a combination of the foregoing securities;
- subscription rights to purchase any of the foregoing securities; or
- any combination of these securities.

The terms of any securities we offer will be determined at the time of sale. We may issue debt securities that are exchangeable for and/or convertible into common stock or any of the other securities that may be sold under this prospectus. When particular securities are offered, a supplement to this prospectus will be filed with the SEC, which will describe the terms of the offering and sale of the offered securities. The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement will offer a security that is not included in the Registration Statement at the time of its effectiveness or offer a security of a type that is not described in this prospectus.

DESCRIPTION OF OUR COMMON STOCK

The following summary of the terms of our common stock is subject to and qualified in its entirety by reference to our certificate of incorporation and by-laws, copies of which are on file with the SEC as exhibits to previous SEC filings. Please refer to "Where You Can Find More Information" below for directions on obtaining these documents.

As of April 24, 2019, we are authorized to issue 500,000,000 shares of common stock, $0.01 par value per share. As of April 22, 2019, we had 230,436,601 shares of common stock outstanding.

General

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer and Trust Company.

The NASDAQ Global Market

Our common stock is listed on the NASDAQ Global Market under the symbol "FOLD."

DESCRIPTION OF OUR PREFERRED STOCK

We are authorized to issue up to 10,000,000 shares of preferred stock, par value $0.01 per share. As of April 24, 2019, there were no shares of our preferred stock outstanding.

Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine the rights, preferences and limitations of each series, including voting rights, dividend rights and redemption and liquidation preferences. Satisfaction of any dividend preferences of outstanding shares of our preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of our preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of the Company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. Upon the affirmative vote of our board of directors, without stockholder approval, we may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of the Company, and, if applicable, the conversion price (or how it will be calculated), the conversion period and any other terms of conversion (including any anti-dilution provisions, if any);
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated), the exchange period and any other terms of exchange (including any anti-dilution provisions, if any);
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;

- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company;

- any material limitations on issuance of any series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company; and

- any other affirmative, negative or other covenants or contractual rights which might be attendant with the specific series of preferred stock.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Transfer Agent and Registrar

The transfer agent and registrar for any series of preferred stock will be set forth in each applicable prospectus supplement.

DESCRIPTION OF OUR WARRANTS

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;

- the currency or currency units in which the offering price, if any, and the exercise price are payable;

- the designation, amount and terms of the securities purchasable upon exercise of the warrants;

- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;

- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise of the warrants, and a description of that series of our preferred stock;

- if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise of the warrants, and a description of that series of debt securities;

- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;

- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;

- any applicable material U.S. federal income tax consequences;

- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange or market;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF OUR DEBT SECURITIES

This section describes the general terms and provisions of the debt securities that we may offer under this prospectus, any of which may be issued as convertible or exchangeable debt securities. We will set forth the particular terms of the debt securities we offer in a prospectus supplement. The extent, if any, to which the following general provisions apply to particular debt securities will be described in the applicable prospectus supplement. The following description of general terms relating to the debt securities and the indenture under which the debt securities will be issued are summaries only and therefore are not complete. You should read the indenture and the prospectus supplement regarding any particular issuance of debt securities.

We will issue any debt securities under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture any amendment or supplement thereto and those made part of the indenture by reference to the Trust Indenture Act of 1939, or the Trust Indenture Act, as in effect on the date of the indenture. We have filed or will file a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety by reference to the detailed provisions of the indenture and the final form indenture which will be filed with a future prospectus supplement and any amendment or supplement thereto.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the SEC.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

- the title of the series;
- the aggregate principal amount;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- the date or dates on which principal is payable;
- the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;
- the place or places where principal and, if applicable, premium and interest, is payable;
- the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;
- the denominations in which such debt securities may be issuable, if other than denominations of $1,000 or any integral multiple of that number;
- whether the debt securities are to be issuable in the form of certificated securities (as described below) or global securities (as described below);
- the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;
- the currency of denomination;
- the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;
- if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;
- if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;
- the provisions, if any, relating to any collateral provided for such debt securities;
- any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;
- any events of default, if not otherwise described below under "Events of Default";
- the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents
- any guarantees of the debt securities;

- the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company; and

- the terms and conditions, if any, pursuant to which the debt securities, in whole or in part, shall be defeasible.

All debt securities of one series need not be issued at the same time and, unless otherwise provided, a series may be reopened, without the consent of any holder, for issuances of additional debt securities of that series with the same terms as the original debt securities of that series (other than the issue price and the interest accrued prior to the issue date of the additional debt securities). We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement. We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of our common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

- "book-entry securities," which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or

- "certificated securities," which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

Certificated Debt Securities

If you hold certificated debt securities issued under an indenture, you may transfer or exchange such debt securities in accordance with the terms of the indenture. You will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Global Securities

The debt securities of a series may be issued in the form of one or more global securities that will be deposited with a depositary or its nominees identified in the prospectus supplement relating to the debt securities. In such a case, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding debt securities of the series to be represented by such global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a global security may not be registered for transfer or exchange except as a whole by the depositary for such global security to a nominee of the depositary and except in the circumstances described in the prospectus supplement relating to the debt securities. The specific terms of the depositary arrangement with respect to a series of debt securities will be described in the prospectus supplement relating to such series.

Protection in the Event of Change of Control

Any provision in an indenture that governs our debt securities covered by this prospectus that includes any covenant or other provision providing for a put or increased interest or that would otherwise afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control of the Company, or a highly leveraged transaction will be described in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities may not have the benefit of any covenant that limits or restricts our business or operations, the pledging of our assets or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger and Sale of Assets

We may agree in any indenture that governs the debt securities of any series covered by this prospectus that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless:

- we are the surviving entity of any such merger or consolidation or the entity formed by such merger or consolidation shall be organized under the laws of the United States of America, or any state thereof or the District of Columbia, and shall expressly assume by a supplemental indenture all of our obligations related to such debt securities; and

- immediately before and immediately after the merger or consolidation, no default or event of default shall have occurred and be continuing.

Notwithstanding the foregoing, the indenture may allow certain transactions, including, but not limited to, a merger between us and our wholly owned subsidiary or a merger between us and our affiliate for the purpose of converting us into a corporation under the laws of the United States of America, or any state thereof or the District of Columbia, or for the purpose of creating or collapsing a holding company structure.

Defaults and Notice

The debt securities of any series will contain events of default to be specified in the applicable prospectus supplement, which may include, without limitation:

- failure to pay the principal of, or premium, if any, on any debt security of such series when due and payable (whether at maturity, upon redemption, acceleration or otherwise);

- failure to make a payment of any interest on any debt security of such series when due and payable and such failure continues for a period of 30 days;

- our failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series and such failure continues for a period of 60 days

after written notice from the trustee or holders of 25% in the aggregate principal amount of the then-outstanding debt securities of such series; and

- certain events relating to our or our significant subsidiaries' bankruptcy, insolvency or reorganization.

If an event of default with respect to debt securities of any series shall occur and be continuing, we may agree that the trustee or the holders of at least 25% in aggregate principal amount of the then-outstanding debt securities of such series may declare the principal amount of all debt securities of such series or such other amount or amounts as the debt securities or supplemental indenture with respect to such series may provide, to be due and payable immediately. Any provisions pertaining to events of default and any remedies associated therewith will be described in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus may require that the trustee under such indenture shall, within 90 days after the trustee knows of the occurrence of a default, give to holders of debt securities of any series notice of all uncured defaults with respect to such series known to it. However, except in the case of a default that results from the failure to make any payment of the principal of, or interest or premium, if any, on the debt securities of any series, the trustee may withhold such notice if it in good faith determines that the withholding of such notice is in the interest of the holders of debt securities of such series. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus will contain a provision entitling the trustee to be indemnified by holders of debt securities before instituting a proceeding or pursuing a remedy under the indenture at the request of such holders. Any such indenture may provide that the holders of at least a majority in aggregate principal amount of the then-outstanding debt securities of any series may direct the time, method and place of conducting any proceedings for any remedy available to the trustee, or of exercising any trust or power conferred upon the trustee with respect to the debt securities of such series. However, the trustee under any such indenture may decline to follow any such direction if, among other reasons, the trustee determines that the actions or proceedings as directed may not lawfully be taken, would involve the trustee in personal liability or would be unduly prejudicial to the holders of the debt securities of such series not joining in such direction.

Any indenture that governs our debt securities covered by this prospectus may permit the holders of such debt securities to institute a proceeding with respect to such indenture, subject to certain conditions, which will be specified in the applicable prospectus supplement and which may include that the holders of at least 25% in aggregate principal amount of the debt securities of such series then-outstanding make a prior written request upon the trustee to exercise its power under the indenture, and offer reasonable indemnity to the trustee. Even so, such holders may have an absolute right to receipt of the principal of, or premium, if any, and interest when due, to require conversion or exchange of debt securities if such indenture provides for convertibility or exchangeability at the option of the holder and to institute suit for the enforcement of such rights. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Modification of the Indenture

We and the trustee may modify any indenture that governs our debt securities of any series covered by this prospectus with or without the consent of the holders of such debt securities, under certain circumstances to be described in a prospectus supplement.

Defeasance; Satisfaction and Discharge

The prospectus supplement will outline the conditions under which we may elect to have certain of our obligations under the indenture discharged and under which the indenture obligations will be deemed to be satisfied.

Any indenture that governs our debt securities covered by this prospectus may provide that we may discharge our obligations under such debt securities and the indenture with respect to such debt securities if:

- either (A) there shall have been canceled by the trustee under the indenture, or delivered to the trustee for cancellation, all debt securities of such series theretofore authenticated and delivered or (B) all such debt securities not theretofore delivered to the trustee for cancellation have become due and payable or will become due and payable within one year or are to be called for redemption within one year under irrevocable arrangements for the giving of notice of redemption by the trustee;

- we have irrevocably deposited or caused to be deposited with the trustee funds in an amount sufficient to pay and discharge the entire indebtedness on the debt securities not theretofore delivered to the trustee for cancellation, for principal, premium, if any, and interest to the maturity or date of redemption;

- we have paid all other sums payable by us under the indenture or deposited all other required sums with the trustee; and

- the deposit will not result in a breach or violation of, or constitute a default under, any other instrument or agreement to which we are a party or to which we are bound.

Any indenture that governs our debt securities covered by this prospectus may provide that we may be discharged from our obligations with respect to any debt securities, subject to certain exceptions. Further, any indenture that governs our debt securities covered by this prospectus may provide that we may be released from our obligations under certain sections of such indenture, subject to certain exceptions. In either case, such indenture may provide that certain conditions must be satisfied prior to such discharge or release, including, but not limited to:

- we shall have irrevocably deposited with the trustee, in trust, for the purpose of making the following payments, specifically pledged as security for, and dedicated solely to, the benefit of the holders of the debt securities, (a) money, (b) U.S. or foreign government obligations which through the scheduled payment of principal and interest in respect thereof in accordance with their terms will provide, not later than the due date of any payment, money, or (c) a combination thereof, in an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal, accrued interest and premium, if any;

- there shall be no continuing default or event of default with respect to such debt securities at the time of the deposit or after giving effect thereto;

- there shall not be certain conflicting interest for purposes of the Trust Indenture Act;

- such actions shall not result in a breach or violation of, or constitute a default under, any other agreement or instrument to which we are bound;

- we shall have delivered a legal opinion relating to certain tax matters; and

- we shall have delivered a legal opinion and certain other certificates relating to the satisfaction of the required conditions.

Regarding the Trustee

We will identify the trustee and any relationship that we may have with such trustee, with respect to any series of debt securities, in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of the Company, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any "conflicting interest" within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

Governing Law

The law governing the indenture and the debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

DESCRIPTION OF OUR UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. Units may be offered independently or together with common stock, preferred stock, debt securities and/or warrants offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will generally apply to any future units that we may offer under this prospectus, we will describe the particular terms of any series of units that we may offer in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of unit agreement, including a form of unit certificate if any, that describes the terms of the series of units we are offering before the issuance of the related series of units. The following summaries of material provisions of the units, and the unit agreements, are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the units that we sell under this prospectus, as well as the complete unit agreements that contain the terms of the units.

General

We may issue units comprised of one or more shares of common stock or preferred stock, debt securities and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether, and under what circumstances, those securities may be held or transferred separately;
- the rights and obligations of the unit agent, if any;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under "Description of Our Common Stock," "Description of our Preferred Stock," "Description of Our Debt Securities" and "Description of Our Warrants," will apply to each unit and to any common stock, preferred stock, debt securities or warrants included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

DESCRIPTION OF OUR SUBSCRIPTION RIGHTS

As specified in any applicable prospectus supplement, we may issue subscription rights consisting of one or more debt securities, shares of preferred stock, shares of common stock or any combination of such securities.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon for us by Pepper Hamilton LLP, Philadelphia, Pennsylvania. As appropriate, legal counsel representing the underwriters, dealers or agents will be named in the accompanying prospectus supplement and may opine to certain legal matters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018 and the effectiveness of our internal control over financial reporting as of December 31, 2018, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated herein by reference for a copy of such contract, agreement or other document.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. We also maintain a website at amicusrx.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider such information contained on, or accessed through, our website as part of this prospectus.

In addition, you may request copies of these filings at no cost, by writing or telephoning us at the following address or telephone number:

Office of the Corporate Secretary
Amicus Therapeutics, Inc.
1 Cedar Brook Drive
Cranbury, NJ 08512
(609) 662-2000

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus. This means that we can disclose important information to you by referring you to other documents we have filed separately with the SEC, without actually including the specific information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC (and that is deemed to be "filed" with the SEC) will automatically update, and may supersede, information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-33497):

- Our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on February 28, 2019;
- Our Current Reports on Form 8-K filed with the SEC on January 3, 2019, January 7, 2019, January 18, 2019, January 24, 2019, February 5, 2019, February 8, 2019, February 25, 2019, February 26, 2019, February 28, 2019 (Film Number 19645014), March 13, 2019 and March 20, 2019; and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed with the SEC on May 23, 2007, under the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference any future filings (except as specifically enumerated above, other than any filings or portions of such reports that are not deemed "filed" under the Exchange Act in accordance with the Exchange Act and applicable SEC rules, including current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus forms a part, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see "Where You Can Find More Information" on page 18 of this prospectus.

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16,279,070 Shares

AMICUS THERAPEUTICS, INC.

Common Stock

Prospectus supplement

J.P. Morgan **Goldman Sachs & Co. LLC** **SVB Leerink**

May 30, 2019