AMICUS THERAPEUTICS INC
Form 424B5
June 10, 2015

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Filed pursuant to Rule 424(b)(5)
Registration No.: 333-202474

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, nor are they soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated June 10, 2015

Preliminary prospectus supplement
(To Prospectus dated May 4, 2015)

AMICUS THERAPEUTICS, INC.

$150,000,000

We are offering shares of our common stock, par value $0.01 per share, at an aggregate public offering price of up to $150,000,000.

Our common stock is listed on The NASDAQ Global Market under the symbol "FOLD." On June 10, 2015, the last reported sale price of our common stock on The NASDAQ Global Market was $13.09 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-7 of this prospectus supplement, page 4 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	$	$
Underwriting discounts and commissions	$	$
Proceeds to us before expenses	$	$

The underwriters may also purchase up to an additional $22,500,000 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 will be $, and our total proceeds before expenses, will be $.

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 , 2015.

J.P. Morgan **Goldman, Sachs & Co.**

Cowen and Company

Janney Montgomery Scott

The date of this prospectus supplement is June , 2015.

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Prospectus supplement

Prospectus

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About this prospectus supplement

This prospectus supplement and the accompanying prospectus are part of a "shelf" registration statement on Form S-3 (File No. 333-202474) that we initially filed with the Securities and Exchange Commission, or the SEC, on March 3, 2015, and that was declared effective by the SEC on May 4, 2015. 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

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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. and its wholly owned subsidiary, Callidus Biopharma, Inc. ("Callidus").

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 registered or filed applications to register certain trademarks in the United States and abroad, including AMICUS , AMICUS THERAPEUTICS (and design), CHART (and design) and Galafold . All other trademarks or trade names referred to in this prospectus are the property of their respective owners.

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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-7 of this prospectus supplement, and the information incorporated by reference in this prospectus, 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 biopharmaceutical company focused on the discovery, development and commercialization of next-generation medicines for a range of rare and orphan diseases, with a focus on improved therapies for lysosomal storage disorders ("LSDs"). Galafold , our lead product candidate, is a small molecule that can be used as a monotherapy and in combination with enzyme replacement therapy ("ERT") for Fabry disease. Our development programs also include next-generation ERTs for LSDs, including Pompe disease and Mucopolysaccharidosis Type I ("MPS I"). We believe that our platform technologies and our advanced product pipeline uniquely position us at the forefront of developing therapies for rare and orphan diseases.

Program status

Our personalized medicine approach consists of an oral small molecule pharmacological chaperone monotherapy that is designed to bind to and stabilize a patient's own endogenous target protein. Patients with amenable mutations may respond based on their genetics. Our Chaperone-Advanced Replacement Therapy, or CHART , platform combines chaperones with ERTs independent of a patient's own genetics. In each CHART program, a unique pharmacological chaperone is designed to bind to a specific therapeutic (exogenous) enzyme, stabilizing the enzyme in its properly folded and active form. This may allow for enhanced tissue uptake, greater lysosomal activity, more reduction of substrate, and the potential for lower immunogenicity.

Galafold (migalastat) for Fabry disease

Our Fabry franchise strategy is to develop the pharmacological chaperone migalastat HCl ("migalastat") for all patients with Fabry disease as a monotherapy for patients with amenable mutations and in combination with ERT for all other patients. We recently secured the brand name Galafold for migalastat, which has been approved by both the European Medicines Agency ("EMA") as well as the U.S. Food and Drug Administration ("FDA").

We have completed two Phase 3 global registration studies (Study 011 and Study 012) of Galafold. We submitted a marketing authorization application ("MAA") to the EMA in the second quarter of 2015 to request approval of Galafold in the European Union ("EU") for the treatment of Fabry patients who have amenable mutations. We plan to submit a new drug application ("NDA") to the FDA in the second half of 2015. We have reported Phase 3 data in both treatment naïve patients ("Study 011" or "FACETS") and ERT switch patients ("Study 012" or "ATTRACT"). Positive results from these studies have shown that treatment with Galafold has resulted in reductions in disease substrate, stability of kidney function, reductions in cardiac mass, and improvement in gastrointestinal symptoms in patients with amenable mutations confirmed by a validated assay.

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Study 011 was a 24-month study of Fabry disease patients who were treatment naïve or did not receive ERT, which investigated the safety and efficacy of oral Galafold. The study consisted of a 6-month double-blind, placebo-controlled period, a 6-month open-label period, and a 12-month open-label extension phase. Subjects completing Study 011 were eligible to continue treatment with Galafold in a long-term open-label extension ("Study 041"). 67 subjects (24 male) were enrolled. All subjects enrolled in Study 011 had amenable mutations in the clinical trial human embryonic kidney ("HEK") cell-based in vitro assay that was available at study initiation ("clinical trial assay"). Following the completion of enrollment, a Good Laboratory Practices ("GLP")-validated HEK assay was developed with a third party to measure the criteria for amenability with more quality control and rigor ("GLP HEK assay"). Approximately 10% of mutations in the HEK database switched categorization between "amenable" and "non-amenable" when moving from the clinical trial assay to the GLP HEK assay. Therefore, there were changes in categorization from amenable to non-amenable in 17 of the 67 patients enrolled in Study 011.

Study 011 was designed to measure the reduction of the disease substrate (Globotriaosylceramide, or "GL-3") in the interstitial capillaries of the kidney following treatment with oral Galafold (150 mg, every other day). The study also measured clinical outcomes, including renal function, as secondary endpoints.

Patients on Galafold experienced greater reductions in GL-3 as compared to placebo during the initial 6-month period; however, this difference was not statistically significant under the original analysis of the primary endpoint (responder analysis with a 50% reduction threshold at month 6). The variability and low levels of GL-3 at baseline contributed to a higher-than-anticipated placebo response at month 6.

Following the unblinding of the 6-month data, and while still blinded to the 12-month data, we reported the mean change in GL-3 from the baseline to month 6 as a post-hoc analysis in the subgroup of patients with GLP HEK-amenable mutations. This analysis showed a statistically significant reduction in GL-3 in the Galafold group compared to placebo. The mean change in GL-3 was identified as a more appropriate way to control for the variability in GL-3 levels in Study 011 and to measure the biological effect of Galafold.

Results from this subgroup analysis further support use of the GLP HEK assay in predicting responsiveness to Galafold. Following a Type C Meeting with the FDA (a meeting in which the FDA provides certain guidance on product development and review), we revised our statistical analysis plan to pre-specify the primary analysis at month 12 as mean change in interstitial capillaries GL-3 in patients with GLP HEK amenable mutations.

Throughout 2014 and in early 2015, we announced positive 12- and 24-month data from Study 011 and longer-term data from Study 041 in patients with amenable mutations who were naïve to ERT. Top-line data were announced in April 2014 and presented to the scientific community at the American Society of Human Genetics ("ASHG") in October 2014 and WORLDSymposium in February 2015. Highlights were as follows:

- Subjects who switched from placebo to Galafold after month 6 demonstrated a statistically significant reduction in disease substrate, or kidney interstitial capillary GL-3, at month 12 (p=0.013), and a statistically significant reduction of disease substrate in another important biomarker of disease, plasma lyso-Gb3. Subjects who remained on Galafold demonstrated a durable reduction in kidney interstitial capillary GL-3, as well as a durable reduction in lyso-Gb3.

- Kidney function, as measured by estimated glomerular filtration rate ("eGFR") and iohexol measured GFR ("mGFR"), remained stable following 18-24 months of treatment with Galafold in Study 011. Kidney function, as measured by eGFR, continued to remain stable in patients receiving Galafold in Study 011 for

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at least 18 months and continuing Galafold treatment in Study 041 for an average of 32 months. mGFR was not collected in Study 041.

Reduction in cardiac mass, as measured by left ventricular mass index ("LVMi"), was statistically significant following treatment with Galafold for up to 36 months (average of 22 months) in patients in Studies 011 and 041.

There was a significant decrease in diarrhea (unadjusted p=0.03) in patients treated with Galafold versus placebo during the 6-month double-blind phase (Stage 1). After 18-24 months of treatment with Galafold, significant improvements in diarrhea and indigestion were observed in addition to favorable trends in reflux and constipation. Gastrointestinal symptoms were assessed using the Gastrointestinal Symptoms Rating Scale ("GSRS"), a validated instrument.

Galafold was generally safe and well-tolerated.

Study 012, our second Phase 3 registration switching study, was a randomized, open-label 18-month study that investigated the safety and efficacy of oral Galafold (150 mg, every other day) compared to standard-of-care infused ERTs (agalsidase beta and agalsidase alfa). The study also included a 12-month open-label Galafold extension phase. The study enrolled a total of 60 patients (males and females) with Fabry disease and genetic mutations identified as amenable to Galafold monotherapy in the clinical trial assay. Subjects were randomized 1.5:1 to switch to Galafold or remain on ERT. All subjects had been receiving ERT infusions for a minimum of 12 months (at least 3 months at the labeled dose) prior to entering the study. Based on the GLP HEK assay, there were changes in categorization from amenable to non-amenable in 4 of the 60 patients enrolled in Study 012.

Taking into account scientific advice from European regulatory authorities, the pre-specified co-primary outcome measures of efficacy in Study 012 were the descriptive assessments of comparability of the mean annualized change in mGFR and eGFR for Galafold and ERT. Both mGFR and eGFR are considered important measures of renal function. Success on mGFR and eGFR was prescribed to be measured in two ways: 1) a 50% overlap in the confidence intervals between the Galafold and ERT treatment groups; and 2) whether the mean annualized changes for patients receiving Galafold are within 2.2 mL/min/1.73 m2/yr of patients receiving ERT. We pre-specified that these renal function outcomes would be analyzed in patients with GLP HEK amenable mutations.

In August 2014, we announced positive 18-month data from Study 012. Data from Study 012 were also presented to the scientific community at the American Society of Nephrology ("ASN") in November 2014 and WORLDSymposium in February 2015. Highlights were as follows:

Galafold had a comparable effect to ERT on patients' kidney function as measured by the change in eGFR and mGFR from baseline to month 18.

Levels of plasma lyso-Gb3, an important biomarker of disease, remained low and stable in patients with amenable mutations who switched from ERT to Galafold.

There was a statistically significant decrease in LVMi from baseline to month 18 in patients who switched from ERT to Galafold.

Measures of pain and quality of life from the Brief Pain Inventory ("BPI") and Short Form 36 ("SF36") remained stable when patients switched from ERT to Galafold.

Galafold was generally safe and well-tolerated.

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During the first quarter of 2015, we met with regulatory authorities in Europe and the United States to discuss the approval pathways for Galafold for Fabry patients who have amenable mutations. In the second quarter of 2015, we submitted an MAA to the EMA. In the United States, we plan to submit a NDA for accelerated approval (Subpart H) with the FDA in the second half of 2015.

Migalastat combination programs for Fabry disease

In support of our Fabry franchise strategy to develop migalastat in combination with ERT for Fabry patients with non-amenable mutations, we plan to initiate a longer-term Phase 2 Fabry co-administration study in 2015. In parallel, we are internally developing our own Fabry cell line for co-formulation with migalastat as a next-generation ERT for Fabry disease. We previously completed an open-label Phase 2 safety and pharmacokinetics study ("Study 013") that investigated two oral doses of migalastat (150 mg and 450 mg) co-administered with agalsidase beta or agalsidase alfa in males with Fabry disease. Unlike Study 011 and Study 012, patients in Study 013 were not required to have alpha-Gal A mutations amenable to chaperone therapy because, when co-administered with ERT, migalastat is designed to bind to and stabilize the exogenous enzyme in the circulation in any patient receiving ERT. Each patient received their current dose and regimen of ERT at one infusion. A single oral dose of migalastat (150 mg or 450 mg) was co-administered two hours prior to the next infusion of the same ERT at the same dose and regimen. Preliminary results from Study 013 showed increased levels of active alpha-Gal A enzyme levels in plasma and skin following co-administration compared to ERT alone.

Next-generation ERT for Pompe disease

We are leveraging our biologics capabilities and CHART platform to develop a next-generation Pompe ERT. This ERT consists of a uniquely engineered recombinant human acid alpha-glucosidase ("rhGAA") enzyme (designated "ATB200") with an optimized carbohydrate structure to enhance uptake, administered in combination with a pharmacological chaperone to improve activity and stability. We acquired ATB200 as well as our enzyme targeting technology through our purchase of Callidus.

In preclinical studies, ATB200 demonstrated greater tissue enzyme levels and further substrate reduction compared to the current approved ERT for Pompe disease (alglucosidase alfa), which were further improved with the addition of a chaperone. Clinical studies of pharmacological chaperones in combination with currently marketed ERTs have established initial human proof-of-concept that a chaperone can stabilize enzyme activity and potentially improve ERT tolerability. In 2013, we completed a Phase 2 safety and pharmacokinetics study ("Study 010") that investigated single ascending oral doses of a pharmacological chaperone co-administered with alglucosidase alfa marketed by Genzyme, in patients with Pompe disease. Each patient received one infusion of ERT alone, and then a single oral dose of the pharmacological chaperone just prior to the next ERT infusion. Results from this study showed an increase in GAA enzyme activity in plasma and muscle when co-administered compared to ERT alone.

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.

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The offering

Common stock offered by us pursuant to this prospectus supplement	Shares having an aggregate offering price of up to $150,000,000.
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 $22,500,000 of our common stock at the public offering price less the underwriting discounts and commissions.
Common stock to be outstanding immediately after this offering	shares (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 global commercial infrastructure for Galafold, the continued clinical development of our product candidates and for other general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical and pre-clinical trial expenditures, and commercialization expenditures. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. As a result, our management will retain broad discretion in the allocation and use of the net proceeds from this offering. See "Use of Proceeds" on page S-13 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-7 of this prospectus supplement, page 4 of the accompanying prospectus, page 26 of our Annual Report on Form 10-K for the year ended December 31, 2014 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 96,375,015 shares of common stock outstanding as of March 31, 2015. Unless specifically stated otherwise, the information in this prospectus supplement is as of March 31, 2015 and excludes:

- 10,602,701 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2015, at a weighted average exercise price of $5.56 per share, of which options to purchase 5,260,979 shares of our common stock were then exercisable;

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1,600,000 shares of our common stock to be issued in connection with the exercise of warrants issued in an offering conducted in November 2013, each with an exercise price of $2.50 per share;

955,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2015;

25,562 shares of our common stock issuable as of March 31, 2015 to the former stockholders of Callidus upon the submission to us of properly completed letters of transmittal and certificates representing shares of Callidus common stock held by such former stockholders of Callidus immediately prior to the closing of our acquisition of Callidus on November 19, 2013; and

an aggregate of 5,095,151 shares of our common stock reserved for future grants of stock options (or other similar equity instruments) under the Amicus Therapeutics, Inc. 2007 Amended and Restated Equity Incentive Plan (the "Amended and Restated Equity Incentive Plan").

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.

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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, or 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, 2015, there were outstanding options to purchase an aggregate of 10,602,701 shares of our common stock at a weighted average exercise price of $5.56 per share, of which options to purchase 5,260,979 shares of our common stock were then exercisable and 955,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2015. As of March 31, 2015, there were warrants outstanding to purchase 1,600,000 shares of our common stock, with an exercise price of $2.50 per share, all of which were exercised and became issuable on June 3, 2015. The exercise of options and warrants 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 in the future and those options or warrants are exercised 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.

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

The public offering price of $ 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 $ per share of common stock, or approximately % 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, your percentage of ownership will be diluted. You may also experience additional dilution if stock options or warrants to purchase our shares are exercised at less than the offering price. As of March 31, 2015, we had reserved 5,095,151 shares of our common stock for issuance under our Amended and Restated Equity Incentive Plan, and 1,600,000 shares of our common stock for issuance upon exercise of outstanding warrants (all of which were exercised and became issuable on June 3, 2015).

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 global commercial infrastructure for Galafold, the continued clinical development of our product candidates, research and development expenditures, clinical and pre-clinical trial expenditures, commercialization expenditures and for other general corporate purposes, 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-13 of this prospectus supplement for further information.

Risks related to our business

We have identified the following changes to the risk factors previously disclosed in our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 (the "2014 Annual Report"). The risk factors listed below should be read in conjunction with the risk factors set forth in the 2014 Annual Report.

Even if we are able to commercialize Galafold or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations and practices that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch

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of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize Galafold or any other product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the EU and U.S. healthcare industries and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for Galafold or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining reimbursement for Galafold may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

If the FDA does not grant accelerated approval for Galafold, the timing and approval of the NDA will be significantly delayed.

We plan to submit a NDA for accelerated approval (Subpart H) of Galafold with the FDA in the second half of 2015. Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening disease or condition that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA

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has broad discretion over whether to grant approval based on a surrogate endpoint. Accordingly, even though we believe Galafold will meet the criteria for accelerated approval, the FDA may disagree and may determine not to grant such approval. If the FDA does not grant accelerated approval of Galafold, we will need to complete a Phase 3 clinical trial and will need to expend significantly more capital to obtain approval of Galafold.

If Galafold is approved by the FDA under the accelerated approval regulations, it will be subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint, which should be underway at the time of approval, and FDA review of all promotional materials prior to their dissemination. If we fail to promptly conduct required post-approval studies, do not confirm a clinical benefit during post-marketing studies, other evidence shows that Galafold is not shown to be safe or effective under the conditions of use, or we disseminate promotional materials relating to Galafold that are found by the FDA to be false and misleading, the FDA could withdraw Galafold from the market on an expedited basis.

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

If Galafold is approved for commercialization in Europe, we intend to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international operations or entering into international business relationships, including:

- different regulatory requirements for maintaining approval of drugs in foreign countries;
- reduced protection for contractual and intellectual property rights in some countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions;
- tighter restrictions on privacy and the collection and use of patient data; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the European Union and many of the individual countries in Europe with which we will need to comply. Many U.S.-based biopharmaceutical companies have found the process of marketing their own products in Europe to be very challenging.

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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 and uncertainties. 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 "anticipate," "believe," "estimate," "expect," "potential," "intend," "may," "plan," "predict," "project," "will," "should," "would" and similar expressions 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, including Galafold;
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the significant cost of new Fabry ERT cell line development and manufacturing as well as the cost of manufacturing Pompe ERT;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of LSDs;
- 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;
- our ability to obtain reimbursement for Galafold;
- our ability to commercialize Galafold in the EU;
- the emergence of competing technologies and other adverse market developments;
- 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; and
- our ability to establish collaborations and obtain milestone, royalty or other payments from any such collaborators.

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. Our forward-looking

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statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make.

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.

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Use of proceeds

We expect to receive net proceeds of approximately $ from the sale of shares of our common stock in this offering, or $ if the underwriters exercise in full their option to purchase additional shares of common stock, based on a public offering price of $ 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, if any, for, without limitation:

- investment in the global commercial infrastructure for Galafold;
- the continued clinical development of our product candidates;
- research and development expenditures;
- clinical and pre-clinical trial expenditures;
- commercialization expenditures; and
- for other general corporate purposes, 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.

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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, 2015 was approximately $69 million, or $0.72 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, 2015. After giving effect to the sale by us of shares of common stock at the public offering price of $ per share of common stock and after deducting the underwriting discount and commissions and estimated offering expenses, our net tangible book value as of March 31, 2015 would have been approximately $ million, or $ per share of common stock. This represents an immediate increase in net tangible book value of $ per share to our existing stockholders and an immediate dilution of $ 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		$
Net tangible book value per share as of March 31, 2015	$ 0.72	
Increase per share attributable to new investors	$	
Net tangible book value per share after this offering		$
Dilution per share to new investors		$

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

The number of shares of our common stock to be outstanding immediately after this offering is based on 96,375,015 shares of common stock outstanding as of March 31, 2015. Unless specifically stated otherwise, the information in this prospectus supplement is as of March 31, 2015 and excludes:

- 10,602,701 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2015, at a weighted average exercise price of $5.56 per share, of which options to purchase 5,260,979 shares of our common stock were then exercisable;
- 1,600,000 shares of our common stock to be issued in connection with the exercise of warrants issued in an offering conducted in November 2013, each with an exercise price of $2.50 per share;
- 955,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2015;
- 25,562 shares of our common stock issuable as of March 31, 2015 to the former stockholders of Callidus upon the submission to us of properly completed letters of transmittal and certificates representing shares of Callidus common stock held by such former stockholders of Callidus immediately prior to the closing of our acquisition of Callidus on November 19, 2013; and

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an aggregate of 5,095,151 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.

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.

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Underwriting

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC and Goldman, Sachs & Co. 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	
Goldman, Sachs & Co.	
Cowen and Company, LLC	
Janney Montgomery Scott LLC	
Total	

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 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 $ 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 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 $ 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	$	$
Total	$	$

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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 $.

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 J.P. Morgan Securities LLC and Goldman, Sachs & Co. for a period of 90 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; (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; or (D) shares of our common stock to be issued to the former stockholders of Callidus. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

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 for at least 30 days after the lock-up period), for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co., (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

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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. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

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

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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.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), from and including the date on which the European Union Prospectus Directive (the "EU Prospectus Directive") was implemented in that Relevant Member State (the "Relevant Implementation Date") an offer of securities described in this prospectus supplement may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus supplement may be made to the public in that Relevant Member State at any time:

to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;

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to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or

in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus supplement shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an "offer of securities to the public" in relation to any securities 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 the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression "EU Prospectus Directive" means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

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.

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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

The consolidated financial statements of Amicus Therapeutics, Inc. appearing in Amicus Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2014, and the effectiveness of Amicus Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2014, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm 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. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the U.S. Securities and Exchange Commission. Please note, however, that we have not incorporated any other information by reference from our website, other than the documents listed under the heading "Incorporation of Certain Information by Reference." 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

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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, 2014 filed with the SEC on March 3, 2015;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 5, 2015;

Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 29, 2015, to the extent incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2014;

Our Current Reports on Form 8-K filed with the SEC on January 12, 2015, January 15, 2015, February 27, 2015, April 13, 2015, April 28, 2015, May 19, 2015, June 4, 2015 and June 10, 2015; 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-21 of this prospectus supplement.

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PROSPECTUS

AMICUS THERAPEUTICS, INC.

$250,000,000
Common Stock
Preferred Stock
Warrants
Debt Securities
Units
Subscription Rights

1,000,000 Shares of Common Stock
Offered by
Selling Stockholders

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.

The aggregate initial offering price of all securities sold by us pursuant to this prospectus will not exceed $250,000,000.

Selling stockholders may also offer up to 1,000,000 shares of our common stock from time to time in connection with one or more offerings. We will not receive any proceeds from the sale of any securities by the selling stockholders. We have paid the fees and expenses incident to the registration of the shares of common stock for sale by the selling stockholders.

This prospectus provides a general description of the securities that we or the selling stockholders 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. Depending on the method of distribution, a prospectus supplement may also be required in connection with certain sales of common stock by the selling stockholders. 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 or the selling stockholders 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 February 27, 2015, the closing price of our common stock was $8.76.

As of February 27, 2015, the aggregate market value of our outstanding common stock held by non-affiliates was approximately $546,171,388, based on 95,624,073 shares of outstanding common stock, of which approximately 62,348,332 shares were held by non-affiliates, and a per share price of $8.76 based on the closing sale price of our common stock on February 27, 2015.

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 4.

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 May 4, 2015.

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Prospectus

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the Commission, using a "shelf" registration process. Under this shelf registration process, we may offer to sell any of the securities, or any combination of the securities, described in this prospectus, in each case in one or more offerings, up to a total dollar amount of $250,000,000 and the selling stockholders may sell up to 1,000,000 shares of our common stock in one or more offerings.

This prospectus provides you only with a general description of the securities that we and the selling stockholders may offer. Each time securities are 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.

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THE COMPANY

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of next-generation medicines for a range of rare and orphan diseases, with a focus on improved therapies for lysosomal storage disorders ("LSDs"). Our lead product candidate is a small molecule that has completed late stage clinical trials to support the candidate being used as a monotherapy and in combination with enzyme replacement therapy ("ERT") for Fabry disease. Our development programs also include next-generation ERTs for LSDs, including Fabry disease, Pompe disease and Mucopolysaccharoidosis Type I ("MPS I"). We believe that our platform technologies and our advanced product pipeline uniquely position us at the forefront of developing therapies for rare and orphan diseases.

In LSDs such as Fabry and Pompe, a mutation in the specific disease-causing gene can lead to the production in the body of a mutant form of the enzyme that is less stable than the normal form, and that may be prematurely degraded before reaching the location in the cell where it is needed. For patients with LSDs who are receiving ERT, the infused (exogenous) protein may also unfold and lose activity at any stage in the process from the infusion bag to the bloodstream, to the eventual uptake into cells and tissue. The result is a loss of enzyme activity and disruption of proper trafficking of the enzyme to lysosomes. Our novel treatment approach consists of using pharmacological chaperones that are designed to selectively bind and stabilize either the endogenous or exogenous target proteins and facilitate trafficking to the location in cells where these proteins are needed (the lysosome).

Our precision medicine approach consists of an oral small molecule pharmacological chaperone monotherapy that is designed to bind to and stabilize a patient's own endogenous target protein. Patients with "amenable mutations" may respond based on their genetics.

Our Chaperone-Advanced Replacement Therapy, or CHART , platform combines chaperones with ERTs independent of a patient's own genetics. In each CHART program, a unique pharmacological chaperone is designed to bind to a specific therapeutic (exogenous) enzyme, stabilizing the enzyme in its properly folded and active form. This may allow for enhanced tissue uptake, greater lysosomal activity, more reduction of substrate, and the potential for lower immunogenicity.

Our Fabry franchise strategy is to develop the pharmacological chaperone migalastat HCl ("migalastat") for all patients with Fabry disease as a monotherapy for patients with amenable mutations and in combination with ERT for all other patients. We have completed two Phase 3 global registration studies (Study 011 and Study 012) of migalastat monotherapy and plan to submit marketing applications in 2015. We have reported Phase 3 data in both treatment naïve patients ("Study 011" or "FACETS") and enzyme replacement therapy ("ERT") switch patients ("Study 012" or "ATTRACT"). Positive results from these studies have shown that treatment with migalastat has resulted in reductions in disease substrate, stability of kidney function, reductions in cardiac mass, and improvement in gastrointestinal symptoms in patients with amenable mutations in a validated assay ("GLP HEK assay"). Data from the Fabry Registry indicate that the leading cause of death in patients is from cardiovascular disease (source: Mehta 2009).

Following a meeting with the European Medicines Agency ("EMA") held in the fourth quarter of 2014, we are on track to submit a marketing application in Europe in mid-2015. We have also scheduled a meeting with the US FDA in the first quarter of 2015 as we work to make migalastat available for all amenable Fabry patients as quickly as possible.

We expect to initiate a longer-term Phase 2 Fabry co-administration study in 2015 in support of our Fabry franchise strategy to develop migalastat in combination with ERT for Fabry patients with non-amenable mutations. Preliminary results from our previously completed open-label Phase 2 safety and pharmacokinetics

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study ("Study 013") in Fabry patients showed increased levels of active alpha-Gal A enzyme levels in plasma and increased alpha-Gal A enzyme in skin following co-administration compared to ERT alone.

We are leveraging our biologics capabilities and CHART to develop a next-generation Pompe ERT. This ERT consists of a uniquely engineered recombinant human acid alpha-glucosidase ("rhGAA") enzyme (designated "ATB200") with an optimized carbohydrate structure to enhance uptake, administered in combination with a pharmacological chaperone to improve activity and stability. Acid alpha-glucosidase ("GAA") is the enzyme deficient in Pompe patients. In preclinical studies, ATB200 demonstrated greater tissue enzyme levels and further substrate ("glycogen") reduction compared to the current approved ERT for Pompe disease ("alglucosidase alfa"), which was further improved in combination with a chaperone. Clinical studies of pharmacological chaperones in combination with currently marketed ERTs have also previously established initial human proof-of-concept that a chaperone can stabilize enzyme activity and potentially improve ERT tolerability.

Additional preclinical programs include a next-generation ERT for MPS I. In addition, our enzyme targeting technology is applicable to multiple ERTs and complementary to our CHART platform for the development of next-generation therapies for multiple LSDs. We believe that together these platform technologies may provide a unique tool set to address some of the major challenges with currently marketed ERT products enzyme activity and stability; targeting and uptake; and tolerability and immunogenicity.

Although LSDs are relatively rare diseases, they represent a substantial commercial opportunity due to the severity of the symptoms and the chronic nature of the diseases. The publicly reported worldwide net product sales for currently approved treatments for three LSDs were approximately $1.9 billion in 2014.

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, and you should not consider information contained on our website as part of this prospectus.

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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, 2014 filed on March 3, 2015, with the Commission, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the Commission 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, and any prospectus supplement and the documents incorporated therein may contain, forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus, any prospectus supplement or the documents incorporated herein and therein by reference regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward- looking statements contain these identifying words.

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

- the progress and results of our clinical trials of our drug candidates, including migalastat HCl ("migalastat");
- the cost of manufacturing drug supply for our clinical and preclinical studies, including the significant cost of new enzyme replacement therapy ("ERT") cell line development and manufacturing as well as the cost of manufacturing Pompe ERT;
- 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 diseases ("LSDs");
- 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;
- 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; and our ability to establish collaborations and obtain milestone, royalty or other payments from any such collaborators.

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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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make.

You should read this prospectus, any prospectus supplement 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. We do not assume any obligation to update any forward-looking statements.

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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, clinical trial expenditures, commercial expenditures, 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 may be set forth in the prospectus supplement relating to the specific offering. We will not receive any of the proceeds from the sale of any securities offered pursuant to this prospectus by any selling stockholder.

RATIO OF EARNINGS TO FIXED CHARGES

Our ratio of earnings to fixed charges for each of the five most recently completed fiscal years and any required interim periods will each be specified in a prospectus supplement or in a document that we file with the Commission and incorporate by reference pertaining to the issuance, if any, by us of debt securities in the future.

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SELLING STOCKHOLDERS

This prospectus also relates to the possible resale by certain of our stockholders of up to an aggregate of 1,000,000 shares of our common stock which were previously acquired by such stockholders through several private placements of our convertible preferred stock completed by us prior to our initial public offering, or the IPO, in 2007, which were all converted to shares of our common stock in connection with our IPO. Specifically, the selling stockholders acquired the convertible preferred stock in our Series B convertible preferred stock offerings in May 2004 and April 2005, our Series C convertible preferred stock offerings in August 2005 and April 2006, and our Series D convertible preferred stock offerings in September 2006 and March 2007. In connection with such private placements, these persons have registration rights with respect to their shares as described further below under the heading "Certain Relationships and Related Party Transactions." Information about selling stockholders, if any, including their identities and the number of shares of common stock to be registered on their behalf, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are incorporated by reference into this prospectus. Selling stockholders shall not sell any shares of our common stock pursuant to this prospectus until we have identified such selling stockholders and the shares being offering for resale by such selling stockholders in a subsequent prospectus supplement. However, the selling stockholders may sell or transfer all or a portion of their shares of our common stock pursuant to any available exemption from the registration requirements of the Securities Act of 1933, as amended, or the Securities Act.

Certain Relationships and Related Party Transactions

Pursuant to a third amended and restated investor rights agreement, dated as of September 13, 2006, by and among entities who held our redeemable convertible preferred stock (which was converted to common stock at our IPO) and us, we granted registration rights to all such holders and to certain other persons, most of whom have subsequently waived their registration rights.

Subject to certain limitations, these stockholders may demand that, on up to two occasions, we register all or part of their securities for sale under the Securities Act as long as the aggregate price to the public for the securities to be sold in each instance is $5,000,000 or more. If we are eligible to register any of our common stock on Form S-3, these stockholders may make the same demand; provided, however, that we will not be required to register their securities if (i) we have already effected a registration within 90 days prior to the request or have effected two or more registrations on Form S-3 within the preceding 12 month period, or (ii) if the aggregate price to the public for the securities to be sold is less than $2,500,000. Additionally, if we believe that such registration would have a materially detrimental effect on any material corporate event, we may delay the request for up to three months, but not more than once in any twelve month period.

These stockholders may also request registration of their shares if we register any of our common stock, either for our own account or for the account of other securityholders. In such an event, these stockholders are entitled to notice of the registration and to include their shares of common stock in such registration. In the case of an underwritten registration, we must use our reasonable best efforts to obtain the permission of the underwriters to the inclusion of these stockholder's shares in the offering on the same terms.

With specified exceptions, these stockholders' right to include shares in a registration is subject to the right of the underwriters to limit the number of shares included in the offering. All fees, costs and expenses of any registrations will generally be paid by us.

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PLAN OF DISTRIBUTION

Amicus, and any selling stockholders and their successors, including their permitted transferees, 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 selling stockholders 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 or any selling stockholder against certain civil liabilities, including liabilities under the Securities Act, or to contribution from us or any selling stockholder 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 or any selling stockholders 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

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

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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 selling stockholders may also offer shares of our common stock from time to time. The terms of any securities we offer or offered by the selling stockholders 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.

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 Commission as exhibits to previous SEC filings. Please refer to "Where You Can Find More Information" below for directions on obtaining these documents.

As of February 27, 2015, we are authorized to issue 125,000,000 shares of common stock, $0.01 par value per share. As of February 27, 2015, we had 95,624,073 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."

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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 February 27, 2015, 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 our 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;

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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;

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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 Outstanding Warrants

On November 20, 2013, we entered into a securities purchase agreement with certain investors for the private placement of (a) shares of our common stock and (b) a combination of shares of common stock and warrants to purchase shares of Common Stock. Each of the investors were stockholders of ours prior to consummation of the transactions contemplated by the private placement. Pursuant to the securities purchase agreement, we agreed to issue 1,500,000 shares of common stock at $2.00 per share and (b) 6,000,000 units at $2.00 per unit, with each unit consisting of one share of common stock and .267 warrants resulting in an aggregate of 6,000,000 shares of common stock and 1,600,000 warrants underlying the units to be issued. Each warrant is exercisable between July 1, 2014 and June 30, 2015 with an exercise price of $2.50, subject to certain adjustments. As of the date hereof, the number of shares underlying the warrants is 1,600,000 and the exercise price is $2.50 per share.

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 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 and those made part of the indenture by reference to the Trust Indenture Act of 1939, 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 indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

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We may offer under this prospectus up to an aggregate principal amount of $250,000,000 in debt securities, or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an aggregate initial public offering price of up to $250,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent direct, unsecured obligations of the Company and will rank equally with all of our other unsecured indebtedness.

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 as may be filed with a future prospectus supplement.

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 Commission.

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;

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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; and

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

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

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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 otherwise that would 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 such person and such proposed transaction meets various criteria, which we will describe in detail in the applicable prospectus supplement.

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 or make-whole amount, if any, on any debt security of such series when due and payable (whether at maturity, by call for redemption, through any mandatory sinking fund, by redemption at the option of the holder, by declaration or acceleration or otherwise);
- failure to make a payment of any interest on any debt security of such series when due;
- our failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series;
- certain events relating to our bankruptcy, insolvency or reorganization; and
- certain cross defaults, if and as applicable.

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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 (or, if the debt securities of such series are issued at an original issue discount, such portion of the principal amount as may be specified in the terms of the debt securities of such series) 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 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, in the case of a default that results from the failure to make any payment of the principal of, premium or make-whole amount, if any, or interest on the debt securities of any series, or in the payment of any mandatory sinking fund installment with respect to debt securities of such series, if any, 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 proceeding to exercise any trust or power 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 in good faith 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 endow 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 a majority in aggregate principal amount of the debt securities of such series then outstanding make a written request upon the trustee to exercise its power under the indenture, indemnify the trustee and afford the trustee reasonable opportunity to act. Even so, such holders may have an absolute right to receipt of the principal of, premium or make-whole amount, 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.

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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.

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 Amicus, 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 identified in the prospectus supplement relating to the applicable indenture and debt securities.

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;

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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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the Commission. You may read and copy information filed by us with the Commission at the Commission's public reference section, 100 F Street, N.E., Washington, D.C. 20549. Information regarding the operation of the public reference section can be obtained by calling 1-800-SEC-0330. The Commission also maintains an Internet site at http://www.sec.gov that contains reports, statements and other information about issuers, such as us, who file electronically with the Commission. We maintain an Internet site at http://www.amicusrx.com. However, the information on our Internet site is not incorporated by reference in this prospectus and any prospectus supplement and you should not consider it a part of this prospectus or any accompanying prospectus supplement.

The Commission allows us to "incorporate by reference" into this prospectus the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the Commission will automatically update and supersede information contained in documents filed earlier with the Commission or contained in this prospectus. We incorporate by reference in this prospectus (i) the documents listed below, (ii) all documents that we file with the Commission under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is included and prior to the effectiveness of such registration statement, and (iii) and any future filings that we may make with the Commission under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of the offering under this prospectus; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed in accordance with Commission rules:

Our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the Commission on March 3, 2015;

Our Current Reports on Form 8-K filed with the Commission on January 12, 2015, January 15, 2015 and February 27, 2015; and

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The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed with the Commission on May 23, 2007, including any amendment or report filed for the purpose of updating such description.

You may obtain a copy of any or all of the documents referred to above which may have been or may be incorporated by reference into this prospectus, except for exhibits to those documents (unless the exhibits are specifically incorporated by reference into those documents) at no cost to you by writing or telephoning us at the following address: Office of the Corporate Secretary, Amicus Therapeutics, Inc., 1 Cedar Brook Drive, Cranbury, NJ 08512, telephone (609) 662-2000.

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 selling stockholders, 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, 2014 and the effectiveness of our internal control over financial reporting as of December 31, 2014, as set forth in their reports, which are incorporated by reference in the prospectus and elsewhere in this registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

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AMICUS THERAPEUTICS, INC.

$150,000,000

Prospectus Supplement

J.P. Morgan **Goldman, Sachs & Co.**

Cowen and Company

Janney Montgomery Scott

June , 2015