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As filed with the Securities and Exchange Commission on December 16, 2013

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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

WASHINGTON, D.C. 20549

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**FORM S-3**  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

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**AMICUS THERAPEUTICS, INC.**

(Exact name of registrant as specified in its charter)

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**Delaware**  
(State of incorporation)

**71-0869350**  
(IRS Employer  
Identification Number)

**1 Cedar Brook Drive, Cranbury, NJ 08512**  
**(609) 662-2000**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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**John F. Crowley**  
**Chief Executive Officer**  
**Amicus Therapeutics, Inc.**  
**1 Cedar Brook Drive**  
**Cranbury, New Jersey 08512**  
**(609) 662-2000**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public:  
From time to time after the effective date of this Registration Statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer

Accelerated filer

Non-accelerated filer   
(Do not check if a  
smaller reporting company)

Smaller reporting company

**CALCULATION OF REGISTRATION FEE**

Title of each class of securities to be registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Security(2)	Proposed Aggregate Maximum Offering Price(2)	Amount of Registration fee(2)
Common Stock, par value \$0.01 per share	9,100,000	\$2.095	\$19,064,500	\$2,456

The Registrant is hereby registering for resale (a) 7,500,000 shares of common stock, (b) 1,600,000 shares of common stock issuable upon the exercise of warrants and (c) an indeterminate number of shares of common stock as may be issuable from time to time as a result of a stock split, stock dividend, capitalization or similar event.

- (2) Estimated pursuant to Rule 457(c) solely for purposes of calculating the amount of the registration fee, based on the average of the high and low prices of the Registrant's common stock reported as of December 11, 2013 on The NASDAQ Global Market.

**The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

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**The information contained in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting offers to buy these securities in any jurisdiction where such offer or sale is not permitted.**

**Subject to Completion, Dated December 16, 2013**

**PROSPECTUS**

**AMICUS THERAPEUTICS, INC.  
9,100,000 Shares of Common Stock**

We are registering our common stock, par value \$0.01 per share, for resale by the selling stockholders identified in this prospectus. We are not selling any shares of our common stock under this prospectus and we will not receive any of the proceeds from the sale of shares by the selling stockholders. Specifically, this prospectus relates to the resale of 7,500,000 shares of our common stock and 1,600,000 shares of our common stock issuable upon the exercise of warrants. The selling stockholders acquired these shares of common stock and warrants from us in a private placement that closed on November 20, 2013.

For a description of the plan of distribution of the resale shares, see page 10 of this prospectus.

The selling stockholders identified in this prospectus, or their pledges, donees, transferees or other successors in interest, may offer and sell the shares of common stock being offered by this prospectus from time to time in public or private transactions, or both. These sales may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices, or at negotiated prices. The selling stockholders may sell shares being offered by this prospectus to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling stockholders, the purchasers of such shares, or both. See "Plan of Distribution" for a more complete description of the ways in which the shares being offered by this prospectus may be sold.

Our common stock is traded on The NASDAQ Global Market under the symbol "FOLD." On December 13, 2013, the closing price of our common stock was \$2.05.

**INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. BEFORE INVESTING, YOU SHOULD REFER TO THE RISK FACTORS ON PAGE 5 OF THIS PROSPECTUS.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

The date of this prospectus is \_\_\_\_\_, 2013.

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## ABOUT THIS PROSPECTUS

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 does 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 its wholly-owned subsidiaries, Amicus Therapeutics UK Limited and Callidus Biopharma, Inc., unless we state otherwise or the context indicates otherwise.

## 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 development programs include next-generation enzyme replacement therapies (ERTs) for LSDs, including Fabry disease, Pompe disease and Mucopolysaccharoidosis Type I (MPS I). We are also developing novel small molecules as monotherapy treatments for Fabry disease and Parkinson's disease. 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 Pompe and Fabry, 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 lysosomal storage diseases who are receiving ERT, the infused (exogenous) protein may 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. In both instances, 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.

Our Chaperone-Advanced Replacement Therapy, or CHART™, platform has been used to develop our next-generation ERTs by identifying and co-formulating therapeutic enzymes with our proprietary pharmacological chaperones. 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 lead CHART program is a next-generation ERT in preclinical development for Fabry disease. This next-generation ERT consists of a proprietary human recombinant alpha-Gal A (alpha-Gal) enzyme (JR-051, manufactured by JCR Pharmaceutical Co Ltd) co-formulated with our pharmacological chaperone migalastat HCl. We completed an initial human proof-of-concept Phase 2 study (Study 013) that evaluated the effects of a single oral dose of migalastat HCl co-administered with the currently marketed ERTs for Fabry disease (Fabrazyme® or Replagal®) in males with Fabry disease. Results from this study demonstrated a consistent increase in levels of active alpha-Gal activity, the enzyme deficient in Fabry patients, in plasma and increased uptake of alpha-Gal enzyme in skin compared to ERT alone. This study has served as the foundation for further development of our next-generation Fabry ERT, which is expected to enter the clinic in 2014.

We are also developing migalastat HCl as a monotherapy in two Phase 3 global registration studies for Fabry patients with genetic mutations that were amenable to this pharmacological chaperone in a cell-based assay (Study 011 and Study 012). In Study 011, we are comparing migalastat HCl to placebo. In December 2012, we announced top-line six-month (Stage 1) results from Study 011. While encouraging, these results did not achieve statistical significance ( $p=0.3$ ) according to the pre-specified primary endpoint analysis. This responder analysis compared the number of patients in the migalastat HCl group to the number of patients in the placebo group who showed a 50% or greater reduction in interstitial capillary GL-3 in the kidney biopsies from baseline to month 6. In the 6-month open-label follow up period in Study 011 (Stage 2), all patients received migalastat HCl. Data from Stage 2 and the open label extension for months 13-24 are anticipated in the first half of 2014.

In Study 012, we are comparing open-label migalastat HCl to current standard of care ERTs (Fabrazyme® and Replagal®) to potentially support global registration. In December 2012, this study achieved full enrollment of 60 patients, who were randomized 1.5:1 to switch from ERT to migalastat HCl or remain on ERT. Data are anticipated in the second half of 2014 on the primary outcome measure, which is renal function assessed by measured Glomerular Filtration Rate (GFR) at 18 months.

We are also utilizing our CHART platform to advance a next-generation ERT for Pompe disease. Similar to Study 013 in Fabry disease, we completed a Phase 2 (Study 010) safety and PK study of our pharmacological chaperone AT2220 (duvoglustat HCl) co-administered with currently approved recombinant human acid-alpha glucosidase (rhGAA) Myozyme®/Lumizyme® in Pompe patients. GAA is the enzyme deficient in Pompe patients. Results from Study 010 demonstrated initial human proof-of-concept for this chaperone-ERT combination in Pompe disease, showing an increase in GAA enzyme activity in plasma and muscle compared to ERT alone.

Through our acquisition of Callidus Biopharma, Inc. we now own a uniquely-engineered, proprietary recombinant human acid-alpha glucosidase (rhGAA) for Pompe disease in late preclinical development. This Pompe ERT has shown promise in preclinical studies, and will be further evaluated with the addition of Amicus' pharmacological chaperone AT2220.

In addition, through our acquisition of Callidus, we have an enzyme targeting technology that is applicable to multiple ERTs and complementary to our CHART platform for the development of next-generation therapies for multiple LSDs. We believe this approach has the potential to improve the properties of the therapeutic enzymes alone while incorporating small molecule stabilizers to increase circulating exposure and tissue uptake.

Additional preclinical CHART programs include a next-generation ERT for MPS I. We also plan to continue our commitment to the broader application of the CHART technology as a potential next-generation treatment approach for other LSDs.

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 six LSDs were approximately \$3.5 billion in 2012.

In September 2013, we entered into a collaboration agreement with Biogen Idec ("Biogen") to discover, develop and commercialize novel small molecules for the treatment of Parkinson's disease. Under terms of the multi-year agreement, we will collaborate in the discovery of a new class of small molecules that target the GCase enzyme, for further development and commercialization by Biogen. Biogen will be responsible for funding all discovery, development, and commercialization activities.

#### **Collaboration with GSK**

On November 19, 2013, we entered into a Revised Agreement with GlaxoSmithKline PLC (GSK) pursuant to which we have obtained global rights to develop and commercialize the investigational pharmacological chaperone migalastat HCl as a monotherapy and in combination with ERT for Fabry disease. The Revised Agreement amends and replaces in its entirety the Expanded Collaboration Agreement entered into between Amicus and GSK on July 17, 2012 for the development and commercialization of migalastat HCl. Under the terms of the Revised Agreement, there is no upfront payment from Amicus to GSK. For the next-generation Fabry ERT (migalastat HCl co-formulated with ERT), GSK is eligible to receive single-digit royalties on net sales in eight major markets outside the U.S. We may also be responsible for milestone payments and single-digit royalties on the net sales of the next-generation Fabry ERT payable to a third party. For migalastat HCl monotherapy, GSK is

eligible to receive post-approval and sales-based milestones, as well as tiered royalties in the mid-teens in eight major markets outside the U.S.

Additionally, simultaneous with entry into the Revised Agreement, we entered into a Stock Purchase Agreement with GSK pursuant to which GSK purchased approximately 1.5 million shares of Amicus common stock at a price of \$2.00 per share. The Stock Purchase Agreement provides GSK with customary registration rights for the shares and includes a six-month lock-up provision. As of December 16, 2013, GSK's ownership position in Amicus is 17.6%.

### **Recent Acquisition**

On November 19, 2013, we acquired Callidus Biopharma, Inc., a privately-held drug discovery company focused on ERTs for lysosomal storage disorders. Under terms of the Merger Agreement, Callidus shareholders received at closing \$15 million in unregistered shares of our common stock. Callidus shareholders are eligible for up to \$10 million in milestone payments through Phase 2 development of the Pompe program and up to \$105 million for the achievement of late-stage development, regulatory, and approval milestones spread across three products. The Company is permitted, at its election, to make certain of these milestone payments in shares of its common stock.

### **Corporate Information**

Our principal executive offices are located at 1 Cedar Brook Drive, Cranbury, NJ 08512, and our phone number is (609) 662-2000.



## **RISK FACTORS**

Investing in our securities involves risk. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2012 filed on March 13, 2013 with the Securities and Exchange Commission (Commission), and in our Registration Statement on Form S-3 filed on December 10, 2013 with the Commission, both of which are 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. Our business, financial condition or results of operations could be materially adversely affected by any one or more of the risks incorporated herein by reference. The trading price of our common stock could decline due to any one or more of the risks, and you may lose all or part of your investments.

The risks and uncertainties we have described therein are those currently known to us but 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 herein by reference contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus or the documents incorporated by reference herein 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 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;
- the continuation of our collaboration with GSK and GSK's achievement of milestone payments thereunder;
- 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 diseases of neurodegeneration;
- 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;
- our ability to successfully incorporate Callidus and its products and technology into our business; 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 Part I Item 1A—"Risk Factors" of the Annual Report on Form 10-K for the year ended December 31, 2012 and in the "Risk Factors" section of the Registration Statement on Form S-3 that we filed on December 10, 2013, 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 and the documents that we incorporate by reference herein 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.

## USE OF PROCEEDS

We will not receive any proceeds from the sale or other disposition by the selling stockholders of the shares of our common stock covered hereby, or interests therein.

The selling stockholders will pay any expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of these shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration fees, listing fees of The NASDAQ Global Market (NASDAQ) and fees and expenses of our counsel and our accountants.

A portion of the shares of common stock covered by this prospectus are issuable upon exercise of warrants to purchase common stock. Upon any cash exercise of the warrants, the selling stockholders will pay us the exercise price of the warrants. The exercise price of the warrants is \$2.00. We will use any cash we receive upon the exercise of the warrants to advance the clinical and preclinical programs and for other general corporate purposes.

## SELLING STOCKHOLDERS

The shares of common stock covered hereby consist of:

- 7,500,000 shares of our common stock that we issued to the selling stockholders in the private placement that closed on November 20, 2013 (the Private Placement); and
- 1,600,000 shares of our common stock issuable to certain selling stockholders upon exercise of warrants to purchase our common stock issued in the Private Placement.

In connection with certain registration rights we granted to the selling stockholders in the Private Placement, we filed with the SEC a registration statement on Form S-3, of which this prospectus forms a part, with respect to the resale or other disposition of the shares of common stock offered by this prospectus from time to time on NASDAQ, in privately negotiated transactions or otherwise. We have also agreed to prepare and file amendments and supplements to the registration statement to the extent necessary to keep the registration statement effective for the period of time required under our agreement with the selling stockholders. The warrants held by the selling stockholders are exercisable between July 1, 2014 and June 30, 2015.

Beneficial ownership is determined in accordance with the rules of the Commission, and includes voting or investment power with respect to our common stock. To our knowledge, the selling stockholders have sole voting and investment power with respect to their respective shares of common stock, unless otherwise noted below. The number representing the number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes (i) all shares held by a selling stockholder prior to the private placement, plus (ii) all shares purchased by the selling stockholder pursuant to the private placement and being offered pursuant to this prospectus, as well as (iii) all shares issuable in connection with the exercise or conversion of all options, warrants or other derivative securities or securities convertible into our common stock which are exercisable or convertible within 60 days of December 13, 2013. The percentages of shares owned after the offering are based on 64,360,571 shares of our common stock outstanding as of December 13, 2013, which includes the outstanding shares of common stock offered by this prospectus (but not the shares issuable upon exercise of the warrants purchased in the Private Placement).

Except as noted in the footnotes below, none of the selling stockholders has held any position or office with us or our affiliates within the last three years or has had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities.

The selling stockholders may sell some, all or none of their respective shares of common stock offered by this prospectus from time to time. We do not know how long the selling stockholders will hold their respective shares of common stock covered hereby before selling them. Other than the Securities Purchase Agreement among us and the selling stockholders pursuant to which the Private Placement occurred, we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock being offered hereunder. The shares offered by this prospectus may be offered from time to time by the selling stockholders, although the shares of our common stock underlying the warrants will not be eligible to be offered pursuant to this prospectus until the warrants are exercised. Accordingly, for purposes of this table, we have assumed that, after completion of the offering, the only shares that will continue to be held by the selling stockholders are those that were owned immediately prior to the private placement.

The selling stockholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act of 1933, as amended (Securities Act), some or all of their shares of common stock since the date on which the information in the table below is presented. Information about the selling stockholders may change over time. Unless otherwise indicated below, the address of

each person listed below is c/o Amicus Therapeutics, Inc., 1 Cedar Brook Drive, Cranbury, New Jersey 08512.

Name of Selling Stockholder	Number of Shares of Common Stock Beneficially Owned Prior to the Offering	Number of Shares of Common Stock Registered for Sale Hereby	Number of Shares of Common Stock Underlying Warrants Registered for Sale Hereby	Shares Beneficially Owned After Offering	
				Number	Percent
Redmile Capital Fund, LP	2,142,388(1)	1,581,200	421,653	561,188	*
Redmile Capital Offshore Fund, Ltd.	4,800,491(2)	3,517,700	938,053	1,282,791	2.0
Redmile Capital Offshore Fund II, Ltd.	913,206(3)	659,500	175,867	253,706	*
Redmile Special Opportunities Fund, Ltd.	290,480(4)	241,600	64,427	48,880	*
Glaxo Group Ltd	11,315,825(5)	1,500,000	—	9,815,825	15.3

\* Less than 1 percent.

- (1) Redmile Group, LLC is the investment manager of Redmile Capital Fund, LP and as such possesses the sole power to vote and dispose of such securities.
- (2) Redmile Group, LLC is the investment manager of Redmile Capital Offshore Fund, LP and as such possesses the sole power to vote and dispose of such securities.
- (3) Redmile Group, LLC is the investment manager of Redmile Capital Offshore Fund II, Ltd. and as such possesses the sole power to vote and dispose of such securities.
- (4) Redmile Group, LLC is the investment manager of Redmile Special Opportunities Fund, LP and as such possesses the sole power to vote and dispose of such securities.
- (5) Glaxo Group Limited is an affiliate of GlaxoSmithKline plc.

## PLAN OF DISTRIBUTION

The selling stockholders and any of their pledgees, assignees and successors-in-interest may, from time to time in one or more transactions on NASDAQ or any other organized market where our shares of common stock may be traded, sell any or all of its shares of our common stock offered hereby through underwriters, dealers or agents, directly to one or more purchasers or through a combination of any such methods of sale. The selling stockholders may distribute the shares of our common stock offered hereby from time to time in one or more transactions:

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

The selling stockholders may use any one or more of the following methods when selling the shares offered hereby:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- one or more block trades in which the broker-dealer will attempt to sell such shares as agent or principal of all of such shares held by the selling stockholder;
- purchases by a broker-dealer as principal and resale by such broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- agreements between broker-dealers and the selling stockholder to sell a specified number of such shares at a stipulated price per share; and
- any other method permitted pursuant to applicable law.

If the selling stockholders effect such transactions by selling shares of common stock offered hereby to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock offered hereby for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). In connection with sales of the shares of common stock offered hereby or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of the shares of common stock offered hereby in the course of hedging in positions they assume. The selling stockholders may also sell shares of common stock offered hereby short and deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock offered hereby to broker-dealers that in turn may sell such shares.

The selling stockholders may pledge or grant a security interest in some or all of the shares of common stock offered hereby and owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell such shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling

stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock offered hereby in other circumstances, in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealer participating in the distribution of the shares of common stock offered hereby may be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock offered hereby is made, a prospectus supplement, if required, will be distributed which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling stockholders and any discounts, commissions or concessions allowed or reallocated or paid to broker-dealers.

We agreed to use our commercially reasonable efforts to keep this prospectus effective until the date all resale shares registered by this prospectus have been sold or may be sold pursuant to Rule 144 without regard to volume limitations. Under the securities laws of some states, the shares of common stock offered hereby may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock offered hereby may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that the selling stockholders will sell any or all of the shares of common stock registered pursuant to the registration statement of which this prospectus forms a part.

The selling stockholders and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended (Exchange Act), and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock offered hereby by the selling stockholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock offered hereby to engage in market-making activities with respect to the shares of common stock offered hereby. All of the foregoing may affect the marketability of the shares of common stock offered hereby and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock offered hereby.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock offered hereby will be freely tradable in the hands of persons other than our affiliates.

## 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.amicustherapeutics.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.

## INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

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, 2012 filed with the Commission on March 13, 2013;
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, filed with the Commission on May 9, 2013, August 7, 2013 and November 12, 2013, respectively;
- Our Current Reports on Form 8-K filed with the Commission on January 7, 2013, February 22, 2013, April 24, 2013, May 22, 2013, June 17, 2013, June 18, 2013, September 10, 2013, November 20, 2013, November 21, 2013 and December 5, 2013; and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed May 23, 2007, under the Exchange Act, 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.

You should rely only on the information contained in this prospectus, including information incorporated by reference herein. We have not authorized anyone to provide you with information different from that contained in this prospectus or any prospectus supplement. This prospectus is not an offer of these securities in any jurisdiction where an offer and sale is not permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.



**LEGAL MATTERS**

The validity of the issuance of the securities offered hereby will be passed upon for us by Pepper Hamilton LLP, Philadelphia, Pennsylvania.

**EXPERTS**

The consolidated financial statements of the Company appearing in the Company's Annual Report (Form 10-K) for the year ended December 31, 2012 and the effectiveness of the Company's internal control over financial reporting as of December 31, 2012 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.

**PART II****INFORMATION NOT REQUIRED IN THE PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

Set forth below is an estimate (except in the case of the registration fee) of the amount of fees and expenses to be incurred in connection with the issuance and distribution of the offered securities registered hereby, other than underwriting discounts and commission, if any, incurred in connection with the sale of the offered securities. All such amounts will be borne by Amicus Therapeutics, Inc.

SEC Registration Fee	\$ 2,456
Legal Fees and Expenses	\$ 10,000
Accounting Fees and Expenses	\$ 10,000
Miscellaneous Fees and Expenses	\$ 2,000
Total:	\$ 24,456

**Item 15. Indemnification of Directors and Officers.**

Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. The Registrant's restated certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as director, notwithstanding any provision of law imposing such liability, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Delaware Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Delaware Court of Chancery or such other court shall deem proper.

The Registrant's restated certificate of incorporation provides that the Registrant will, to the fullest extent permitted by Section 145 of the Delaware General Corporation Law and the Registrant's by-laws (each as amended from time to time), indemnify each person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Registrant, or is or was serving, or has agreed to serve, at the

request of the Registrant, as a director, officer, partner, or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, including any employee benefit plan (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by, or on behalf of, the Indemnitee in connection with such action, suit or proceeding and any appeal therefrom. Such indemnification may include payment by the Registrant of expenses in defending an action or proceeding in advance of the final disposition of such action or proceeding upon receipt of an undertaking by the Indemnitee (such undertaking acceptable by the Registrant without reference to the financial ability of the Indemnitee) to repay such payment if it is ultimately determined that the Indemnitee is not entitled to indemnification under the Registrant's restated certificate of incorporation; however, the Registrant will not indemnify any person seeking indemnification in connection with a proceeding (or part thereof) initiated by such person, unless such initiation was approved by the Registrant's board of directors. Also, the indemnification rights provided in the Registrant's restated certificate of incorporation (i) are not exclusive of any other rights to which those indemnified may be entitled under any law, agreement or vote of stockholders or disinterested directors or otherwise, and (ii) will inure to the benefit of the heirs, executors and administrators of such persons. The Registrant may, to the extent authorized from time to time by its board of directors, grant indemnification rights to other employees of the Registrant or other persons serving the Registrant and such rights may be equivalent to, or greater or less than, those set forth in the Registrant's restated certificate of incorporation.

The Registrant has entered into indemnification agreements with each of its directors. These agreements, among other things, require the Registrant to indemnify each director to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director in any action or proceeding, including any action or proceeding by or in right of the Registrant, arising out of the person's services as a director.

The Registrant maintains a general liability insurance policy that covers certain liabilities of the Registrant's directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In any underwriting agreement that the Registrant enters into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, the Registrant, its directors, its officers and persons who control the Registrant within the meaning of the Securities Act, against certain liabilities.

**Item 16. Exhibits**

<u>Exhibit</u>	<u>Description</u>
3.1	Restated Certificate of Incorporation of the registrant (incorporated by reference to Exhibit 3.1 of the registrant's Annual Report on Form 10-K filed with the Commission on February 28, 2012)
3.2	Restated By-laws of the of the registrant (incorporated by reference to Exhibit 3.4 of the registrant's Registration Statement on Form S-1/A (Registration No. 333-141700), as amended, originally filed with the Commission on April 27, 2007)
4.1	See Exhibits 3.1 and 3.2 for instruments defining rights of holders of common stock
4.2	Specimen Stock Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 of the registrant's Registration Statement on Form S-1 (Registration No. 333-141700), as amended, originally filed with the Commission on March 30, 2007)
4.3	Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended, by and among the registrant and certain stockholders of the registrant (incorporated by reference to Exhibit 4.3 of the registrant's Registration Statement on Form S-1 (Registration No. 333-141700), as amended, originally filed with the Commission on March 30, 2007)
4.4	Form of Warrant (incorporated by reference to Exhibit 4.1 of the registrant's Current Report on Form 8-K filed with the Commission on February 26, 2010)
5.1	Opinion of Pepper Hamilton LLP (filed herewith)
10.1	Securities Purchase Agreement by and among Amicus Therapeutics, Inc. and the purchasers appearing on the signature pages thereto dated November 20, 2013 (incorporated by reference to Exhibit 10.1 of the registrant's Current Report on Form 8-K filed with the Commission on November 20, 2013)
10.2	Form of Warrant (incorporated by reference to Exhibit 10.1 of the registrant's Current Report on Form 8-K filed with the Commission on November 20, 2013)
23.1	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
23.2	Consent of Ernst & Young LLP (filed herewith)
24.1	Power of attorney (included on the signature page hereto)

**Item 17. Undertakings.**

(a) The undersigned Registrant hereby undertakes:

(1) to file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of a prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price

represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

*provided, however*, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the registration statement is on Form S-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) that, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) to remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) that, for the purpose of determining liability under the Securities Act to any purchaser:

(A) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions described under Item 15 above, or otherwise, the registrant has been advised that in the opinion of the Securities and

Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.





<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ JAMES BARRETT PH.D.</u>		
James Barrett Ph.D.	Director	December 16, 2013
<u>/s/ ROBERT ESSNER</u>		
Robert Essner	Director	December 16, 2013
<u>/s/ DONALD J. HAYDEN , JR.</u>		
Donald J. Hayden , Jr.	Director	December 16, 2013
<u>/s/ TED W. LOVE, M.D.</u>		
Ted W. Love, M.D.	Director	December 16, 2013
<u>/s/ MARGARET G. MCGLYNN, R.PH.</u>		
Margaret G. McGlynn, R.Ph.	Director	December 16, 2013
<u>/s/ MICHAEL G. RAAB</u>		
Michael G. Raab	Director	December 16, 2013
<u>/s/ GLENN SBLENDORIO</u>		
Glenn Sblendorio	Director	December 16, 2013
<u>/s/ JAMES N. TOPPER, M.D., PH.D.</u>		
James N. Topper, M.D., Ph.D.	Director	December 16, 2013

**EXHIBIT INDEX**

<b>Exhibit</b>	<b>Description</b>
5.1	Opinion of Pepper Hamilton LLP
23.1	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
23.2	Consent of Ernst & Young LLP
24.1	Power of attorney (included on the signature page hereto)



[Letterhead of Pepper Hamilton LLP]

December 16, 2013

Amicus Therapeutics, Inc.  
1 Cedar Brook Drive  
Cranbury, NJ 08512

Re: *Resale Registration*

Ladies and Gentlemen:

We have acted as counsel to Amicus Therapeutics, Inc., a Delaware corporation (the "**Company**"), in connection with the preparation of a registration statement (the "**Registration Statement**") of the Company on Form S-3 under the Securities Act of 1933, as amended (the "**Act**"), and the filing of the Registration Statement with the Securities and Exchange Commission. The Registration Statement relates to offer and sale from time to time by certain stockholders of the Company of up to 9,100,000 shares of the Company's common stock, par value \$0.01 per share (the "**Common Stock**"), which includes an aggregate 7,500,000 shares of Common Stock (the "**Shares**") held by such stockholders and up to 1,600,000 shares of Common Stock (the "**Warrant Shares**") issuable upon the exercise of certain warrants held by certain of such stockholders.

In connection with this opinion, we have examined the originals or copies, certified or otherwise identified to our satisfaction, of the Registration Statement, the Restated Certificate of Incorporation and the Amended and Restated By-laws of the Company, as amended to date, resolutions of the Company's Board of Directors and such other documents and corporate records relating to the Company as we have deemed appropriate. We have assumed that all signatures are genuine, that all documents submitted to us as originals are authentic, and that all copies of documents submitted to us conform to the originals. We have relied as to certain matters on information obtained from public officials, officers of the Company, and other sources believed by us to be reliable.

We express no opinion herein as to the law of any state or jurisdiction other than the laws of the State of Delaware, including statutory provisions and all applicable provisions of the Delaware Constitution and reported judicial decisions interpreting such laws of the State of Delaware, and the federal laws of the United States of America.

Based on the foregoing, and in reliance thereon, we are of the opinion that (i) the Shares are validly issued, fully paid and nonassessable, and (ii) subject to the availability of a sufficient number of then authorized and unissued shares of Common Stock, the Warrant Shares, when duly issued and sold in accordance with the terms of the warrants and assuming compliance with the Act, will be validly issued, fully paid and nonassessable.

We assume no obligation to supplement this opinion if any applicable law changes after the date hereof or if we become aware of any fact that might change the opinion expressed herein after the date hereof.

We hereby consent to the reference to our firm under the section "Legal Matters" in the prospectus included in the Registration Statement and to the filing of this opinion as an exhibit to the Registration Statement. In giving this consent, we do not admit that we are an "expert" within the meaning of the Act.

Very truly yours,

/s/ Pepper Hamilton LLP

Pepper Hamilton LLP

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## QuickLinks

[Exhibit 5.1](#)

[\[Letterhead of Pepper Hamilton LLP\]](#)

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the reference to our firm under the caption "Experts" in this Registration Statement (Form S-3) and related Prospectus of Amicus Therapeutics, Inc. for the registration of 9,100,000 shares of common stock of Amicus Therapeutics, Inc. and to the incorporation by reference therein of our reports dated March 12, 2013, with respect to the consolidated financial statements of Amicus Therapeutics, Inc., and the effectiveness of internal control over financial reporting of Amicus Therapeutics, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2012, filed with the Securities and Exchange Commission.

/s/ ERNST & YOUNG LLP

MetroPark, New Jersey  
December 10, 2013

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QuickLinks

[Exhibit 23.2](#)

[CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM](#)