Filed pursuant to Rule 424(b)(5)
Registration No.: 333-262987

Prospectus Supplement
(to prospectus dated February 24, 2022)

AMICUS THERAPEUTICS, INC.

Up to $250,000,000 of Shares of Common Stock

We have entered into an equity distribution agreement with Goldman Sachs & Co. LLC, or Goldman Sachs, as our sales agent, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the equity distribution agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $250,000,000 from time to time through Goldman as our sales agent. Goldman Sachs may act as agents on our behalf or purchase shares of our common stock as principal.

Our common stock is listed on The NASDAQ Global Market under the symbol “FOLD.” The last reported sale price of our common stock on The NASDAQ Global Market on November 3, 2022 was $10.10 per share.

Sales of our common stock, if any, under the equity distribution agreement will be made in sales deemed to be an “at the market offering” as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, in ordinary brokers’ transactions, to or through a market maker, on or through The Nasdaq Global Select Market or any other market venue where the securities may be traded, in the over-the-counter market, in privately negotiated transactions, or through a combination of any such methods of sale. Goldman Sachs may also sell our common stock by any other method permitted by law. Goldman Sachs is not required to sell any specific amount of securities but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Goldman Sachs and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Pursuant to the terms of the equity distribution agreement, Goldman Sachs will be entitled to compensation at a commission rate of up to 3.0% of the gross offering proceeds of shares sold under the equity distribution agreement. In connection with the sale of our common stock on our behalf, Goldman Sachs & Co. LLC may be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation paid to Goldman Sachs may be deemed to be underwriting commissions or discounts.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “Risk Factors” on page S-8 of this prospectus supplement, page 3 of the accompanying prospectus and under similar headings in the other documents that are incorporated by reference in this prospectus supplement and the accompanying prospectus.

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

Goldman Sachs & Co. LLC

The date of this prospectus supplement is November 7, 2022.

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Prospectus supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a universal shelf registration statement on Form S-3 (File No.333-262987) that we filed with the U.S. Securities and Exchange Commission (the "SEC") on February 24, 2022, which became effective automatically upon the filing thereof. This document is in two parts. The first part is this prospectus supplement which describes the terms of this offering of our common stock and adds to and updates the information contained in the accompanying prospectus. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or in any document incorporated by reference into this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, you should rely on the information in this prospectus supplement. In addition, any statement in a filing we make with the SEC after the date of this prospectus supplement that adds to, updates or changes information contained in this prospectus supplement, the accompanying prospectus or an earlier filing we made with the SEC shall be deemed to modify and supersede such information in this prospectus supplement, the accompanying prospectus or the earlier filing.

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

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

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

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

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

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

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

Unless the context otherwise requires, in this prospectus supplement the “Company,” “we,” “us,” “our” and similar names refer to Amicus Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries. This prospectus supplement and the accompanying prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. We have registrations and/or filed applications to register certain trademarks in the U.S. and abroad, including AMICUS THERAPEUTICS and design, AMICUS ASSIST and design, CHART and design, AT THE FOREFRONT OF THERAPIES FOR RARE AND ORPHAN DISEASES, HEALING BEYOND DISEASE, OUR GOOD STUFF and Galafold® and design. All other trademarks or trade names referred to in this prospectus supplement are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus supplement, including the risks of investing in our securities discussed under the heading "Risk Factors" on page S-8 of this prospectus supplement and under similar headings in the other documents that are incorporated by reference herein.

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We have a portfolio including the first, oral monotherapy for Fabry disease that has achieved widespread global approval and a differentiated biologic for Pompe disease that is under review with the U.S. Food and Drug Administration ("FDA") as well as the European Medicines Agency ("EMA"). We are committed to discovering and developing next generation therapies in Fabry and Pompe diseases.

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, two-component, potential best-in-class treatment for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation ("BTD") to AT-GAA for the treatment of late onset Pompe disease. In September 2021, the FDA set the Prescription Drug User Fee Act ("PDUFA") target action date of May 29, 2022 for the New Drug Application ("NDA") for miglustat and July 29, 2022 for the Biologics License Application ("BLA") for cipaglucosidase alfa. The EMA validated the Marketing Authorization Application ("MAA") in the fourth quarter of 2021. On May 9, 2022, the FDA extended the review period for the NDA for miglustat and the BLA for cipaglucosidase alfa resulting in revised PDUFA action dates of August 29, 2022 and October 29, 2022, respectively. In October 2022, the FDA deferred action on the BLA for cipaglucosidase alfa, citing the inability to complete the manufacturing facility inspection prior to the PDUFA action date. We are actively engaged with the FDA on developing an inspection plan.

Our Strategy

Our strategy is to create, manufacture, test, and deliver the highest quality medicines for people living with rare diseases through internally developed, jointly developed, acquired, or in-licensed products and product candidates that have the potential to obsolete current treatments, provide significant benefits to patients, and be first- or best-in-class. We are leveraging our global capabilities to develop and broaden our lead franchises in Fabry and Pompe disease, with focused discovery work on next generation therapies and novel platform technologies.

We continue to monitor the novel coronavirus ("COVID-19") pandemic. Our commercial operations have not been significantly impacted by the COVID-19 pandemic thus far. We continue to observe increased lag time between patient identification and Galafold® initiation due to the continued prevalence of COVID-19 and its ongoing impact on access to treatment for people living with Fabry disease in certain markets. We have maintained operations in all geographies, secured our global supply chain for our commercial and clinical products, as well as maintained the operational integrity of our clinical trials, with minimum disruptions. Our ability to continue to operate without any significant disruptions will depend on the continued health of our employees, the ongoing demand for Galafold® and the continued operation of our global supply chain. We have continued to provide uninterrupted access to medicines for those in need of treatment, while prioritizing the health and safety of our global workforce. In regard to our regulatory operations, the FDA deferred action on the pending BLA for cipaglucosidase alfa, as a facility inspection was necessary, however, could not be completed by the PDUFA action

date due to COVID-19 related travel restrictions. Per FDA guidance relating to pre-approval inspections during the COVID-19 pandemic, receipt of a deferral action indicates no deficiencies have been identified and the application otherwise satisfies the requirements for approval.

Highlights of our progress include:

- *Commercial and regulatory success in Fabry disease*. For the nine months ended September 30, 2022, Galafold® revenue totaled $241.1 million, an increase of $17.8 million compared to the same period in the prior year. We continue to see strong commercial momentum and expansion into additional geographies. In countries where we have been operating the longest, we see an increasing proportion of previously untreated patients come onto Galafold®. In the U.S., we continue to see a significant increase in patients from a growing and very wide prescriber base. Across all markets, we see a high rate of compliance and adherence to this oral treatment option.
- *Pompe disease clinical program milestones*. In February 2021, we reported topline results from the Phase 3 study of AT-GAA (ATB200-03, also known as "PROPEL"). In June 2021, the MHRA granted AT-GAA a positive scientific opinion through the Early Access to Medicines Scheme ("EAMS") which permits eligible adults living with late-onset Pompe disease ("LOPD") who have received alglucosidase alfa for at least 2 years to switch to AT-GAA prior to marketing authorization in the U.K. We completed the submission of the rolling BLA and NDA to the FDA, which was accepted for review in September 2021, and in the fourth quarter of 2021, the MAA was submitted and validated by the EMA. In June 2022, the French National Agency for the Medicines and Health Products Safety granted the first reimbursed access to AT-GAA under their compassionate access program.
- *Pipeline advancement and growth*. We are leveraging our global capabilities to develop and broaden our lead franchises in Fabry and Pompe disease, with focused discovery work on next generation therapies and novel platform technologies.
- *Manufacturing*. We have managed our clinical and commercial supply chains during the COVID-19 pandemic such that as of the date hereof we have not experienced supply impacts. We have been able to continue to meet required commercial demand for Galafold® as well as supply our ongoing Pompe disease clinical studies and access programs including EAMS without interruption. We have secured supply for our continued needs for the Pompe disease program through a long-term supply agreement with Wuxi Biologics. The agreement allows for the continuous manufacture of our biologic to support future clinical needs and our anticipated commercial requirements should we garner regulatory approvals as planned. We have contracts in place to supply miglustat, our small molecule component of AT-GAA, to support both clinical and future commercial requirements.
- *Financial strength*. Total cash, cash equivalents, and marketable securities as of September 30, 2022 was $354.7 million. Based on the current operating model, we believe that the current cash position, which includes expected revenues, is sufficient to fund our operations and ongoing research programs to achieve self-sustainability. Potential impacts of the COVID-19 pandemic, business development collaborations, pipeline expansion, and investment in manufacturing capabilities could impact our future capital requirements.

Our Commercial Product and Product Candidates

Galafold® (migalastat HCl) for Fabry Disease

Our oral precision medicine Galafold® was granted accelerated approval by the FDA in August 2018 under the brand name Galafold® for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene ("GLA") variant based on in vitro assay data. The FDA has approved Galafold® for 350 amenable GLA variants. Galafold® was approved in the E.U. and U.K. in May 2016 as a first-line therapy for long-term treatment of adults and adolescents, aged 16 years and older, with a confirmed diagnosis of Fabry disease and who have an amenable mutation (variant). The approved E.U. and U.K. labels include 1,384 mutations amenable to Galafold® treatment, which

represent up to half of all patients with Fabry disease. In countries where mutations are provided only on the amenability website, these 1,384 amenable mutations are now available. Marketing authorization approvals have been granted in over 40 countries around the world, including the U.S., E.U., U.K., Japan, and others. In July 2021, Galafold® was approved in the E.U. for adolescents aged 12 years and older weighing 45 kg or more. We plan to continue to launch Galafold® in additional countries during 2022, including for adolescents aged 12 years and older.

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

The Galafold® U.S. patent portfolio encompasses 46 Orange Book listed patents, including 5 composition-of-matter patents, of which 30 provide protection through at least 2038.

In the fourth quarter, we received Paragraph IV Certification Notice Letters from Teva Pharmaceuticals USA, Inc., Aurobindo Pharma Limited, and Lupin Limited in connection with Abbreviated New Drug Applications ("ANDA") filed with the FDA requesting approval to market generic migalastat. We intend to file lawsuits against the ANDA filers within 45 days of the receipt of the notice letters and to vigorously enforce our Galafold® intellectual property rights.

Next Generation for Fabry Disease

We are committed to continued innovation for all people living with Fabry disease. Our pipeline includes a Fabry gene therapy and an academic research collaboration agreement with the University of Seville to explore next generation pharmacological chaperones for Fabry disease.

Novel ERT for Pompe Disease

We are leveraging our biologics capabilities to develop AT-GAA, a novel treatment paradigm for Pompe disease. AT-GAA consists of a uniquely engineered rhGAA enzyme, ATB200, or cipaglucosidase alfa, with an optimized carbohydrate structure to enhance lysosomal uptake, administered in combination with AT2221, or miglustat, that functions as an enzyme stabilizer. Miglustat binds to and stabilizes ATB200 preventing inactivation of rhGAA in circulation to improve the uptake of active enzyme in key disease-relevant tissues, resulting in increased clearance of accumulated substrate, ("glycogen"). Miglustat is not an active ingredient that contributes directly to glycogen reduction.

In February 2021, we reported topline results from the Phase 3 PROPEL study. Of the Pompe disease patients enrolled, 77% were being treated with alglucosidase alfa (n=95) immediately prior to enrollment ("Switch") and 23% had never been treated with any ERT (n=28) ("Naïve"). Nearly all patients from the PROPEL study continue to be treated with AT-GAA in the extension clinical study. The clinical data from the PROPEL study, the extension study as well as the Phase 1/2 study were included in the AT-GAA submissions to the FDA and the EMA.

In October 2022, we reported positive long-term data from our ongoing phase 1/2 clinical study. Study participants treated with AT-GAA for up to 48 months demonstrated persistent and durable effects on six-minute walk test distance and measures of motor function and muscle strength, stability, or increase in forced vital capacity, and reductions in biomarkers of muscle damage and disease substrate.

In addition, we are conducting ongoing clinical studies in pediatric patients for both LOPD and infantile-onset Pompe disease ("IOPD") populations.

Next Generation for Pompe Disease

As part of our long-term commitment to provide multiple solutions to address the significant unmet needs of the Pompe disease community, we are also continuing discovery for next-generation genetic medicines for Pompe disease.

CDKL5 Deficiency Disorder

We are researching a potential first-in-class genetic medicine for CDKL5 deficiency disorder consisting of a CDKL5 protein engineered for cross correction, delivered as either a protein replacement or as a gene therapy through our collaboration with Penn. We are collaborating with the LouLou Foundation to assess the natural history of the disease to identify endpoints for potential use in future studies.

Additional Next Generation Programs

We have a number of additional gene therapies in clinical and preclinical development, including potential gene therapies in multiple forms of Batten disease.

Strategic Alliances and Arrangements

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

Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our principal executive offices are located at 3675 Market Street, Philadelphia, PA 19104 and our telephone number is (215) 921-7600. Our website address is www.amicusrx.com. We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus, and you should not consider information contained on our website as part of this prospectus supplement or the accompanying prospectus.

THE OFFERING

Common stock offered by us	Shares of common stock having an aggregate offering price of up to $250,000,000.
Manner of offering	"At the market" offering that may be made from time to time through our sales agent, Goldman Sachs & Co. LLC. See "Plan of Distribution" on page S-15 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds of this offering for general corporate purposes, including for the support of the launch of our Pompe disease treatment, AT-GAA, in the United States, European Union and various other jurisdictions where we may seek approval, the continued expansion and commercialization of Galafold, manufacturing capabilities for AT-GAA and our gene therapy product candidates, including contract manufacturing partnerships, and for other general corporate and product development purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements, business combinations or business collaborations for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. As a result, our management will retain broad discretion in the allocation and use of the net proceeds from this offering. See "Use of Proceeds" on page S-13 of this prospectus supplement.
Risk Factors	An investment in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under "Risk Factors" on page S-8 of this prospectus supplement, page 3 of the accompanying prospectus, page 29 of our Annual Report on Form 10-K for the year ended December 31, 2021, and under similar headings in the other documents that are incorporated by reference herein, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus.
Market for the common stock	Our common stock is quoted and traded on The NASDAQ Global Market under the symbol "FOLD."

RISK FACTORS

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

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

Risks Related to this Offering

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

We currently intend to use the net proceeds of this offering for support of the launch of our Pompe disease treatment, AT-GAA, in the United States, European Union and various other jurisdictions where we may seek approval, the continued expansion and commercialization of Galafold, manufacturing capabilities for AT-GAA and our gene therapy product candidates, including contract manufacturing partnerships, and for other general corporate and product development purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements, business combinations or business collaborations for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses. However, we have not determined the specific allocation of the net proceeds among these potential uses. Our management will have broad discretion over the use and investment of the net proceeds of this offering, and, accordingly, investors in this offering will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning our specific intentions. These proceeds could be applied in ways that do not improve our operating results or increase the value of your investment. Please see the section entitled “Use of Proceeds” on page S-13 of this prospectus supplement for further information.

If you purchase the common stock sold in this offering, you will experience immediate dilution as a result of this offering and future equity issuances.

Because the price per share of our common stock being offered may be higher than the book value per share of our common stock, you may suffer immediate substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section entitled “Dilution” on page S-14 of this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing stockholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

The issuance of additional shares of our common stock in future offerings could be dilutive to stockholders if they do not invest in future offerings. Moreover, to the extent that we issue options or warrants to purchase, or securities convertible into or exchangeable for, shares of our common stock in the future and those options, warrants or other securities are exercised, converted or exchanged, stockholders may experience further dilution.

The common stock offered hereby will be sold in "at the market offerings," and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold in this offering. In addition, subject to the final determination by our board of directors, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

Risks Related to our Business

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

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

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

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

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

- launching commercial sales of Galafold®, where approved, whether alone or in collaboration with others;
- acceptance of Galafold®, where approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including potential generics and potential gene therapies;
- a continued acceptable safety profile of Galafold®;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting and enforcing our rights in our intellectual property portfolio;
- obtaining and maintaining a commercially viable price for our products; and
- continuing to successfully mitigate the impact of the COVID-19 pandemic.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

- our expectations related to the use of proceeds, if any, from this offering;
- the scope, progress, results and costs of our clinical trials of our drug candidates;
- the cost of manufacturing drug supply for our commercial, clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200" or "cipaglucosidase alfa");
- the future results of preclinical research and subsequent clinical trials for pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates, including AT-GAA;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales, and distribution;
- the emergence of competing technologies and other adverse market developments;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl") and, if our regulatory applications are approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and AT-GAA;
- our ability to obtain reimbursement for Galafold® and, if our regulatory applications are approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold®, and, if approved and applicable, AT-GAA;
- our ability to obtain market acceptance of Galafold® and, if our regulatory applications are approved AT-GAA;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims, including Hatch-Waxman litigation;
- the impact of litigation that has been or may be brought against us or of litigation that we are pursuing or may pursue against others;

- the extent to which we acquire or invest in businesses, products, and technologies;
- our ability to successfully integrate our acquired products and technologies into our business, or successfully divest or license existing products and technologies from our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish licensing agreements, collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;
- the extent to which our business could be adversely impacted by the effects of the novel coronavirus ("COVID-19") outbreak, including due to actions by us, governments, our customers, our suppliers, or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards;
- our ability to accurately forecast revenue, operating expenditures, or other metrics impacting profitability;
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

In light of these risks and uncertainties, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement and the accompanying prospectus, particularly under "Risk Factors", that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Those factors and the other risk factors described herein are not necessarily all of the important factors that could cause actual results or developments to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors also could harm our results. Our forward-looking statements do not reflect the potential impact of any future collaborations, alliances, business combinations, partnerships, strategic out-licensing of certain assets, the acquisition of preclinical-stage, clinical-stage, marketed products or platform technologies or other investments we may make. Consequently, there can be no assurance that actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, us. Given these uncertainties, investors are cautioned not to place undue reliance on such forward-looking statements.

You should read this prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect.

These forward-looking statements speak only as of the date of this prospectus supplement. We undertake no obligation, and specifically decline any obligation, to publicly update or revise any forward-looking statements, even if experience or future developments make it clear that projected results expressed or implied in such statements will not be realized, except as may be required by law. You should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to purchase our securities, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus supplement and the accompanying prospectus and in the registration statement of which this prospectus supplement and the accompanying prospectus form a part.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to $250,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

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

- for support of the launch of our Pompe disease treatment, AT-GAA, in the United States, European Union and various other jurisdictions where we may seek approval;
- continued expansion and commercialization of Galafold®;
- manufacturing capabilities for AT-GAA and our gene therapy product candidates, including contract manufacturing partnerships; and
- for other general corporate and product development purposes, which may include working capital, capital expenditures, the funding of in-licensing agreements, business combinations or business collaborations for product candidates, additional technologies or other forms of intellectual property, the acquisition of assets or businesses that are complementary to our existing business and general and administrative expenses.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our products and product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the shares of common stock offered by us hereunder.

Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the offering price per share and the as adjusted net tangible book value per share of our common stock immediately after this offering. We calculate net tangible book value per share by dividing our net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock.

Our net tangible book value (deficit) as of September 30, 2022 was approximately ($88.0 million), or ($0.31) per share. After giving effect to the assumed sale by us of an aggregate of $250,000,000 in shares of common stock in this offering at an assumed offering price of $10.10 per share, which was the last reported sale price of our common stock on The NASDAQ Global Market on November 3, 2022, and after deducting estimated commissions and offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2022, would have been approximately $154.0 million, or $0.50 per share of common stock. This represents an immediate increase in the net tangible book value of $0.81 per share to our existing stockholders and an immediate dilution in the net tangible book value of $9.60 per share of common stock to investors purchasing common stock in this offering. The following table illustrates this calculation on a per share basis:

Assumed offering price per share of common stock		$ 10.10
Net tangible book value per share as of September 30, 2022	$(0.31)	
Increase in net tangible book value per share after this offering	$ 0.81	
As adjusted net tangible book value per share as of September 30, 2022 after giving effect to this offering		$ 0.50
Dilution per share to investors participating in this offering		$ 9.60

The number of shares of our common stock to be outstanding immediately after this offering is based on 280,887,136 shares of common stock outstanding as of September 30, 2022. Unless specifically stated otherwise, the information in this prospectus supplement is as of September 30, 2022 and excludes, as of such date:

- 19,235,568 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2022, at a weighted average exercise price of $11.30 per share, of which options to purchase 10,655,322 shares of our common stock were then exercisable;
- 8,349,705 shares of our common stock issuable upon the exercise of warrants to purchase common stock, at a weighted average exercise price of $0.01 per share;
- 9,838,707 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2022;
- an aggregate of 15,428,394 shares of our common stock reserved for future grants of stock options (or other similar equity instruments) under the Amended and Restated 2007 Equity Incentive Plan;
- 67,928 shares of our common stock issued since September 30, 2022 upon the exercise of outstanding stock options or vesting of restricted stock units.

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

PLAN OF DISTRIBUTION

We have entered into an equity distribution agreement with Goldman Sachs & Co. LLC, as our sales agent, under which we may offer and sell from time to time our common stock having an aggregate offering price of up to $250,000,000. The sales agent may act as agent on our behalf or purchase shares of our common stock as principal.

Sales, if any, of common stock under the equity distribution agreement may be made in ordinary brokers' transactions, to or through a market maker, on or through The NASDAQ Global Market or any other market venue where the securities may be traded, in the over-the-counter market, in privately negotiated transactions, or through a combination of any such methods of sale. The sales agent may also sell our common stock by any other method permitted by law.

The securities may be sold at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices.

We will designate the maximum amount of common stock to be sold through the sales agent on a daily basis or otherwise as we and the sales agent agree and the minimum price per share at which such common stock may be sold. Subject to the terms and conditions of the equity distribution agreement, the sales agent will use its commercially reasonable efforts consistent with its normal sales and trading practices to sell on our behalf all of the designated shares of common stock. We may instruct the sales agent not to sell any common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or the sales agent, with respect to itself only, may suspend the offering of our common stock by notifying the other party.

The sales agent will provide to us written confirmation following the close of trading on The NASDAQ Global Market each day on which shares of common stock are sold under the equity distribution agreement. Each confirmation will include the number of shares of common stock sold on such day, the gross offering proceeds and the compensation payable by us to the sales agent. We will report at least quarterly the number of shares of common stock sold through the sales agent under the equity distribution agreement, the net proceeds to us (before expenses) and the compensation paid by us to the sales agent in connection with the sales of the shares of common stock.

We will pay the sales agent a commission of up to 3.0% of the gross offering proceeds of shares of common stock sold through such agent under the equity distribution agreement. We have also agreed to reimburse the sales agent for certain of its expenses in an amount up to $250,000, in addition to an amount not to exceed $25,000 per each quarter thereafter.

Settlement of any sales of common stock will occur on the third business day following the date on which such sales were made (or such earlier day as is industry practice for regular-way trading). There is no arrangement for funds to be received in an escrow, trust or similar arrangement. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and the sales agent may agree.

The offering of our common stock pursuant to the equity distribution agreement will terminate upon the earlier of (i) the sale of all of our shares of common stock subject to the equity distribution agreement, or (ii) termination of the equity distribution agreement by us or by the sales agent as provided therein.

In connection with the sale of the shares of common stock on our behalf, the sales agent may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to the sales agent may be deemed to be an underwriting commission or discount.

We have agreed to provide indemnification and contribution to the sales agent against certain liabilities, including civil liabilities under the Securities Act.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement is being passed upon for us by Troutman Pepper Hamilton Sanders LLP. Certain matters will be passed upon for Goldman Sachs & Co. LLC by Latham & Watkins 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, 2021, and the effectiveness of our internal control over financial reporting as of December 31, 2021, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

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

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

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

Office of the Corporate Secretary
Amicus Therapeutics, Inc.
3675 Market Street
Philadelphia, PA 19104
(215) 921-7600

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

- Our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 24, 2022;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021 from our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 26, 2022;
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022 filed with the SEC on May 10, 2022, August 4, 2022 and November 7, 2022, respectively;
- Our Current Reports on Form 8-K filed with the SEC on January 10, 2022, February 24, 2022, May 10, 2022, June 10, 2022, August 1, 2022 and September 14, 2022; and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed with the SEC on May 23, 2007, under the Exchange Act, including any amendment or report filed for the purpose of updating such description, including Exhibit 4.8 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 2, 2020.

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

Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see "Where You Can Find More Information" on page S-17 of this prospectus supplement.

PROSPECTUS

AMICUS THERAPEUTICS, INC.

Common Stock
Preferred Stock
Warrants
Debt Securities
Units
Subscription Rights

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

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

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

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

Our common stock is traded on the NASDAQ Global Market under the symbol "FOLD." On February 23, 2022, the closing price of our common stock was $8.25.

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

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

The date of this prospectus is February 24, 2022.

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Prospectus

ABOUT THIS PROSPECTUS

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

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

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

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

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

THE COMPANY

Overview

We are a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering novel medicines for rare diseases. We have a portfolio of product opportunities including the first, oral monotherapy for Fabry disease that has achieved widespread global approval and a differentiated biologic for Pompe disease that is under review with the U.S. Food and Drug Administration ("FDA") as well as the European Medicines Agency ("EMA"). We are committed to discovering and developing next generation therapies in Fabry and Pompe diseases.

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

The lead biologics program of our pipeline is Amicus Therapeutics GAA ("AT-GAA", also known as ATB200/AT2221, or cipaglucosidase alfa/miglustat), a novel, two-component, potential best-in-class treatment for Pompe disease. In February 2019, the FDA granted Breakthrough Therapy designation to AT-GAA for the treatment of late onset Pompe disease. In September 2021, the FDA set the Prescription Drug User Fee Act target action date of May 29, 2022 for the New Drug Application for miglustat and July 29, 2022 for the Biologics License Application for cipaglucosidase afla. The EMA validated the Marking Authorization Application in the fourth quarter of 2021.

On February 24, 2022, we announced, with ARYA Sciences Acquisition Corp IV, a special purpose acquisition company, sponsored by Perceptive Advisors, we have agreed to mutually terminate the previously announced definitive business combination agreement, originally executed in September 2021.

Additionally, in September 2021, we entered into securities purchase agreements with certain investors for the private placement of an aggregate of 11,296,660 shares of our common stock, at a purchase price of $10.18 per share and pre-funded warrants to purchase an aggregate of 8,349,705 shares of common stock, at a purchase price of $10.17 per pre-funded warrant. The net proceeds from these private placements were approximately $199.8 million. We expect to use the net proceeds to further fund initiatives in the global commercialization of Galafold® and the anticipated global launch of AT-GAA and to further support our discovery work on next generation therapies in Fabry and Pompe diseases.

Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our global headquarters are located at 3675 Market Street Philadelphia, PA 19104 and our telephone number is (215) 921-7600. Our website address is www.amicusrx.com. We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider information contained on our website as part of this prospectus.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 filed on February 24, 2022, with the SEC, which is incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

FORWARD-LOOKING STATEMENTS

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

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

- the scope, progress, results and costs of our clinical trials of our drug candidates;
- the cost of manufacturing drug supply for our commercial, clinical and preclinical studies, including the cost of manufacturing Pompe Enzyme Replacement Therapy ("ERT" or "ATB200" or "cipaglucosidase alfa");
- the future results of preclinical research and subsequent clinical trials for pipeline candidates we may identify from time to time, including our ability to obtain regulatory approvals and commercialize these therapies and obtain market acceptance for such therapies;
- the costs, timing, and outcome of regulatory review of our product candidates, including AT-GAA;
- any changes in regulatory standards relating to the review of our product candidates, including AT-GAA;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales, and distribution;
- the emergence of competing technologies and other adverse market developments;
- our ability to successfully commercialize Galafold® (also referred to as "migalastat HCl") and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to manufacture or supply sufficient clinical or commercial products, including Galafold® and AT-GAA;
- our ability to obtain reimbursement for Galafold® and, if our regulatory filings are accepted and approved, AT-GAA;
- our ability to satisfy post-marketing commitments or requirements for continued regulatory approval of Galafold® and, if approved and applicable, AT-GAA;
- our ability to obtain market acceptance of Galafold® and, if our regulatory filings are accepted and approved, AT-GAA;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims, including Hatch-Waxman litigation;
- the impact of litigation that has been or may be brought against us or of litigation that we are pursuing or may pursue against others;
- the extent to which we acquire or invest in businesses, products, and technologies;

- our ability to successfully integrate our acquired products and technologies into our business, or successfully divest or license existing products and technologies from our business, including the possibility that the expected benefits of the transactions will not be fully realized by us or may take longer to realize than expected;
- our ability to establish licensing agreements, collaborations, partnerships or other similar arrangements and to obtain milestone, royalty, or other payments from any such collaborators;
- the extent to which our business could be adversely impacted by the effects of the novel coronavirus ("COVID-19") outbreak, including due to actions by us, governments, our customers, our suppliers, or other third parties to control the spread of COVID-19, or by other health epidemics or pandemics;
- the costs associated with, and our ability to comply with, emerging environmental, social and governance standards;
- our ability to accurately forecast revenue, operating expenditures, or other metrics impacting profitability
- fluctuations in foreign currency exchange rates; and
- changes in accounting standards.

In light of these risks and uncertainties, we may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly 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. Those factors and the other risk factors described herein and in documents incorporated herein by reference are not necessarily all of the important factors that could cause actual results or developments to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors also could harm our results. Our forward-looking statements do not reflect the potential impact of any future collaborations, alliances, business combinations, partnerships, strategic out-licensing of certain assets, the acquisition of preclinical-stage, clinical-stage, marketed products or platform technologies or other investments we may make. Consequently, there can be no assurance that actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, us. Given these uncertainties, investors are cautioned not to place undue reliance on such forward-looking statements.

You should read this prospectus and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. These forward-looking statements speak only, as applicable, as of the date of this prospectus, any prospectus supplement or the documents incorporated by reference therein. We undertake no obligation, and specifically decline any obligation, to publicly update or revise any forward-looking statements, even if experience or future developments make it clear that projected results expressed or implied in such statements will not be realized, except as may be required by law. Before deciding to purchase our securities, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus and in the registration statement of which this prospectus is a part.

USE OF PROCEEDS

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

PLAN OF DISTRIBUTION

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

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

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

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

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

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

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

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

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

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

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

The securities we offer may be new issues of securities and may have no established trading market. The securities may or may not be listed on a securities exchange. Underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of, or the existence of trading markets for, any of the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying

security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

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

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

GENERAL DESCRIPTION OF SECURITIES

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

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

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

DESCRIPTION OF OUR COMMON STOCK

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

As of February 24, 2022, we are authorized to issue 500,000,000 shares of common stock, $0.01 par value per share. As of February 23, 2022, we had 280,044,586 shares of common stock outstanding.

General

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

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

Transfer Agent and Registrar

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

The NASDAQ Global Market

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

DESCRIPTION OF OUR PREFERRED STOCK

We are authorized to issue up to 10,000,000 shares of preferred stock, par value $0.01 per share. As of February 24, 2022, there were no shares of our preferred stock outstanding.

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

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

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of the Company, and, if applicable, the conversion price (or how it will be calculated), the conversion period and any other terms of conversion (including any anti-dilution provisions, if any);
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated), the exchange period and any other terms of exchange (including any anti-dilution provisions, if any);
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company;
- any material limitations on issuance of any series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company; and
- any other affirmative, negative or other covenants or contractual rights which might be attendant with the specific series of preferred stock.

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

Transfer Agent and Registrar

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

DESCRIPTION OF OUR WARRANTS

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

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

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise of the warrants, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise of the warrants, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange or market;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

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

DESCRIPTION OF OUR DEBT SECURITIES

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

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

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

General

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

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

- the title of the series;
- the aggregate principal amount;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- the date or dates on which principal is payable;
- the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;
- the place or places where principal and, if applicable, premium and interest, is payable;
- the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;
- the denominations in which such debt securities may be issuable, if other than denominations of $1,000 or any integral multiple of that number;
- whether the debt securities are to be issuable in the form of certificated securities (as described below) or global securities (as described below);
- the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;
- the currency of denomination;
- the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;

- if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;
- if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;
- the provisions, if any, relating to any collateral provided for such debt securities;
- any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;
- any events of default, if not otherwise described below under "Events of Default";
- the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents
- any guarantees of the debt securities;
- the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company; and
- the terms and conditions, if any, pursuant to which the debt securities, in whole or in part, shall be defeasible.

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

Exchange and/or Conversion Rights

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

Transfer and Exchange

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

- "book-entry securities," which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or
- "certificated securities," which means that they will be represented by a certificate issued in definitive registered form.

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

Certificated Debt Securities

If you hold certificated debt securities issued under an indenture, you may transfer or exchange such debt securities in accordance with the terms of the indenture. You will not be charged a service charge for

any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Global Securities

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

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

Protection in the Event of Change of Control

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

Covenants

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

Consolidation, Merger and Sale of Assets

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

- we are the surviving entity of any such merger or consolidation or the entity formed by such merger or consolidation shall be organized under the laws of the United States of America, or any state thereof or the District of Columbia, and shall expressly assume by a supplemental indenture all of our obligations related to such debt securities; and
- immediately before and immediately after the merger or consolidation, no default or event of default shall have occurred and be continuing.

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

Defaults and Notice

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

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

- failure to make a payment of any interest on any debt security of such series when due and payable and such failure continues for a period of 30 days;
- our failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series and such failure continues for a period of 60 days;
- after written notice from the trustee or holders of 25% in the aggregate principal amount of the then-outstanding debt securities of such series; and
- certain events relating to our or our significant subsidiaries' bankruptcy, insolvency or reorganization.

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

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

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

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

Modification of the Indenture

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

Defeasance; Satisfaction and Discharge

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

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

- either (A) there shall have been canceled by the trustee under the indenture, or delivered to the trustee for cancellation, all debt securities of such series theretofore authenticated and delivered or (B) all such debt securities not theretofore delivered to the trustee for cancellation have become due and payable or will become due and payable within one year or are to be called for redemption within one year under irrevocable arrangements for the giving of notice of redemption by the trustee;
- we have irrevocably deposited or caused to be deposited with the trustee funds in an amount sufficient to pay and discharge the entire indebtedness on the debt securities not theretofore delivered to the trustee for cancellation, for principal, premium, if any, and interest to the maturity or date of redemption;
- we have paid all other sums payable by us under the indenture or deposited all other required sums with the trustee; and
- the deposit will not result in a breach or violation of, or constitute a default under, any other instrument or agreement to which we are a party or to which we are bound.

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

- we shall have irrevocably deposited with the trustee, in trust, for the purpose of making the following payments, specifically pledged as security for, and dedicated solely to, the benefit of the holders of the debt securities, (a) money, (b) U.S. or foreign government obligations which through the scheduled payment of principal and interest in respect thereof in accordance with their terms will provide, not later than the due date of any payment, money, or (c) a combination thereof, in an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal, accrued interest and premium, if any;
- there shall be no continuing default or event of default with respect to such debt securities at the time of the deposit or after giving effect thereto;
- there shall not be certain conflicting interest for purposes of the Trust Indenture Act;
- such actions shall not result in a breach or violation of, or constitute a default under, any other agreement or instrument to which we are bound;
- we shall have delivered a legal opinion relating to certain tax matters; and
- we shall have delivered a legal opinion and certain other certificates relating to the satisfaction of the required conditions.

Regarding the Trustee

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

Governing Law

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

DESCRIPTION OF OUR UNITS

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

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

General

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

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

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

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

Issuance in Series

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

DESCRIPTION OF OUR SUBSCRIPTION RIGHTS

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

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021 and the effectiveness of our internal control over financial reporting as of December 31, 2021, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

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

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

Office of the Corporate Secretary
Amicus Therapeutics, Inc.
3675 Market Street
Philadelphia, PA 19104
(215) 921-7600

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

- Our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 24, 2022;
- Our Current Reports on Form 8-K filed with the SEC on January 10, 2022 and February 24, 2022 (except for information furnished in Item 2.02 therein and all exhibits related thereto); and
- The description of our common stock contained in our registration statement on Form 8-A (File No. 001-33497) filed with the SEC on May 23, 2007, under the Exchange Act, and any amendment or report filed for the purpose of updating such description, including Exhibit 4.8 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, as filed with the SEC on March 2, 2020.

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

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

$250,000,000

Common Stock

Prospectus Supplement

Goldman Sachs & Co. LLC

November 7, 2022

Exhibit 107.1

Calculation of Filing Fee Table

424(b)(5)
(Form Type)

Amicus Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee (1)
Equity	Common Stock, $0.01 par value per share	457(o)	—	$ —	$ 250,000,000	0.00011020	$ 27,550
	Total Offering Amounts				$ 250,000,000		$ 27,550
	Total Fee Offsets						—
	Net Fee Due						$ 27,550

(1) Calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act"), based on the maximum aggregate offering price, and Rule 457(r) under the Securities Act. This "Calculation of Registration Fee" table shall be deemed to update the "Calculation of Registration Fee" table in the registrant's Registration Statement on Form S-3 (File No. 333-262987) in accordance with Rules 456(b) and 457(r) under the Securities Act.