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As filed with the Securities and Exchange Commission on July 6, 2016

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

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

AMICUS THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State of incorporation)

71-0869350
(I.R.S. 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)

John F. Crowley
Chief Executive Officer
Amicus Therapeutics, Inc.
1 Cedar Brook Drive
Cranbury, New Jersey 085124
(609) 662-2000

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

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, check the following box and list the Securities Act registration statement number of the earlier effective 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(1)	Amount to be Registered(2)	Proposed Maximum Offering Price Per Share(3)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee
Common Stock, \$0.01 par value per share	825,603	\$5.57	\$4,598,608.71	\$463.08

- (1) All shares of common stock registered hereby are offered for the account of certain selling stockholders who acquired such shares in a private transaction.
 - (2) Pursuant to Rule 416 under the securities act of 1933, as amended (the "Securities Act"), this registration statement also covers an indeterminate number of additional shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of a stock split, stock dividend, recapitalization or other similar event.
 - (3) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) under the Securities Act, based upon the average of the high and low prices of the registrant's common stock on July 1, 2016, as reported on the NASDAQ Global Market.
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AMICUS THERAPEUTICS, INC.



825,603 Shares of Common Stock

This prospectus relates to the resale of up to 825,603 shares of common stock, par value \$0.01 per share, of Amicus Therapeutics, Inc., by the selling stockholders identified beginning on page 8 of this prospectus, together with any additional selling stockholders identified in any applicable prospectus supplement. The selling stockholders acquired these shares from us in connection with our acquisition of MiaMed, Inc., or MiaMed, pursuant to the terms of the Agreement and Plan of Merger, dated as of July 5, 2016, by and among Amicus Therapeutics, Inc., Minervas Merger Sub, Inc., MiaMed, Inc., and MM Stockholders Representative LLC, in its capacity as the stockholders representative.

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. The selling stockholders may sell the shares of common stock described in this prospectus through public or private transactions at market prices prevailing at the time of sale or at negotiated prices. Additional information about how the selling stockholders may sell their shares of common stock is provided in the section of this prospectus entitled "Plan of Distribution."

Our common stock is listed on The NASDAQ Global Market under the symbol "FOLD." On July 5, 2016, the last reported sale price for our common stock on The NASDAQ Global Market was \$5.58 per share.

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 4 of this prospectus and under similar headings in the other documents filed with the Securities and Exchange Commission that are incorporated by reference in 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.

Prospectus dated July 6, 2016.

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We are responsible for the information contained and incorporated by reference in this prospectus, any accompanying prospectus supplement and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to provide you with any other information, and we take no responsibility for any other information that others may provide you. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell, or a solicitation of an offer to purchase, any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying prospectus supplement constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered hereby, or thereby in any jurisdiction to or from any person whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information appearing or incorporated by reference in this prospectus, any accompanying prospectus supplement, and any related free writing prospectus, is accurate only as of the date thereof, regardless of the time of delivery of this prospectus, any accompanying prospectus supplement, or any related free writing prospectus, or of any sale of our securities. Our business, financial condition, and results of operations may have changed since those dates. It is important for you to read and consider all the information contained in this prospectus and in any accompanying prospectus supplement, including the documents incorporated by reference herein or therein, before making your investment decision.

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission (the "SEC"), as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"), utilizing a "shelf" registration process. Under this process, selling stockholders named in this prospectus or in one or more supplements to this prospectus may offer or sell shares of our common stock, as described in this prospectus, in one or more offerings from time to time. Each time any selling stockholder not named in this prospectus (or in any supplement to this prospectus), sells shares of common stock under the registration statement of which this prospectus is a part, such selling stockholder must provide a copy of this prospectus and any applicable prospectus supplement, to a potential purchaser, as required by law.

We may also authorize one or more free writing prospectuses or prospectus supplements to be provided to you in connection with these offerings. Any related free writing prospectus or prospectus supplement may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in any prospectus supplement or any related free writing prospectus and any documents incorporated by reference.

The selling stockholders may offer and sell shares of our common stock directly to purchasers through agents selected by the selling stockholders, or to or through underwriters or dealers. A prospectus supplement, if required, may describe the terms of the plan of distribution and set forth the names of any agents, underwriters or dealers involved in the sale of shares of our common stock. See "Plan of Distribution."

You should read this prospectus together with any applicable prospectus supplement, as well as additional information described under the heading "Where You Can Find More Information." You should only rely on the information contained or incorporated by reference in this prospectus, and any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. We have not authorized, and no selling stockholder has authorized, any other person to provide you with different or additional information. If anyone provides you with different or inconsistent information, you should not rely on it. No offer of shares of common stock is being made in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information in this prospectus, any applicable prospectus supplement, any related free writing prospectus or any document incorporated by reference herein or therein is accurate as of any date other than the date on the cover of the applicable document. Our business, financial condition, results of operations and prospects may have changed since those dates. We urge you to read carefully this prospectus, the documents incorporated by reference in this prospectus, any applicable prospectus supplement and any applicable free writing prospectus before making an investment decision.

Unless the context requires otherwise, references in this prospectus to "the Company," "Amicus," "we," "our," "us," and other similar terms mean Amicus Therapeutics, Inc. and our wholly owned subsidiaries.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference into this prospectus, and does not contain all the information that you should consider before investing in our common stock. You should carefully read the entire prospectus, including the risks of investing on our common stock discussed under the heading "Risk Factors" on page 4 of this prospectus and under similar headings in the other documents that are incorporated by reference herein.

Overview

We are a global, late-stage, patient-focused biotechnology company engaged in the discovery and development of a diverse set of novel treatments for patients living with devastating rare and orphan diseases. We own exclusive global rights to three clinical programs that have the potential to address significant unmet needs, each with \$500 million to \$1 billion estimated global market opportunities.

Our lead product candidate, migalastat HCl ("migalastat"), is an orally administered small molecule pharmacological chaperone for the treatment of Fabry disease, a Lysosomal Storage Disorder ("LSD"). On May 27, 2016, the European Commission granted full approval for Galafold™ (migalastat) as a first line therapy for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease (alpha-galactosidase A deficiency) and who have an amenable mutation. We are also in Phase 3 clinical development of a novel topical cream, SD-101 (allantoin 6%), for the treatment of the genetic connective tissue disorder Epidermolysis Bullosa ("EB") for which no other pharmacological therapies are approved. We have also initiated a clinical study in patients with Pompe disease, another LSD, to investigate our novel treatment paradigm that consists of ATB200, a uniquely engineered recombinant human acid alpha-glucosidase (rhGAA) enzyme with an optimized carbohydrate structure to enhance uptake, co-administered with a pharmacological chaperone, AT2221, designed to improve activity and stability. Leveraging our biologics capabilities and platform technologies, we have the potential to develop additional novel enzyme replacement therapies ("ERTs") for Fabry disease and other LSDs. We believe that our platform technologies and our advanced product pipeline uniquely position us at the forefront of developing therapies to address significant unmet needs for devastating rare and orphan diseases.

Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our principal executive offices are located at 1 Cedar Brook Drive, Cranbury, NJ 08512 and our telephone number is (609) 662-2000. Our website address is www.amicusrx.com. We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider information contained on our website as part of this prospectus.

Recent Developments

Acquisition of MiaMed, Inc. On July 5, 2016, we entered into an Agreement and Plan of Merger (the "Merger Agreement"), by and among us, Minervas Merger Sub, Inc., MiaMed, Inc. ("MiaMed"), and MM Stockholders Representative LLC, solely in its capacity as stockholders representative and on the same day, the transactions contemplated by the Merger Agreement closed and Minervas Merger Sub, Inc. merged with and into MiaMed, with MiaMed as the surviving corporation and our wholly-owned subsidiary.

Pursuant to the terms of the Merger Agreement, in connection with the closing of the transactions contemplated by the Merger Agreement, the former holders of MiaMed's capital stock (collectively, the "MiaMed Stockholders") received (i) an aggregate amount of cash equal to approximately \$1.8 million

(plus MiaMed's cash and cash equivalents at closing and less any of MiaMed's unpaid third-party fees and expenses related to the transaction) and (ii) an aggregate of 825,603 shares of our common stock.

Pursuant to the terms of the Merger Agreement, we have also agreed to pay up to an additional \$83.0 million to the MiaMed Stockholders upon achievement of certain development, regulatory and commercial milestones (together the "Milestone Payments"). The Milestone Payments may be made in cash, shares of Amicus common stock, or a combination of cash and stock, at our election, subject to certain exceptions, at the time each Milestone Payment is due.

In addition, each MiaMed Stockholder receiving stock consideration under the Merger Agreement is required to enter into a lock-up agreement in order to receive shares of our common stock. The lock-up agreement provides for, among other things, a lock-up period of 60 days with respect to all of the shares of our common stock issued upon closing of the merger, 90 days for two-thirds of the shares issued upon closing of the merger and 120 days with respect to one-third of the shares of our common stock issued upon closing of the merger. The lock-up agreement also applies to any shares of common stock we may issue in connection with any Milestone Payment, with the lock-up period beginning on the date such shares are issued. Under the terms of the Merger Agreement, we agreed to file with the SEC, a registration statement on Form S-3 covering the resale of the shares of common stock received by MiaMed Stockholders as part of the closing merger consideration.

The foregoing is a summary of the material provisions of the Merger Agreement and is not intended to be complete and is qualified in its entirety by reference to the Merger Agreement, which has been filed with the SEC as an exhibit to our current report on Form 8-K dated as of July 6, 2016. Our stockholders are not considered third-party beneficiaries under the Merger Agreement and should not rely on the representations, warranties, covenants or any descriptions thereof as characterization of the actual state of facts of condition of Amicus, MiaMed or any of their respective subsidiaries.

Throughout this prospectus, when we refer to the shares of our common stock, the offer and sale of which are being registered on behalf of the selling stockholders on the registration statement of which this prospectus is a part, we are referring to the shares of common stock held by former holders of the capital stock of MiaMed, that we agreed to register pursuant to the Merger Agreement. When we refer to the "selling stockholders" in this prospectus, we are referring to former holders of the capital stock of MiaMed.

The Offering

Common Stock offered by the selling stockholders	825,603 shares
Use of Proceeds	All shares of common stock offered hereby are being sold by the selling stockholders. Accordingly, we will not receive any proceeds from the sale of these shares.
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 4 of this prospectus 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.
NASDAQ Global Market symbol	Our common stock is quoted and traded on The NASDAQ Global Market under the symbol "FOLD."

RISK FACTORS

Investing in our common stock involves risks. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed below and any factors discussed under the heading "Risk Factors" in any prospectus supplement, together with all of the other information contained or incorporated by reference in this prospectus or any prospectus supplement. 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, 2015, filed on February 29, 2016, with the SEC, and our quarterly report on Form 10-Q for the period ended March 31, 2016, filed on May 3, 2016, with the SEC, each of which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described therein and below 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 by reference 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 or the documents incorporated herein or 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," 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 our pharmacological chaperone migalastat HCl;
- 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 future results of clinical trials for products containing the TATk-CDKL5 Fusion Protein, including our ability to obtain necessary regulatory approvals, commercialize and obtain market acceptance of such products;
- the future results of on-going or later clinical trials for SD-101 ("Zorblisa"), including our ability to obtain regulatory approvals and commercialize Zorblisa and obtain market acceptance of Zorblisa;
- the costs, timing and outcome of regulatory review of our product candidates, including, without limitation, the FDA and EMA.;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the emergence of competing technologies and other adverse market developments;
- our ability to obtain reimbursement for Galafold™;
- our ability to commercialize Galafold™ ;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property related claims;
- the extent to which we acquire or invest in businesses, products and technologies;
- our ability to successfully incorporate MiaMed and its products and technology into our business, including the possibility that the expected benefits of the transaction will not be fully realized by us or may take longer to realize than expected; 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, particularly those incorporated by reference in the section captioned "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 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.

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 and in the registration statement of which this prospectus is a part.

USE OF PROCEEDS

The selling stockholders will make offers and sales pursuant to this prospectus and any applicable prospectus supplement. 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 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 statement of which this prospectus forms a part, including, without limitation, all registration fees, listing fees of the NASDAQ Global Market and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDERS

We are registering for resale an aggregate of 825,603 shares of our common stock that may be sold by the selling stockholders set forth herein. The shares registered hereby were issued to the former stockholders of MiaMed in connection with the closing of the merger pursuant to the Merger Agreement.

Pursuant to Section 5.04 of the Merger Agreement, we agreed to file with the SEC, a registration statement, or prospectus supplement under an existing "shelf" registration statement, to register for resale the shares of our common stock that we issued as part of the consideration for the merger at closing as well as any shares we may issue in satisfaction of any Milestone Payment. We agreed to use reasonable best efforts to keep such registration statement effective until the earlier of (i) the date on which all such shares of common stock having been sold pursuant to an effective registration statement, or prospectus supplement, or (ii) at such time as such shares of common stock are eligible for resale under Rule 144 of the Securities Act.

Beneficial ownership is determined in accordance with the rules of the SEC, and includes voting or investment power with respect to our common stock. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares of common stock that they beneficially own, subject to applicable community property laws.

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. The selling stockholders have agreed, subject to certain exceptions, to limitations on their ability to sell all, two-thirds and one-third of the shares issued to them upon closing of the merger for a period of 60, 90 and 120 days following the closing of the merger, respectively. Other than the Merger Agreement and the agreements contemplated thereby, 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.

Name of Selling Stockholder	Shares Beneficially Owned Prior to the Offering		Number of Shares Being Registered for Resale(5)	Shares Beneficially Owned After the Offering	
	Shares	Percentage(4)		Shares(6)	Percentage
Michael Jasulavic(1)	255,267	*	255,267	—	*
Sandra Wihbey(2)	283,630	*	283,630	—	*
Other Selling Stockholders(3)	286,706	*	286,706	—	*

* Represents less than 1% of the total aggregate amount of shares of our common stock

(1) Mr. Jasulavic has sole voting and investment power over the shares.

(2) Ms. Wihbey has sole voting and investment power over the shares.

(3) Represents shares held by 16 selling stockholders not listed above, who, as a group own less than 1% of our shares of common stock prior to this offering.

(4) Based on 134,408,526 shares outstanding as of June 28, 2016, plus 825,603 shares issued in connection with the acquisition of MiaMed.

(5) Represents the number of shares being registered on behalf of the selling stockholder pursuant to the registration statement, of which this prospectus forms a part, which may be less than the total number of shares beneficially owned by such selling stockholder.

(6) Assumes the selling stockholders dispose of all of the shares of common stock covered by this prospectus and do not acquire beneficial ownership of any additional shares. The registration of these shares does not necessarily mean that the selling stockholders will sell all or any portion of the shares covered by this prospectus.

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 their 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:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing or settlement of options, whether such options are listed on an options exchange or otherwise;
- 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 the shares as agent or principal of all such shares held by the selling stockholder;
- purchases by a broker-dealer as principal and resale by the 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 or combination of methods of sale permitted pursuant to applicable law.

The selling stockholders may also sell shares pursuant to Rule 144 under the Securities Act, if available, rather than under this prospectus.

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 from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus or any amendment to this prospectus under Rule 424(b)(3), or other applicable provision of the Securities Act, supplementing or 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 the shares of common stock in other circumstances, in which case the transferees, 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 in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Any such discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person 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.

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 any selling stockholder 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 the applicable provisions of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the rules and regulations promulgated 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 shelf registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus has been passed upon for Amicus by Pepper Hamilton LLP.

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, 2015, and the effectiveness of our internal control over financial reporting as of December 31, 2015, as set forth in their reports, which are incorporated by reference in this 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.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 filed with the SEC under the Securities Act and does not contain all of the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated herein by reference for a copy of such contract, agreement or other document. We are subject to the information and reporting requirements of the Exchange Act, and as such, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public via the Internet on the SEC's website at 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 1-800-SEC-0330 for further information regarding the operation of the Public Reference Room.

We make available free of charge on our website at www.amicusrx.com, our annual, quarterly and current reports, including any amendments thereto, as soon as reasonably practicable after these materials are filed with or furnished to the SEC. The information on our website, other than the information identified below under the caption "Information Incorporated Reference," is not incorporated by reference in this prospectus, or any prospectus supplement and you should not consider it a part of this prospectus or any accompanying prospectus supplement. Additionally, you may obtain documents incorporated by reference in this prospectus by writing to us at the following address or by calling us at the telephone number listed below:

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

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front page of those documents.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus the information in other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference in this prospectus and the registration statement of which this prospectus forms a part, the information or documents listed below that we have filed with the SEC (Commission File No. 001-33497):

- Our Annual Report on Form 10-K for the year ended December 31, 2015 filed with the SEC on February 29, 2016;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2016 filed with the SEC on May 3, 2015;
- Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 29, 2016, to the extent incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015;
- Our Current Reports on Form 8-K filed with the SEC on January 11, 2016, February 22, 2016, February 26, 2016, March 3, 2016, March 15, 2016, April 1, 2016, May 3, 2016, May 11, 2016, June 7, 2016, June 9, 2016, June 13, 2016, July 1, 2016 and July 6, 2016;
- 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 (other than any filings or portions of such reports that are not deemed "filed" under the Exchange Act in accordance with the Exchange Act and applicable SEC rules, including current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus forms a part, until the selling stockholders identified herein sell all of the common stock covered by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

825,603 Shares



Common Stock

PROSPECTUS

July 6, 2016

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.**

The Registrant will pay all reasonable expenses incident to the registration of the shares other than any commissions and discounts of underwriters, dealers or agents. Such expenses are set forth in the following table. All of the amounts shown are estimates except the SEC registration fee.

	<u>Amount to be Paid</u>
SEC registration fee	\$ 463.08
Printing fees and expenses	15,000
Legal fees and expenses	25,000
Accounting fees and expenses	10,000
Miscellaneous fees and expenses	10,000
Total	<u>\$ 60,463.08</u>

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.

A list of exhibits filed herewith is contained in the exhibit index that immediately precedes such exhibits and is incorporated herein by reference.

ITEM 17. UNDERTAKINGS.

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 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 (i), (ii) and (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 SEC 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; and

(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 SEC such

indemnification is against public policy as expressed in the Securities 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 Securities Act and will be governed by the final adjudication of such issue.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<hr/> <i>/s/ ROBERT ESSNER</i> <hr/> Robert Essner	Director	July 6, 2016
<hr/> <i>/s/ DONALD J. HAYDEN, JR.</i> <hr/> Donald J. Hayden, Jr.	Director	July 6, 2016
<hr/> <i>/s/ TED W. LOVE, M.D.</i> <hr/> Ted W. Love, M.D.	Director	July 6, 2016
<hr/> <i>/s/ MARGARET G. MCGLYNN, R.PH.</i> <hr/> Margaret G. McGlynn, R.PH.	Director	July 6, 2016
<hr/> <i>/s/ MICHAEL G. RAAB</i> <hr/> Michael G. Raab	Director	July 6, 2016
<hr/> <i>/s/ GLEN SBLENDORIO</i> <hr/> Glen Sblendorio	Director	July 6, 2016
<hr/> <i>/s/ CRAIG A. WHEELER</i> <hr/> Craig A. Wheeler	Director	July 6, 2016

EXHIBIT INDEX

Exhibit	Description	Incorporated by reference herein		
		Form	Date	Exhibit Number
2.1*†	Agreement and Plan of Merger dated as of July 5, 2016, by and among Amicus Therapeutics, Inc., Minervas Merger Sub, Inc., MiaMed, Inc., and MM Stockholders Representative LLC, in its capacity as stockholders representative	8-K	July 6, 2016	2.1
3.1*	Restated Certificate of Incorporation of Amicus Therapeutics, Inc.	10-K	February 28, 2012	3.1
3.2*	Certificate of Amendment to the Restated Certificate of Incorporation of Amicus Therapeutics, Inc.	8-K	June 10, 2015	3.2
3.3*	Restated Bylaws of Amicus Therapeutics, Inc.	S-1/A	April 27, 2007	3.4
4.1	See Exhibits 3.1, 3.2 and 3.3 for instruments defining the rights of holders of Amicus common stock			
4.2*	Specimen Stock Certificate evidencing shares of common stock	S-1/A	May 17, 2007	4.1
5.1**	Opinion of Pepper Hamilton LLP			
23.1**	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm			
23.2**	Consent of Pepper Hamilton LLP (included in Exhibit 5.1 to this Registration Statement)			
24.1**	Power of Attorney (included on the signature page hereto)			

* Incorporated by reference herein.

** Filed herewith.

† Portions of this exhibit have been redacted pursuant to a request for confidential treatment submitted to the Securities and Exchange Commission. The schedules and exhibits to the Agreement and Plan of Merger have been omitted from this filing pursuant to Item 601(b) (2) of Regulation S-K under the Securities Act of 1933, as amended. Amicus agrees to furnish as a supplement a copy of any omitted schedules or exhibits to the Agreement and Plan of Merger to the Securities and Exchange Commission upon request, provided that Amicus may request confidential treatment for any schedule or exhibit so furnished.

Pepper Hamilton LLP
Attorneys at Law

3000 Two Logan Square
Eighteenth and Arch Streets
Philadelphia, PA 19103-2799
215.981.4000
Fax 215.981.4750

July 6, 2016

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

Re: Securities Registered under Registration Statement
on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Amicus Therapeutics, Inc., a Delaware corporation (the "**Company**"), in connection with the registration of 825,603 shares (the "**Shares**") of the Company's common stock, par value \$0.01 per share (the "**Common Stock**"), that were issued to the selling stockholders of MiaMed, Inc., a Delaware corporation ("**MiaMed**"), pursuant to the Agreement and Plan of Merger, dated as of July 5, 2016, by and among the Company, Minervas Merger Sub, Inc., a Delaware corporation, MiaMed, and MM Stockholders Representative LLC, a Delaware limited liability company, as Stockholders' Representative (the "**Merger Agreement**") on a registration statement on Form S-3 (the "**Registration Statement**") filed with the U.S. Securities and Exchange Commission (the "**Commission**"), under the Securities Act of 1933, as amended (the "**Securities Act**").

In connection with this opinion, we have examined all such documents as we considered necessary to enable us to render this opinion, including but not limited to the Registration Statement, the Merger Agreement, the Company's Restated Certificate of Incorporation, as amended, and the Company's Amended and Restated By-laws, as amended, in effect on the date hereof, certain resolutions of the Board of Directors of the Company, corporate records, and instruments, and such laws and regulations as we have deemed necessary for purposes of rendering the opinions set forth herein.

In rendering this opinion, we have assumed: (a) the legal capacity of all natural persons; (b) the genuineness of all signatures; (c) the authenticity of all documents submitted to us as originals; (d) the conformity to original documents of all documents submitted to us as certified, conformed, photostatic or facsimile copies; (e) the authenticity of the originals of such latter documents; (f) the truth, accuracy and completeness of the information, representations and warranties contained in the records, documents, instruments, certificates and records we have reviewed; and (g) the absence of any undisclosed modifications to the agreements and instruments reviewed by us. As to any facts material to the opinions expressed herein, which were not independently established or verified, we have relied upon statements and representations of officers and other representatives of the Company and others.

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.

	Boston	Washington, D.C.	Los Angeles	New York	Pittsburgh	
Detroit	Berwyn	Harrisburg	Orange County	Princeton	Silicon Valley	Wilmington

www.pepperlaw.com

Based upon the foregoing, we are of the opinion that, as of the date hereof, the Shares have been duly authorized and that the Shares already issued or when issued in accordance with the terms of the Merger Agreement, are or will be, as applicable, validly issued, fully paid and non-assessable.

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 filing of this opinion as a part of the Registration Statement and to the reference of our firm under the caption "Legal Matters" in the Prospectus. In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission. Except as otherwise set forth herein, this opinion may not be used, circulated, quoted or otherwise referred to for any purpose or relied upon by any other person without the express written permission of this firm.

Very truly yours,

/s/ Pepper Hamilton LLP

Pepper Hamilton LLP

QuickLinks

[Exhibit 5.1](#)

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Amicus Therapeutics, Inc. for the registration of 825,603 shares of its common stock and to the incorporation by reference therein of our reports dated February 29, 2016, 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, 2015, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP
Metropark, New Jersey
July 6, 2016

QuickLinks

[Exhibit 23.1](#)

[Consent of Independent Registered Public Accounting Firm](#)