AMICUS THERAPEUTICS INC
Form S-1/A
May 25, 2007

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As filed with the Securities and Exchange Commission on May 25, 2007
Registration No. 333-141700

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Amendment No. 3
to
Form S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

AMICUS THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**2834**	**20-0422823**
(State or Other Jurisdiction of Incorporation or Organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

6 Cedar Brook Drive
Cranbury, New Jersey 08512
(609) 662-2000
(Address, including zip code, and telephone number, including area code, of Registrant s principal executive offices)

John F. Crowley
Chief Executive Officer
Amicus Therapeutics, Inc.
6 Cedar Brook Drive
Cranbury, New Jersey 08512
(609) 662-2000
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Julio E. Vega	**Douglas A. Branch**	**Patrick O Brien**
Bingham McCutchen LLP	**Vice President, General**	**Ropes & Gray LLP**
150 Federal Street	**Counsel and Secretary**	**One International Place**
Boston, Massachusetts 02110-1726	**Amicus Therapeutics, Inc.**	**Boston, Massachusetts 02110-1726**
(617) 951-8000	**6 Cedar Brook Drive**	**(617) 951-7000**
	Cranbury, New Jersey 08512	
	(609) 662-2029	

Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the Securities Act), please check the following box. o

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

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

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

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

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

PROSPECTUS (Subject to Completion)
Issued May 25, 2007

5,000,000 Shares

Common Stock

This offering is our initial public offering of shares of our common stock. We are offering 5,000,000 shares of common stock.

We expect the initial public offering price to be between $14.00 and $16.00 per share. Currently, no public market exists for our shares. After pricing of the offering, we expect that the shares will be quoted on The NASDAQ Global Market under the symbol FOLD .

Investing in our common stock involves risks. See Risk Factors beginning on page 8.

	Per Share	Total
Public offering price	$	$
Underwriting discount	$	$
Proceeds, before expenses	$	$

The underwriters may also purchase up to an additional 750,000 shares of common stock from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus to cover over-allotments.

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

The underwriters expect to deliver the shares to purchasers on or about , 2007.

Morgan Stanley **Merrill Lynch & Co.**

JPMorgan

Lazard Capital Markets **Pacific Growth Equities, LLC**

, 2007

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock. In this prospectus, unless otherwise stated or the context otherwise requires, references to Amicus Therapeutics, Amicus, we, us, our and similar references refer to Amicus Therapeutics, In

Until , 2007, 25 days after the commencement of this offering, all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary may not contain all of the information that is important to you. Before investing in our common stock, you should read this prospectus carefully in its entirety, especially the risks of investing in shares of our common stock that we discuss in the Risk Factors section of this prospectus beginning on page 8 and our financial statements and related notes beginning on page F-1.

AMICUS THERAPEUTICS, INC.

Our Company

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule, orally-administered drugs, known as pharmacological chaperones, for the treatment of a range of human genetic diseases. Our lead products in development are Amigal for Fabry disease, Plicera for Gaucher disease and AT2220 for Pompe disease. Fabry, Gaucher and Pompe are relatively rare disorders but represent substantial commercial markets due to the severity of the symptoms and the chronic nature of the diseases. The worldwide net product sales for the five approved therapeutics to treat Fabry, Gaucher and Pompe disease totaled more than $1.5 billion in 2006, as publicly reported by companies that market these therapeutics. We hold worldwide commercialization rights to Amigal, Plicera and AT2220 and we intend to establish a commercial infrastructure and targeted sales force to market some or all of our products. Currently, none of our product candidates are approved for commercial sale or have generated any revenue from commercial sales.

We have completed enrollment of our Phase II clinical trials of Amigal, and have obtained initial results in the first eleven patients who have completed at least 12 weeks of treatment. These initial results suggest that treatment with Amigal causes an increase in the activity of -galactosidase A, or -GAL, the enzyme deficient in Fabry disease. We believe this increase is likely to be clinically meaningful for a wide range of Fabry patients. Data for the three patients from whom we have kidney biopsies suggest that the increased level of -GAL that occurs after treatment with Amigal may result in a decrease of globotriaosylceramide, or GL-3. GL-3 is the substrate that accumulates in the cells of patients with Fabry disease and is believed to cause the majority of disease symptoms. Reduction of the level of GL-3 in a specific cell type of the kidney was the basis of prior regulatory approval by the FDA of an enzyme replacement therapy for the treatment of Fabry disease. We expect to complete our Phase II clinical trials of Amigal by the end of 2007.

We are currently conducting two Phase II clinical trials of Plicera in Type I Gaucher patients. We expect to obtain preliminary results from the first of these Phase II clinical trials by the end of 2007. We are currently conducting Phase I trials of AT2220 for Pompe disease and expect to initiate a Phase II clinical trial by the end of 2007.

Certain human diseases result from mutations in specific genes that, in many cases, lead to the production of proteins with reduced stability. Proteins with such mutations may not fold into their correct three-dimensional shape and are generally referred to as misfolded proteins. The cell ensures that proteins are folded into their correct shape before they can move from where they are made, the endoplasmic reticulum, or ER, to the appropriate destination in the cell, a process referred to as protein trafficking. Proteins that do not achieve their correct shape are often eliminated by the cell, resulting in reduced biological activity that can lead to impaired cellular function and ultimately to disease. In certain instances, misfolded proteins can accumulate in the ER instead of being eliminated. This accumulation of misfolded proteins may lead to various types of stress on cells, which may also contribute to cellular dysfunction and disease.

Our novel approach to the treatment of human genetic diseases consists of using pharmacological chaperones that selectively bind to the target protein, increasing the stability of the protein and helping it fold into the correct three-dimensional shape. This allows proper trafficking of the protein, thereby increasing protein activity, improving cellular function and potentially reducing cell stress.

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The current standard of treatment for Fabry, Gaucher and Pompe is enzyme replacement therapy. This therapy compensates for the reduced level of activity of specialized proteins called enzymes through regular infusions of recombinant enzyme. Instead of adding enzyme from an external source by intravenous infusion, our approach uses small-molecule, orally-administered pharmacological chaperones to restore the function of the enzyme that is already made by the patient s own body. We believe our product candidates may have advantages relative to enzyme replacement therapy relating to biodistribution and ease of use, potentially improving treatment of these diseases. In addition, we believe our technology is broadly applicable to other diseases for which protein stabilization and improved folding may be beneficial, including certain types of neurological disease, metabolic disease, cardiovascular disease and cancer.

Our Lead Programs

Our three most advanced product development programs target lysosomal storage disorders, which are chronic genetic diseases that frequently result in severe symptoms. Each of these disorders results from the deficiency of a single enzyme.

Amigal for Fabry disease. We are developing Amigal for the treatment of patients with Fabry disease, which commonly causes kidney failure and increased risk of heart attack and stroke. We are currently conducting multiple Phase II clinical trials of Amigal. We expect to complete our Phase II trials of Amigal by the end of 2007.

Plicera for Gaucher disease. We are developing Plicera for the treatment of Gaucher disease, which commonly causes an enlarged liver and spleen, abnormally low levels of red blood cells and platelets, and skeletal complications. Some patients also present with neurological complications. We are currently conducting two Phase II clinical trials of Plicera in Type I Gaucher patients. We expect to obtain preliminary results from the first of these two trials by the end of 2007.

AT2220 for Pompe disease. We are developing AT2220 for the treatment of Pompe disease, which commonly causes progressive muscle weakness, particularly affecting breathing, mobility and heart function. We are currently conducting Phase I clinical trials of AT2220 and expect to initiate a Phase II clinical trial by the end of 2007.

Preliminary Data from our Ongoing Phase II Clinical Trials in Fabry Disease

We have completed enrollment of our four Phase II clinical trials of Amigal and have obtained initial results for the first eleven patients that have completed at least 12 weeks of treatment. Each of these patients has been treated with various doses and regimens of Amigal for various periods of time in accordance with the Phase II protocols. Amigal has been well-tolerated to date with no reported drug-related serious, adverse events.

The eleven patients represent ten different genetic mutations and have baseline levels of -GAL in white blood cells of between 0% and 30% of normal. An increase in -GAL enzyme levels in white blood cells has been observed in ten out of the eleven patients. These initial results suggest that treatment with Amigal causes an increase in the level of -GAL, the enzyme deficient in Fabry disease, in a wide range of Fabry patients. In addition, we believe that this increase is likely to be therapeutically meaningful because it is generally believed that even small increases in lysosomal enzyme levels may have clinical benefits.

GL-3, the lipid substrate broken down by -GAL in the lysosome, accumulates in the cells of patients with Fabry disease and is believed to be the cause of the majority of disease symptoms. Reduction of the level of GL-3 in a specific cell type of the kidney was the basis of prior regulatory approval by the FDA of an enzyme replacement

therapy for the treatment of Fabry disease. Kidney GL-3 levels are available for three patients and were assessed by an independent expert using light and electron microscopy. A decrease in GL-3 was observed in multiple cell types of the kidney of one patient after 12 weeks of treatment. A second patient showed a decrease of GL-3 levels in the same kidney cell types after 24 weeks of treatment, but these decreases were not independently conclusive because of the patient s lower levels of GL-3 at baseline. An increase in the level of -GAL in white blood cells was observed in both of these two patients after treatment

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with Amigal. A third patient showed an increase in GL-3 levels in some cell types of the kidney and no change or a decrease in others after 12 weeks of treatment. Of the eleven patients who have completed at least 12 weeks of treatment to date in our ongoing clinical trials, this is the one patient who did not show an increase in the level of -GAL in white blood cells after treatment with Amigal.

Amigal has been well-tolerated to date with no reported drug-related serious adverse events. Four patients have been on Amigal for over a year. Adverse events were mostly mild and reported by the investigators as unlikely to be related to Amigal. One patient with a history of hypertension discontinued study treatment due to increased blood pressure, which was reported by the investigator as possibly related to the study drug.

The results of our Phase II clinical trials to date do not necessarily predict final results for our Phase II clinical trials. The results from additional patients in our ongoing Phase II clinical studies or additional data from these first eleven patients may cause the results of our Phase II studies to differ from or be less favorable than the preliminary results presented above. We cannot guarantee that our Phase II clinical studies will ultimately be successful.

Data from our Phase I Clinical Trials in Gaucher Disease

We recently completed two double-blind, placebo-controlled, dose escalation Phase I clinical trials in healthy volunteers. These trials were designed to evaluate the safety, tolerability and pharmacokinetics of Plicera. In the first study, 36 subjects received a single dose of one of five dose levels of Plicera. This was followed by a multiple-dose study in which 18 subjects received one of three dose levels of Plicera once daily for 7 consecutive days. The data from our Phase I clinical trials in healthy volunteers showed that Plicera was generally safe and well tolerated at all doses. There were no serious adverse events and no subjects withdrew or discontinued due to an adverse event. The trials also demonstrated that Plicera has good oral bioavailability, and linear pharmacokinetics with a terminal half-life in plasma of approximately fourteen hours. Also, the data from the multiple-dose Phase I clinical trial showed a statistically significant, dose-related increase in -glucocerebrosidase, or GCase, levels in the white blood cells of normal, healthy volunteers who received oral administration of Plicera for seven days. GCase is the enzyme deficient in Gaucher disease.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the discovery, development and commercialization of pharmacological chaperone therapies for the treatment of a wide range of human diseases. The introduction of pharmacological chaperones as a treatment option has the potential to address significant unmet medical needs and improve the quality of life for patients.

To achieve this goal, we intend to:

- focus our initial efforts on developing pharmacological chaperones for severe genetic diseases called lysosomal storage disorders;
- rapidly advance our lead programs;
- leverage our proprietary approach to the discovery and development of additional small molecules; and
- build a targeted sales and marketing infrastructure.

Our success in achieving our goal, however, depends in part on the risks and uncertainties described in this prospectus in the section entitled Risk Factors, including, without limitation, those relating to our ability to conduct preclinical

and clinical trials that demonstrate safety and efficacy of our product candidates, our ability to obtain regulatory approvals and our ability to attract and retain effective sales and marketing personnel.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. We discuss these risks more fully in the Risk Factors section of this prospectus immediately following this prospectus summary. We have a limited operating history and have not yet commercialized any

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products. We have incurred substantial operating losses in each year since inception. Our net loss attributable to common stockholders was $65.9 million for the year ended December 31, 2006 and $9.7 million for the three months ended March 31, 2007. As of March 31, 2007, we had an accumulated deficit of $93.4 million. We expect to incur significant and increasing net losses for at least the next several years. It is uncertain whether any of our product candidates under development will become effective treatments. All of our product candidates are undergoing clinical trials or are in earlier stages of development, and failure in the development of new drugs is common and can occur at any stage of development. None of our product candidates has received regulatory approval for commercialization, and we do not expect that any drugs resulting from our research and development efforts will be commercially available for a number of years, if at all. We may never generate any revenues or achieve profitability.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on February 4, 2002. Our principal executive offices are located at 6 Cedar Brook Drive, Cranbury, New Jersey 08512, and our telephone number is (609) 662-2000. Our website address is *www.amicustherapeutics.com*. The information on, or that can be accessed through, our website is not part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

We have filed applications to register certain trademarks in the United States and abroad, including AMICUS™, AMICUS THERAPEUTICS™ (and design), AMIGAL™ and PLICERA™. Fabrazyme®, Cerezyme®, Myozyme®, Replagal™ and Zavesca® are the property of their respective owners.

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THE OFFERING

Common stock we are offering	5,000,000 shares
Common stock to be outstanding after this offering	22,234,426 shares
Over-allotment option	750,000 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $67.9 million, or approximately $78.3 million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of $15.00 per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect to use most of the net proceeds from this offering to fund clinical trial activities and preclinical research and development activities, and the balance for other general corporate purposes. See Use of Proceeds.
Risk factors	You should read the Risk Factors section of this prospectus for a discussion of the factors to consider carefully before deciding to purchase any shares of our common stock.
Proposed NASDAQ Global Market symbol	FOLD

The number of shares of common stock to be outstanding immediately after the offering is based on 1,162,502 shares of common stock outstanding as of April 25, 2007 and the issuance of 16,071,924 shares of common stock issuable upon the automatic conversion of all shares of our redeemable convertible preferred stock outstanding upon the closing of this offering. The number of shares of common stock to be outstanding after this offering excludes:

- 2,549,950 shares of common stock issuable upon the exercise of stock options outstanding as of April 25, 2007, with a weighted average exercise price of $7.56 per share;
- 5,333 shares of common stock issuable upon exercise of a warrant to purchase common stock at an exercise price of $5.63 per share;
- shares of common stock issuable in connection with the exercise of outstanding warrants to purchase shares of series B redeemable convertible preferred stock. Upon the closing of this offering, these warrants will be automatically exercised and the shares of series B redeemable convertible preferred stock automatically converted into between 34,309 and 59,674 shares of common stock, depending on whether such warrants are exercised for cash or on a net issue basis. In the case of exercises on a net issue basis, we have assumed a price to the public of $15.00 per share, which is the mid-point of the price range as set forth on the cover page of this prospectus;
- an aggregate of 966,667 shares of common stock reserved for future issuance under our 2007 equity incentive plan as of the closing of this offering;
- an aggregate of 200,000 shares of common stock reserved for future issuance under our 2007 director option plan as of the closing of this offering; and
- an aggregate of 200,000 shares of common stock reserved for future issuance under our 2007 employee stock purchase plan as of the closing of this offering.

Unless otherwise noted, all information in this prospectus assumes:

- no exercise of the outstanding options or warrants to purchase capital stock described above;
- no exercise by the underwriters of their option to purchase shares of common stock to cover over-allotments; and
- a 1-for-7.5 reverse split of our common stock and preferred stock effected on May 24, 2007.

Entities affiliated with New Enterprise Associates have indicated an interest in purchasing shares of our common stock in this offering at the initial public offering price. Because these indications of interest are not binding

agreements or commitments to purchase, these entities may elect not to purchase any shares in this offering.

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SUMMARY FINANCIAL DATA

The following is a summary of our financial data. You should read the summary financial data together with our financial statements and the related notes appearing at the end of this prospectus, and Management s Discussion and Analysis of Financial Condition and Results of Operations and other financial information appearing elsewhere in this prospectus.

The pro forma net loss and pro forma net loss per share data for the year end December 31, 2006, and the three month period ended March 31, 2007, give effect, as of the beginning of each such period, to the issuance in March 2007 of 1,976,527 shares of our series D redeemable convertible preferred stock, and the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into 16,071,924 shares of common stock upon the closing of this offering. The pro forma balance sheet data set forth below also give effect, as of March 31, 2007, to the foregoing events and the elimination of our warrant liability.

The pro forma as adjusted balance sheet data gives further effect to our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	Year Ended December 31,			Three Months Ended March 31,		Period from February 4, 2002 (Inception) to March 31, 2007
	2004	2005	2006	2006	2007	
				(unaudited)	(unaudited)	(unaudited)
	(in thousands, except shares and per share data)					
Statement of Operations Data:						
Operating expenses:						
Research and development	$ 6,301	$ 13,652	$ 33,630	$ 6,028	$ 7,085	$ 65,889
General and administrative	2,081	6,877	12,277	1,900	2,850	25,642
Impairment of leasehold improvements						1,030
Depreciation and amortization	146	303	952	199	297	1,854
In-process research and development						418
Total operating expenses	8,528	20,831	46,859	8,127	10,232	94,833
Loss from operations	(8,528)	(20,831)	(46,859)	(8,127)	(10,232)	(94,833)
Other income (expenses):						
Interest income	190	610	1,991	238	693	3,501
Interest expense	(550)	(82)	(273)	(52)	(92)	(1,175)
	(2)	(280)	(22)	(343)	(64)	(368)

Change in fair value of warrant liability						
Other expense			(1,182)	(3)		(1,182)
Loss before tax benefit	(8,890)	(20,584)	(46,345)	(8,287)	(9,695)	(94,057)
Income tax benefit	83	612				695
Net loss	(8,807)	(19,972)	(46,345)	(8,287)	(9,695)	(93,362)
Deemed dividend			(19,424)			(19,424)
Preferred stock accretion	(125)	(139)	(159)	(41)	(41)	(492)
Net loss attributable to common stockholders	$ (8,932)	$ (20,111)	$ (65,928)	$ (8,328)	$ (9,736)	$ (113,278)

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	Year Ended December 31,			Three Months Ended March 31,	Period from February 4, 2002 (Inception) to March 31,
	2004	2005	2006	2006	