AMICUS THERAPEUTICS INC
Form S-1
March 30, 2007

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As filed with the Securities and Exchange Commission on March 30, 2007.
Registration No. 333-

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

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 ___

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common Stock, $0.01 par value per share	$86,250,000	$2,647.88

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933.

(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

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 , 2007

Shares

Common Stock

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

We expect the initial public offering price to be between $ and $ 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 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 were 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.

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 alpha 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 two 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.

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

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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 two 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. These initial results are consistent with the GL-3 reductions observed after oral administration of Amigal to mice that produce a form of human -GAL found in some Fabry patients.

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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 demonstrate 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 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. As of December 31, 2006, we had an accumulated deficit of $83.7 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

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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	shares
Common stock to be outstanding after this offering	shares
Over-allotment option	shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $ million, or approximately $ million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of $ 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 7,452,959 shares of common stock outstanding as of March 15, 2007, and gives effect to the automatic exercise for cash upon the closing of this offering of outstanding warrants to purchase 447,583 shares of series B redeemable convertible preferred stock, and the issuance of 120,987,335 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:

- 14,064,554 shares of common stock issuable upon the exercise of stock options outstanding as of March 15, 2007, with a weighted average exercise price of $0.57 per share;
- 40,000 shares of common stock issuable upon exercise of a warrant to purchase common stock at an exercise price of $0.75 per share; and
- an aggregate of shares of common stock reserved for future issuance under our 2007 equity incentive plan as of the closing of this offering.

Unless otherwise noted, all information in this prospectus assumes:

- no exercise of the outstanding options or warrant to purchase common stock described above; and
- no exercise by the underwriters of their option to purchase shares of common stock to cover over-allotments.

We expect to complete a one-for- reverse split of our common stock before completion of this offering. All share numbers will be adjusted to give effect to this reverse stock split.

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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 ended December 31, 2006, give effect, as of the beginning of such period, to the issuance on March 12, 2007 of 14,823,985 shares of our series D redeemable convertible preferred stock, the automatic exercise for cash upon the closing of this offering of all outstanding warrants to purchase 447,583 shares of our series B redeemable convertible preferred stock, and the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into 120,987,335 shares of common stock upon the closing of this offering. The pro forma balance sheet data set forth below also give effect, as of December 31, 2006, to the foregoing events.

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 $ 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,			Period from February 4, 2002 (Inception) to December 31,
	2004	2005	2006	2006
	(in thousands, except shares and per share data)			
Statement of Operations Data:				
Operating expenses:				
Research and development	$ 6,301	$ 13,652	$ 33,630	$ 58,804
General and administrative	2,081	6,877	12,277	22,792
Impairment of leasehold improvements				1,030
Depreciation and amortization	146	303	952	1,557
In-process research and development				418
Total operating expenses	8,528	20,831	46,859	84,601
Loss from operations	(8,528)	(20,831)	(46,859)	(84,601)
Other income (expenses):				
Interest income	190	610	1,991	2,808
Interest expense	(550)	(82)	(273)	(1,083)
Change in fair value of warrant liability	(2)	(280)	(22)	(304)
Other expense			(1,182)	(1,182)
Loss before tax benefit	(8,890)	(20,584)	(46,345)	(84,362)
Income tax benefit	83	612		695

Net loss	(8,807)	(19,972)	(46,345)	(83,667)
Deemed dividend			(19,424)	(19,424)
Preferred stock accretion	(125)	(139)	(159)	(451)
Net loss attributable to common stockholders	$ (8,932)	$ (20,111)	$ (65,928)	$ (103,543)
Net loss attributable to common stockholders per common shares basic and diluted	$ (3.87)	$ (6.54)	$ (11.94)	
Weighted-average common shares outstanding basic and diluted	2,306,541	3,076,649	5,519,749	
Unaudited pro forma net loss			$ (46,345)	
Unaudited pro forma basic and diluted net loss per share			$ (0.37)	
Unaudited shares used to compute pro forma basic and diluted net loss per share			126,507,084	

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	As of December 31, 2006		
	Actual	Pro Forma	Pro Forma as Adjusted
		(unaudited)	
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents and marketable securities	$ 54,699	$ 79,133	
Working capital	44,814	69,247	
Total assets	59,646	84,079	
Total liabilities	13,071	12,463	
Redeemable convertible preferred stock[(1)]	124,091		
Deficit accumulated during the development stage	(83,667)	(83,667)	
Total stockholders (deficiency) equity	(77,515)	71,616	

(1) In March 2007, we issued additional 14,823,985 shares of series D redeemable convertible preferred stock for proceeds of $24.1 million.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information included in this prospectus, including the financial statements and related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, they would materially harm our business, prospects, financial condition and results of operations. In this event, the market price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since our inception. We currently do not, and since inception never have had, any products available for commercial sale. We expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss attributable to common stockholders was $65.9 million for the year ended December 31, 2006. As of December 31, 2006, we had an accumulated deficit of $83.7 million. To date, we have financed our operations primarily through private placements of our redeemable convertible preferred stock. We have devoted substantially all of our efforts to research and development, including our preclinical development activities and clinical trials. We have not completed development of any drugs. We expect to continue to incur significant and increasing operating losses for at least the next several years and we are unable to predict the extent of any future losses. We anticipate that our expenses will increase substantially as we:

- continue our ongoing Phase II clinical trials of Amigal for the treatment of Fabry disease and potentially conduct later-stage clinical trials of Amigal;
- continue our ongoing Phase II clinical trials of Plicera for the treatment of Gaucher disease and potentially conduct later-stage clinical trials of Plicera;
- continue our ongoing Phase I clinical trials of AT2220 for the treatment of Pompe disease and potentially conduct later-stage clinical trials of AT2220;
- continue the research and development of additional product candidates;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- establish a sales and marketing infrastructure to commercialize products for which we may obtain regulatory approval; and
- add operational, financial and management information systems and personnel, including personnel to support our product development efforts and our obligations as a public company.

To become and remain profitable, we must succeed in developing and commercializing drugs with significant market potential. This will require us to be successful in a range of challenging activities, including the discovery of product candidates, successful completion of preclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of these activities. We may never succeed in

these activities and may never generate revenues that are large enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become or remain profitable could depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the market price of our common stock would also cause you to lose a part or all of your investment.

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We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we continue our Phase II clinical trials of Amigal, our Phase II clinical trials of Plicera and our Phase I clinical trials of AT2220, and for any later-stage clinical trials of our product candidates. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales and marketing, securing commercial quantities of product from our manufacturers and product distribution. We currently have no additional commitments or arrangements for any additional financing to fund the research and development and commercial launch of our product candidates.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents and marketable securities, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements until at least . Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to reduce or eliminate research development programs or commercial efforts.

Our future capital requirements will depend on many factors, including:

- the progress and results of our clinical trials of Amigal, Plicera and AT2220;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the number and development requirements of other product candidates that we pursue;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the emergence of competing technologies and other adverse market developments;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property related claims;
- the extent to which we acquire or invest in businesses, products and technologies; and
- our ability to establish collaborations and obtain milestone, royalty or other payments from any such collaborators.

Any additional funds that we obtain may not be on terms favorable to us or our stockholders or may require us to relinquish valuable rights.

Until such time, if ever, as we generate product revenue to finance our operations, we expect to finance our cash needs through public or private equity offerings and debt financings, corporate collaboration and licensing arrangements and grants from patient advocacy groups, foundations and government agencies. If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may include rights that are senior to the holders of our common stock.

Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences, which are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us or our stockholders.

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Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a development stage company. We commenced operations in February 2002. Our operations to date have been limited to organizing and staffing our company, acquiring and developing our technology and undertaking preclinical studies and limited clinical trials of our most advanced product candidates. We have not yet demonstrated our ability to successfully complete large-scale, clinical trials, obtain regulatory approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. If we are successful in obtaining marketing approval for any of our lead product candidates, we will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks Related to the Development and Commercialization of Our Product Candidates

We depend heavily on the success of our most advanced product candidates, Amigal, Plicera and AT2220. All of our product candidates are still in either preclinical or clinical development. Clinical trials of our product candidates may not be successful. If we are unable to commercialize Amigal, Plicera or AT2220, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of our most advanced product candidates, Amigal, Plicera and AT2220. Our ability to generate product revenue, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and commercialization of these product candidates. The successful commercialization of our product candidates will depend on several factors, including the following:

- obtaining supplies of Amigal, Plicera and AT2220 for completion of our clinical trials on a timely basis;
- successful completion of preclinical studies and clinical trials;
- obtaining marketing approvals from the United States Food and Drug Administration, or FDA, and similar regulatory authorities outside the United States;
- establishing commercial-scale manufacturing arrangements with third party manufacturers whose manufacturing facilities are operated in compliance with current good manufacturing practice, or cGMP, regulations;
- launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third party payors;
- competition from other companies and their therapies;
- successful protection of our intellectual property rights from competing products in the United States and abroad; and

a continued acceptable safety and efficacy profile of our product candidates following approval.

If the market opportunities for our product candidates are smaller than we believe they are, then our revenues may be adversely affected and our business may suffer.

Each of the diseases that our product candidates are being developed to address is relatively rare. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates.

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Currently, most reported estimates of the prevalence of these diseases are based on studies of small subsets of the population of specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the broader world population. In addition, as new studies are performed the estimated prevalence of these diseases may change. In fact, as a result of some recent studies, we believe that previously reported studies do not accurately account for the prevalence of Fabry disease and that the prevalence of Fabry disease could be many times higher than previously reported. There can be no assurance that the prevalence of Fabry disease, Gaucher disease or Pompe disease in the study populations, particularly in these newer studies, accurately reflect the prevalence of these diseases in the broader world population.

We estimate the number of potential patients in the broader world population who have those diseases and may respond to treatment with our product candidates by further extrapolating estimates of the prevalence of specific types of genetic mutations giving rise to these diseases. For example, we base our estimate of the percentage of Fabry patients who may respond to treatment with Amigal on the frequency of missense and other similar mutations that cause Fabry disease reported in the Human Gene Mutation Database. As a result of recent studies that estimate that the prevalence of Fabry disease could be many times higher than previously reported, we believe that the number of patients diagnosed with Fabry disease will increase and estimate that the number of Fabry patients who may benefit from the use of Amigal is significantly higher than some previously reported estimates of Fabry disease generally. If our estimates of the prevalence of Fabry disease, Gaucher disease or Pompe disease or of the number of patients who may benefit from treatment with our product candidates prove to be incorrect, the market opportunities for our product candidates may be smaller than we believe they are, our prospects for generating revenue may be adversely affected and our business may suffer.

Initial results from a clinical trial do not ensure that the trial will be successful and success in early stage clinical trials does not ensure success in later-stage clinical trials.

We will only obtain regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable non-United States regulatory authority, in well-designed and conducted clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain results. A failure of one or more of our clinical trials may occur at any stage of testing. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA.

Our efforts to develop all of our product candidates are at an early stage. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and initial results from a clinical trial do not necessarily predict final results. For example, results to date in our Phase II clinical trials of Amigal for the treatment of Fabry disease caused by missense mutations are based on data from only eleven patients and the kidney biopsy data are based on data from only two patients. Additional data from these eleven patients and data from additional patients in these trials may be less favorable than the results to date. No definitive conclusions as to the safety or efficacy of any drug candidate can be drawn from such a small number of patients. We cannot assure you that these trials will ultimately be successful.

Patients may not be compliant with their dosing regimen or trial protocols or they may withdraw from the study at any time for any reason. We note that a patient in the ongoing Phase II clinical trials for Amigal for the treatment of Fabry disease elected to withdraw from the study. This patient had a history of hypertension and discontinued study treatment due to increased blood pressure, which was reported by the investigator as possibly related to the study drug.

Even if our early stage clinical trials are successful, we will need to conduct additional clinical trials with larger numbers of patients receiving the drug for longer periods for all of our product candidates before we are able to seek approvals to market and sell these product candidates from the FDA and regulatory authorities outside the United States. In addition, each of our product candidates is based on our pharmacological chaperone technology. To date, we are not aware that any product based on chaperone technology has been approved by the FDA. As a result, we cannot be sure what endpoints the FDA will require us to measure in later-stage clinical trials of our product candidates. We are aware that the currently available enzyme

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replacement therapy for the treatment of Fabry disease was approved by the FDA based on an endpoint measuring GL-3 levels in a specific type of kidney cell. We cannot be certain that the FDA will permit the use of this endpoint in our Phase III trials of Amigal. If the FDA requires different endpoints than the endpoints we anticipate using, it may be more difficult for us to obtain, or we may be delayed in obtaining, FDA approval of our product candidates. If we are not successful in commercializing any of our lead product candidates, or are significantly delayed in doing so, our business will be materially harmed.

We have limited experience in conducting and managing the preclinical development activities and clinical trials necessary to obtain regulatory approvals, including approval by the FDA.

We have limited experience in conducting and managing the preclinical development activities and clinical trials necessary to obtain regulatory approvals, including approval by the FDA. To date, we have only three lead product candidates: Amigal, Plicera and AT2220. We have not obtained regulatory approval nor commercialized any of these or any other product candidates. We are currently conducting Phase II clinical trials for Amigal and Plicera and a Phase I clinical trial for AT2220 but have not yet initiated a Phase III clinical trial, or even completed a Phase II clinical trial, for any of our product candidates. Our limited experience might prevent us from successfully designing or implementing a clinical trial. We have limited experience in conducting and managing the application process necessary to obtain regulatory approvals and we might not be able to demonstrate that our product candidates meet the appropriate standards for regulatory approval. If we are not successful in conducting and managing our preclinical development activities or clinical trials or obtaining regulatory approvals, we might not be able to commercialize our lead product candidates, or might be significantly delayed in doing so, which will materially harm our business.

We may find it difficult to enroll patients in our clinical trials.

Each of the diseases that our lead product candidates are intended to treat is relatively rare and we expect only a subset of the patients with these diseases to be eligible for our clinical trials. Given that each of our product candidates is in the early stages of required testing, we may not be able to initiate or continue clinical trials for each or all of our product candidates if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other non-United States regulatory agencies. The requirements of our clinical testing mandates that a patient cannot be involved in another clinical trial for the same indication. We are aware that our competitors have ongoing clinical trials for products that are competitive with our product candidates and patients who would otherwise be eligible for our clinical trials may be involved in such testing, rendering them unavailable for testing of our product candidates. Additionally, many patients with Fabry disease, Gaucher disease and Pompe disease may already be receiving existing therapies, such as enzyme replacement therapy, which would render them ineligible for our current clinical trials if they are not willing to stop receiving such therapies. Further, if we are required to include patients in our clinical trials who have never received enzyme replacement therapy, we may experience yet further difficulty and delay enrolling patients in our trials. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

If our preclinical studies do not produce positive results, if our clinical trials are delayed or if serious side effects are identified during drug development, we may experience delays, incur additional costs and ultimately be unable to commercialize our product candidates.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct, at our own expense, extensive preclinical tests to demonstrate the safety of our product candidates in animals, and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, and can take many years to complete. A failure of one or more of our preclinical studies or clinical trials can occur at any stage of testing. We may experience

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numerous unforeseen events during, or as a result of, preclinical testing and the clinical trial process that could delay or prevent our ability to obtain regulatory approval or commercialize our product candidates, including:

- our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials or we may abandon projects that we expect to be promising;
- regulators or institutional review boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- conditions imposed on us by the FDA or any non-United States regulatory authority regarding the scope or design of our clinical trials or may require us to resubmit our clinical trial protocols to institutional review boards for re-inspection due to changes in the regulatory environment;
- the number of patients required for our clinical trials may be larger than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate;
- our third party contractors or clinical investigators may fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner;
- we might have to suspend or terminate one or more of our clinical trials if we, the regulators or the institutional review boards determine that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of our clinical trials may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate or we may not be able to reach agreements on acceptable terms with prospective clinical research organizations; and
- the effects of our product candidates may not be the desired effects or may include undesirable side effects or the product candidates may have other unexpected characteristics.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete our clinical trials or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining, or may not be able to obtain, marketing approval for one or more of our product candidates;
- obtain approval for indications that are not as broad as intended or entirely different than those indications for which we sought approval; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or approvals. We do not know whether any preclinical tests or clinical trials will be initiated as planned, will need to be restructured or will be

completed on schedule, if at all. Significant preclinical or clinical trial delays also could shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. Such delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or product candidates.

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The commercial success of any product candidates that we may develop, including Amigal, Plicera and AT2220, will depend upon the degree of market acceptance by physicians, patients, third party payors and others in the medical community.

Any products that we bring to the market, including Amigal, Plicera and AT2220, if they receive marketing approval, may not gain market acceptance by physicians, patients, third party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the prevalence and severity of any side effects, including any limitations or warnings contained in a product s approved labeling;
- the efficacy and potential advantages over alternative treatments;
- the pricing of our product candidates;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third party insurance coverage or reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical trials, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors.

If we are unable to obtain adequate reimbursement from governments or third party payors for any products that we may develop or if we are unable to obtain acceptable prices for those products, our prospects for generating revenue and achieving profitability will suffer.

Our prospects for generating revenue and achieving profitability will depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third party payors, both in the United States and in other markets. Reimbursement by a third party payor may depend upon a number of factors, including the third party payor s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining reimbursement approval for a product from each government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to each payor. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payors satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payor determines that a product is eligible for reimbursement, the payor may impose coverage limitations

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that preclude payment for some uses that are approved by the FDA or non-United States regulatory authorities. In addition, there is a risk that full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. A primary trend in the United States healthcare industry and elsewhere is toward cost containment. We expect recent changes in the Medicare program and increasing emphasis on managed care to continue to put pressure on pharmaceutical product pricing. For example, the Medicare Prescription Drug Improvement and Modernization Act of 2003 provides a new Medicare prescription drug benefit that began in 2006 and mandates other reforms. While we cannot predict the full outcome of the implementation of this legislation, it is possible that the new Medicare prescription drug benefit, which will be managed by private health insurers and other managed care organizations, will result in additional government reimbursement for prescription drugs, which may make some prescription drugs more affordable but may further exacerbate industry wide pressure to reduce prescription drug prices. If one or more of our product candidates reaches commercialization, such changes may have a significant impact on our ability to set a price we believe is fair for our products and may affect our ability to generate revenue and achieve or maintain profitability.

Governments outside the United States tend to impose strict price controls and reimbursement approval policies, which may adversely affect our prospects for generating revenue.

In some countries, particularly European Union countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time (6 to 12 months or longer) after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our prospects for generating revenue, if any, could be adversely affected and our business may suffer.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate product revenue.

At present, we have no sales or marketing personnel. In order to commercialize any of our product candidates, we must either acquire or internally develop sales, marketing and distribution capabilities, or enter into collaborations with partners to perform these services for us. We may not be able to establish sales and distribution partnerships on acceptable terms or at all, and if we do enter into a distribution arrangement, our success will be dependent upon the performance of our partner.

In the event that we attempt to acquire or develop our own in-house sales, marketing and distribution capabilities, factors that may inhibit our efforts to commercialize our products without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage against companies with broader product lines;
- unforeseen costs associated with creating our own sales and marketing team or with entering into a partnering agreement with an independent sales and marketing organization; and

efforts by our competitors to commercialize products at or about the time when our product candidates would be coming to market.

We may co-promote our product candidates in various markets with pharmaceutical and biotechnology companies in instances where we believe that a larger sales and marketing presence will expand the market or

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accelerate penetration. If we do enter into arrangements with third parties to perform sales and marketing services, our product revenues will be lower than if we directly sold and marketed our products and any revenues received under such arrangements will depend on the skills and efforts of others.

We may not be successful in entering into distribution arrangements and marketing alliances with third parties. Our failure to enter into these arrangements on favorable terms could delay or impair our ability to commercialize our product candidates and could increase our costs of commercialization. Dependence on distribution arrangements and marketing alliances to commercialize our product candidates will subject us to a number of risks, including:

- we may not be able to control the amount and timing of resources that our distributors may devote to the commercialization of our product candidates;
- our distributors may experience financial difficulties;
- business combinations or significant changes in a distributor s business strategy may also adversely affect a distributor s willingness or ability to complete its obligations under any arrangement; and
- these arrangements are often terminated or allowed to expire, which could interrupt the marketing and sales of a product and decrease our revenue.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop and which are approved for sale. We may be exposed to product liability claims and product recalls, including those which may arise from misuse or malfunction of, or design flaws in, such products, whether or not such problems directly relate to the products and services we have provided. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- damage to our reputation;
- regulatory investigations that could require costly recalls or product modifications;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- substantial monetary awards to trial participants or patients, including awards that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available, and would damage our ability to obtain liability insurance at reasonable costs, or at all, in the future;
- loss of revenue;

the diversion of management s attention from managing our business; and

the inability to commercialize any products that we may develop.

We have liability insurance policies for our clinical trials in the geographies in which we are conducting trials. The aggregate annual limit of coverage amount under these policies expressed in United States dollars is approximately $31.4 million, and these policies are also subject to per claim deductibles. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost and we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may

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arise. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or a series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our available cash and adversely affect our business.

We face substantial competition which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drugs is highly competitive and competition is expected to increase. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. For example, several large pharmaceutical and biotechnology companies currently market and sell products for the treatment of Fabry disease. These products include Genzyme Corporation s Fabrazyme and Shire PLC s Replagal. In addition, Genzyme Corporation and Actelion, Ltd. market and sell Cerezyme and Zavesca, respectively, for the treatment of Gaucher disease, and Genzyme Corporation markets and sells Myozyme for the treatment of Pompe disease. We are also aware of other enzyme replacement and substrate reduction therapies in development by third parties.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or noncompetitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. We may also face competition from off-label use of other approved therapies. There can be no assurance that developments by others that will not render our product candidates obsolete or noncompetitive either during the research phase or once the products reach commercialization.

We believe that many competitors, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies, are attempting to develop therapies for many of our target indications.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, prosecuting intellectual property rights and marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs or advantageous to our business. In addition, if we obtain regulatory approvals for our products, manufacturing efficiency and marketing capabilities are likely to be significant competitive factors. We currently have no commercial manufacturing capability, sales force or marketing infrastructure. Further, many of our competitors have substantial resources and expertise in conducting collaborative arrangements, sourcing in-licensing arrangements and acquiring new business lines or businesses that are greater than our own.

Our business activities involve the use of hazardous materials, which require compliance with environmental and occupational safety laws regulating the use of such materials. If we violate these laws, we could be subject to significant fines, liabilities or other adverse consequences.

Our research and development programs involve the controlled use of hazardous materials, including microbial agents, corrosive, explosive and flammable chemicals and other hazardous compounds in addition to certain biological hazardous waste. Ultimately, the activities of our third party product manufacturers when a product candidate reaches commercialization will also require the use of hazardous materials. Accordingly, we are subject to federal, state and local laws governing the use, handling and disposal of these materials. Although we believe that our safety procedures for handling and disposing of these materials comply in all material

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respects with the standards prescribed by local, state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In addition, our collaborators may not comply with these laws. In the event of an accident or failure to comply with environmental laws, we could be held liable for damages that result, and any such liability could exceed our assets and resources or we could be subject to limitations or stoppages related to our use of these materials which may lead to an interruption of our business operations or those of our third party contractors. While we believe that our existing insurance coverage is generally adequate for our normal handling of these hazardous materials, it may not be sufficient to cover pollution conditions or other extraordinary or unanticipated events. Furthermore, an accident could damage or force us to shut down our operations. Changes in environmental laws may impose costly compliance requirements on us or otherwise subject us to future liabilities and additional laws relating to the management, handling, generation, manufacture, transportation, storage, use and disposal of materials used in or generated by the manufacture of our products or related to our clinical trials. In addition, we cannot predict the effect that these potential requirements may have on us, our suppliers and contractors or our customers.

Risks Related to Our Dependence on Third Parties

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, and clinical development and commercialization of our product candidates could be delayed, prevented or impaired.

We do not own or operate manufacturing facilities for clinical or commercial production of our product candidates. We have limited personnel with experience in drug manufacturing and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently outsource all manufacturing and packaging of our preclinical and clinical product candidates and products to third parties. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields and quality control, including stability of the product candidate.

We do not currently have any agreements with third party manufacturers for the long-term commercial supply of any of our product candidates. We may be unable to enter into agreements for commercial supply with third party manufacturers, or may be unable to do so on acceptable terms. Even if we enter into these agreements, the manufacturers of each product candidate will be single source suppliers to us for a significant period of time.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured product candidates or products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- limitations on supply availability resulting from capacity and scheduling constraints of the third parties;
- impact on our reputation in the marketplace if manufacturers of our products, once commercialized, fail to meet the demands of our customers;
- the possible breach of the manufacturing agreement by the third party because of factors beyond our control; and
- the possible termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

The failure of any of our contract manufacturers to maintain high manufacturing standards could result in injury or death of clinical trial participants or patients using products. Such failure could also result in product liability claims, product recalls, product seizures or withdrawals, delays or failures in testing or delivery, cost overruns or other problems that could seriously harm our business or profitability.

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Our contract manufacturers will be required to adhere to FDA regulations setting forth current good manufacturing processes, or cGMP. These regulations cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our product candidates and any products that we may commercialize. Our manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our manufacturers are subject to unannounced inspections by the FDA, state regulators and similar regulators outside the United States. Our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect regulatory approval and supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If the third parties that we engage to manufacture products for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. Later relocation to another manufacturer will also require notification, review and other regulatory approvals from the FDA and other regulators and will subject our production to further cost and instability in the availability of our product candidates. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that obtain regulatory approval on a timely and competitive basis.

Materials necessary to manufacture our product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our product candidates.

We rely on the manufacturers of our product candidates to purchase from third party suppliers the materials necessary to produce the compounds for our preclinical and clinical studies and will rely on these other manufacturers for commercial distribution if we obtain marketing approval for any of our product candidates. Suppliers may not sell these materials to our manufacturers at the time we need them or on commercially reasonable terms and all such prices are susceptible to fluctuations in price and availability due to transportation costs, government regulations, price controls, changes in economic climate or other foreseen circumstances. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these materials. If our manufacturers are unable to obtain these materials for our preclinical and clinical studies, product testing and potential regulatory approval of our product candidates would be delayed, significantly impacting our ability to develop our product candidates. If our manufacturers or we are unable to purchase these materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would materially affect our ability to generate revenues from the sale of our product candidates.

We rely on third parties to conduct certain preclinical development activities and our clinical trials and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such activities and trials.

We do not independently conduct certain preclinical development activities of our product candidates, such as long-term safety studies in animals, or clinical trials for our product candidates. We rely on, or work in conjunction

with, third parties, such as contract research organizations, medical institutions and clinical investigators, to perform this function. Our reliance on these third parties for preclinical and clinical

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development activities reduces our control over these activities. We are responsible for ensuring that each of our preclinical development activities and our clinical trials is conducted in accordance with the applicable general investigational plan and protocols, however, we have no direct control over these researchers or contractors (except by contract), as they are not our employees. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, or GCP, for conducting, recording and reporting the results of our preclinical development activities and our clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical development activities or our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Moreover, these third parties may be bought by other entities or they may go out of business, thereby preventing them from meeting their contractual obligations.

We also rely on other third parties to store and distribute drug supplies for our preclinical development activities and our clinical trials. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

Extensions, delays, suspensions or terminations of our preclinical development activities and our clinical trials as a result of the performance of our independent clinical investigators and contract research organizations will delay, and make more costly, regulatory approval for any product candidates that we may develop. Any change in a contract research organization during an ongoing preclinical development activity or clinical trial could seriously delay that trial and potentially compromise the results of the activity or trial.

We may not be successful in maintaining or establishing collaborations, which could adversely affect our ability to develop and, particularly in international markets, commercialize products.

For each of our product candidates, we are collaborating with physicians, patient advocacy groups, foundations and government agencies in order to assist with the development of our products. We plan to pursue similar activities in future programs and plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies. We also may seek to establish collaborations for the sales, marketing and distribution of our products outside the United States. If we elect to seek collaborators in the future but are unable to reach agreements with suitable collaborators, we may fail to meet our business objectives for the affected product or program. We face, and will continue to face, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts, if any, to establish and implement collaborations or other alternative arrangements. The terms of any collaborations or other arrangements that we establish, if any, may not be favorable to us.

Any collaboration that we enter into may not be successful. The success of our collaboration arrangements, if any, will depend heavily on the efforts and activities of our collaborators. It is likely that any collaborators of ours will have significant discretion in determining the efforts and resources that they will apply to these collaborations. The risks that we may be subject to in possible future collaborations include the following:

- our collaboration agreements are likely to be for fixed terms and subject to termination by our collaborators in the event of a material breach or lack of scientific progress by us;

our collaborators are likely to have the first right to maintain or defend our intellectual property rights and, although we would likely have the right to assume the maintenance and defense of our intellectual property rights if our collaborators do not, our ability to do so may be compromised by our collaborators acts or omissions; and

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our collaborators may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Such terminations or expirations may adversely affect us financially and could harm our business reputation in the event we elect to pursue collaborations that ultimately expire or are terminated.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain protection for the intellectual property relating to our technology and products, the value of our technology and products will be adversely affected.

Our success will depend in large part on our ability to obtain and maintain protection in the United States and other countries for the intellectual property covering or incorporated into our technology and products. The patent situation in the field of biotechnology and pharmaceuticals generally is highly uncertain and involves complex legal, technical, scientific and factual questions. We may not be able to obtain additional issued patents relating to our technology or products. Even if issued, patents issued to us or our licensors may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to stop competitors from marketing similar products or reduce the term of patent protection we may have for our products. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

we or our licensors were the first to make the inventions covered by each of our pending patent applications;

we or our licensors were the first to file patent applications for these inventions;

others will not independently develop similar or alternative technologies or duplicate any of our technologies;

any patents issued to us or our licensors will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;

we will develop additional proprietary technologies that are patentable;

we will file patent applications for new proprietary technologies promptly or at all;

our patents will not expire prior to or shortly after commencing commercialization of a product; or

the patents of others will not have a negative effect on our ability to do business.

In addition, we cannot assure you that any of our pending patent applications will result in issued patents. In particular, we have filed patent applications in the European Patent Office and other countries outside the United States that have not been issued as patents. These pending applications include, among others, the patent applications we license pursuant to a license agreement with Mount Sinai School of Medicine of New York University. If patents are not issued in respect of our pending patent applications, we may not be able to stop competitors from marketing similar products in Europe and other countries in which we do not have issued patents.

The patents and patent applications that we own or have licensed relating to use of Amigal expire in 2018 in the United States and 2019 outside of the United States, and the foreign counterparts, if issued, would expire in 2019. Patents that we own or have licensed relating to Plicera expire between 2015 and 2016 in the United States and in 2015 outside of the United States for composition of matter, and in 2018 in the United States for methods of use. We currently have no issued patents or pending applications covering methods of using Plicera outside of the United States. Patents and patent applications that we own or have licensed relating to the use of AT2220 expire in 2018 in the United States. Further, we currently do not have composition of matter or method of use protection for AT2220 outside of the United States. Where we lack patent protection outside of the United States, we intend to seek orphan medicinal product designation and to

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rely on statutory data exclusivity provisions in jurisdictions outside the United States where such protections are available, including Europe. If we are unable to obtain such protection outside the United States, our competitors may be free to use and sell Plicera and/or AT2220 outside of the United States and there will be no liability for infringement or any other barrier to competition. The patent rights that we own or have licensed relating to our product candidates are limited in ways that may affect our ability to exclude third parties from competing against us if we obtain regulatory approval to market these product candidates. In particular:

- We do not hold composition of matter patents covering Amigal and AT2220, two of our three lead product candidates. Composition of matter patents can provide protection for pharmaceutical products to the extent that the specifically covered compositions are important. For our product candidates for which we do not hold composition of matter patents, competitors who obtain the requisite regulatory approval can offer products with the same composition as our products so long as the competitors do not infringe any method of use patents that we may hold.

- For some of our product candidates, the principal patent protection that covers, or that we expect will cover, our product candidate is a method of use patent. This type of patent only protects the product when used or sold for the specified method. However, this type of patent does not limit a competitor from making and marketing a product that is identical to our product that is labeled for an indication that is outside of the patented method, or for which there is a substantial use in commerce outside the patented method.

Moreover, physicians may prescribe such a competitive identical product for indications other than the one for which the product has been approved, or off-label indications, that are covered by the applicable patents. Although such off-label prescriptions may infringe or induce infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Our patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States and many other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind the actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in our or their issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications. If a third party has also filed a United States patent application covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the United States Patent and Trademark Office to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts could be unsuccessful, resulting in a loss of our United States patent position.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of license agreements including agreements with the Mount Sinai School of Medicine of New York University, the University of Maryland, Baltimore County and Novo Nordisk A/S, pursuant to which we license key intellectual property relating to our lead product candidates. We expect to enter into additional licenses in the future. Under our existing licenses, we have the right to enforce the licensed patent rights. Our existing licenses impose, and we expect that future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

We seek to protect our know-how and confidential information, in part, by confidentiality agreements with our employees, corporate partners, outside scientific collaborators, sponsored researchers, consultants and

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other advisors. We also have confidentiality and invention or patent assignment agreements with our employees and our consultants. If our employees or consultants breach these agreements, we may not have adequate remedies for any of these breaches. In addition, our trade secrets may otherwise become known to or be independently developed by others. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Costly and time consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

If we infringe or are alleged to infringe the intellectual property rights of third parties, it will adversely affect our business.

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be accused of infringing one or more claims of an issued patent or may fall within the scope of one or more claims in a published patent application that may subsequently issue and to which we do not hold a license or other rights. Third parties may own or control these patents or patent applications in the United States and abroad. These third parties could bring claims against us that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering our products, technology or methods. Because of the number of patents issued and patent applications filed in our field, we believe there is a risk that third parties may allege they have patent rights encompassing our products, technology or methods.

We are aware, for example, of United States patents, and corresponding international counterparts, owned by third parties that contain claims related to treating protein misfolding. We have received written notice from one of these third parties indicating that it believes we may need a license to certain of these patents in order to avoid infringing such patents. If any of these third party patents were to be asserted against us we do not believe that our proposed products would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a presumption of validity that attaches to every patent. This burden is high and would require us to present clear and convincing evidence as to the invalidity of the patent s claims. There is no assurance that a court would find in our favor on infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our future collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Others may sue us for infringing their patent rights or file nullity, opposition or interference proceedings against our patents, even if such claims are without merit, which would similarly harm our business. Furthermore, during the course of litigation, confidential information may be disclosed in the form of documents or testimony in connection with discovery requests, depositions or trial testimony. Disclosure of our confidential information and our involvement in intellectual property litigation could materially adversely affect our business.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including interference proceedings

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declared by the United States Patent and Trademark Office and opposition proceedings in the European Patent Office, regarding intellectual property rights with respect to our products and technology. Even if we prevail, the cost to us of any patent litigation or other proceeding could be substantial.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from any litigation could significantly limit our ability to continue our operations. Patent litigation and other proceedings may also absorb significant management time.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We try to ensure that our employees do not use the proprietary information or know-how of others in their work for us. However, we may be subject to claims that we or these employees have inadvertently or otherwise used or disclosed intellectual property, trade secrets or other proprietary information of any such employee s former employer. Litigation may be necessary to defend against these claims and, even if we are successful in defending ourselves, could result in substantial costs to us or be distracting to our management. If we fail to defend any such claims, in addition to paying monetary damages, we may jeopardize valuable intellectual property rights, disclose confidential information or lose personnel.

Risks Related to Regulatory Approval of Our Product Candidates

If we are not able to obtain and maintain required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including Amigal, Plicera and AT2220, and the activities associated with their development and commercialization, including their testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate will prevent us from commercializing the product candidate in the jurisdiction of the regulatory authority. We have not obtained regulatory approval to market any of our product candidates in any jurisdiction. We have only limited experience in filing and prosecuting the applications necessary to obtain regulatory approvals and expect to rely on third party contract research organizations to assist us in this process.

Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate s safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Our future products may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

Our product candidates may fail to obtain regulatory approval for many reasons, including:

- our failure to demonstrate to the satisfaction of the FDA or comparable regulatory authorities that a product candidate is safe and effective for a particular indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable regulatory authorities for approval;
- our inability to demonstrate that a product candidate s benefits outweigh its risks;

our inability to demonstrate that the product candidate presents an advantage over existing therapies;

the FDA s or comparable regulatory authorities disagreement with the manner in which we interpret the data from preclinical studies or clinical trials;

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the FDA s or comparable regulatory authorities failure to approve the manufacturing processes, quality procedures or manufacturing facilities of third party manufacturers with which we contract for clinical or commercial supplies; and

a change in the approval policies or regulations of the FDA or comparable regulatory authorities or a change in the laws governing the approval process.

The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. The FDA and non-United States regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post approval commitments that render the approved product not commercially viable. Any FDA or other regulatory approval of our product candidates, once obtained, may be withdrawn, including for failure to comply with regulatory requirements or if clinical or manufacturing problems follow initial marketing.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. For example, in a clinical trial of Amigal for Fabry disease, one patient with a history of hypertension experienced increased blood pressure during the course of the trial which was reported by the investigator as possibly related to the drug. Further, Amigal has been shown to cause reversible infertility effects in mice.

In addition, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product:

regulatory authorities may require the addition of restrictive labeling statements;

regulatory authorities may withdraw their approval of the product; and

we may be required to change the way the product is administered or conduct additional clinical trials.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product candidate, which in turn could delay or prevent us from generating significant revenues from its sale or adversely affect our reputation.

We may not be able to obtain orphan drug exclusivity for our product candidates. If our competitors are able to obtain orphan drug exclusivity for their products that are the same drug as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. We obtained orphan drug designations from the FDA for Amigal for the treatment of Fabry disease on February 25, 2004 and the active ingredient in Plicera for the treatment of Gaucher disease on January 10, 2006. We also obtained orphan drug designation from the European Medicines Agency, or EMEA, for Amigal on May 22, 2006. We anticipate filing for orphan drug designation from the EMEA for Plicera for the treatment of Gaucher disease and from the FDA and EMEA

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for AT2220 for the treatment of Pompe disease. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the applicable regulatory authority from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. For a drug composed of small molecules, the FDA defines same drug as a drug that contains the same active molecule and is intended for the same use. Obtaining orphan drug exclusivity for Amigal and Plicera may be important to each of the product candidate s success. Even if we obtain orphan drug exclusivity for Amigal or Plicera for these indications, we may not be able to maintain it. For example, if a competitive product that is the same drug as our product candidate is shown to be clinically superior to our product candidate, any orphan drug exclusivity we have obtained will not block the approval of such competitive product and we may effectively lose what had previously been orphan drug exclusivity.

Any product for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product for which we obtain marketing approval, along with the manufacturing processes, post approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post marketing information and reports, registration requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if we obtain regulatory approval of a product, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post marketing testing and surveillance to monitor the safety or efficacy of the product. We also may be subject to state laws and registration requirements covering the distribution of our products. Later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on such products, manufacturers or manufacturing processes;
- warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- voluntary or mandatory recall;
- fines;
- suspension or withdrawal of regulatory approvals or refusal to approve pending applications or supplements to approved applications that we submit;
- refusal to permit the import or export of our products;
- product seizure or detentions;
- injunctions or the imposition of civil or criminal penalties; and

adverse publicity.

If we, or our suppliers, third party contractors, clinical investigators or collaborators are slow to adapt, or are unable to adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, we or our collaborators may lose marketing approval for our products when and if any of them are approved, resulting in decreased revenue from milestones, product sales or royalties.

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Failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our products abroad.

We intend to have our products marketed outside the United States. In order to market our products in the European Union and many other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedures vary among countries and can involve additional testing and clinical trials. The time required to obtain approval may differ from that required to obtain FDA approval. The regulatory approval process outside the United States may include all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement by government-backed healthcare regulators or insurance providers before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our management team and scientific staff. These executives each have significant pharmaceutical industry experience, including our President and Chief Executive Officer, John F. Crowley, with whom we have entered into an employment agreement that runs for successive one year terms until either we or Mr. Crowley elect to terminate the agreement. Mr. Crowley is a commissioned officer in the United States Navy (Reserve). The United States recently called Mr. Crowley to service, which he fulfilled, from September 11, 2006 to March 5, 2007, and he may be called to active duty service again at any time. The loss of Mr. Crowley for protracted military duty could materially adversely affect our business. We do not maintain key person insurance on Mr. Crowley or on any of our other executive officers.

Recruiting and retaining qualified scientific personnel, clinical personnel and sales and marketing personnel will also be critical to our success. Our industry has experienced a high rate of turnover in recent years. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, particularly in New Jersey and surrounding areas. Although we believe we offer competitive salaries and benefits, we may have to increase spending in order to retain personnel.

We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We are a development stage company with 77 full-time employees as of March 15, 2007. Of these employees, 54 work primarily in research and development and 23 provide administrative services. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. Assuming our plans and business conditions progress

consistent with our current projections, we plan to grow to a total of 90-100 employees by the end of 2007 and to a total of 100-120 employees by the end of 2008. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems,

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expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability on the part of our management to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock and This Offering

After this offering, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to our stockholders for approval.

When this offering is completed, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately % of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, will control the election of directors and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization. This concentration of voting power could delay or prevent an acquisition of us on terms that other stockholders may desire. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders, and they may act, whether by meeting or written consent of stockholders, in a manner that advances their best interests and not necessarily those of other stockholders, including obtaining a premium value for their common stock, and might affect the prevailing market price for our common stock.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions:

- establish a classified board of directors, and, as a result, not all directors are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call stockholder meetings;

authorize our board of directors to issue preferred stock, without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

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require the approval of the holders of at least 67% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

We expect the initial public offering price of our common stock to be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent outstanding options or warrants are exercised, you will incur further dilution.

Based on an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately % of the aggregate price paid by all purchasers of our common stock but will own only approximately % of our common stock outstanding after this offering.

An active trading market for our common stock may not develop.

This is our initial public offering of equity securities and prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have applied to have our common stock approved for quotation on The NASDAQ Global Market, an active trading market for our common stock may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for our common stock.

If the price of our common stock is volatile, purchasers of our common stock could incur substantial losses.

The price of our common stock is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their shares of our common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

results of clinical trials of our product candidates or those of our competitors;

our entry into or the loss of a significant collaboration;

regulatory or legal developments in the United States and other countries, including changes in the health care payment systems;

variations in our financial results or those of companies that are perceived to be similar to us;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts reports or recommendations;

general economic, industry and market conditions;

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results of clinical trials conducted by others on drugs that would compete with our product candidates;

developments or disputes concerning patents or other proprietary rights;

public concern over our product candidates or any products approved in the future;

litigation;

future sales or anticipated sales of our common stock by us or our stockholders; and

the other factors described in this Risk Factors section.

For these reasons and others you should consider an investment in our common stock as risky and invest only if you can withstand a significant loss and wide fluctuations in the marked value of your investment.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending the application of these funds, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We intend to use the proceeds from this offering for clinical activities, including clinical supplies, preclinical research and development activities, general and administrative expenses, working capital needs and other general corporate purposes, including capital expenditures. Because of the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. For a further description of our intended use of the proceeds of this offering, see the Use of Proceeds section of this prospectus.

We have never paid cash dividends on our capital stock and we do not anticipate paying any cash dividends in the foreseeable future. You should not invest in us if you require dividend income. Any income from an investment in us would only come from a rise in the market price of our common stock, which is uncertain and unpredictable.

We have paid no cash dividends on our capital stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business and do not foresee payment of a dividend in any upcoming fiscal period. In addition, the terms of existing or any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

A significant portion of our total outstanding shares of common stock is restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. After this offering, we will have outstanding shares

of common stock based on the number of shares outstanding as of , 2007. Of these shares, may be resold in the public market immediately and the remaining shares are currently restricted under securities laws or as a result of lock-up agreements but will be able to be sold after the offering as described in the Shares Eligible for Future Sale section of this prospectus. Moreover, after this offering, holders of an aggregate of 124,769,334 shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation

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plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to the 180 day lock-up periods under the lock-up agreements described in the Underwriters section of this prospectus.

If securities or industry analysts do not publish research or reports or publish unfavorable research about our business, the price of our common stock and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of us the trading price for our common stock would be negatively affected. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our common stock, the price of our common stock would likely decline. If one or more of these analysts ceases to cover us or fails to publish regular reports on us, interest in the purchase of our common stock could decrease, which could cause the price of our common stock or trading volume to decline.

We will incur increased costs as a result of being a public company.

As a public company, we will incur significant legal, accounting, reporting and other expenses that we did not incur as a private company, including costs related to compliance with the regulations of the Sarbanes-Oxley Act of 2002. We expect these rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We also expect these new rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, we may experience more difficulty attracting and retaining qualified individuals to serve on our board of directors or as executive officers. We cannot predict or estimate the amount of additional costs we may incur as a result of these requirements or the timing of such costs.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- our plans to develop and commercialize Amigal, Plicera and AT2220;
- our ongoing and planned discovery programs, preclinical studies and clinical trials;
- our ability to enter into selective collaboration arrangements;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our ability to quickly and efficiently identify and develop product candidates;
- the extent to which our scientific approach may potentially address a broad range of diseases across multiple therapeutic areas;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

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 in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of shares of common stock in this offering will be approximately $ million, or $ million if the underwriters exercise their over-allotment option in full, based on an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund the growth of our business, including:

- $ to $ million for clinical development of Amigal for the treatment of Fabry disease;
- $ to $ million for clinical development of Plicera for the treatment of Gaucher disease;
- $ to $ million for clinical development of AT2220 for the treatment of Pompe disease;
- $ to $ million for research and development activities relating to additional preclinical programs; and
- the balance, if any, to fund working capital and other general corporate purposes, which may include the acquisition or licensing of complementary technologies, products or businesses, the expansion of our current corporate offices and laboratory space in Cranbury, New Jersey, and the leasing of additional space at one or more different facilities.

The expected use of net proceeds of this offering represents our intentions based on our current plans and business conditions. The amount and timing of our actual expenditures will depend on numerous factors, including the progress of our research and development activities and clinical trials, the number and breadth of our product development programs, whether or not we establish corporate collaborations and other arrangements, and the amount of cash, if any, generated by our operations and any unforeseen cash needs. As a result, we will retain broad discretion in the allocation and use of the remaining net proceeds of this offering. We do not expect the net proceeds from this offering and our other available funds to be sufficient to fund the completion of the development of our lead product candidates, and we expect that we will need to raise additional funds prior to being able to market any products. We have no current plans, agreements or commitments for any material acquisitions or licenses of any technologies, products or businesses.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the net proceeds to us from this offering by $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

Pending application of the net proceeds, as described above, we intend to invest any remaining proceeds in a variety of short-term, investment-grade, interest-bearing securities.

DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance our research and development efforts, the further development of our pharmacological chaperone technology, and the expansion of our business. We do not intend to declare or pay cash dividends to our stockholders

in the foreseeable future.

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CAPITALIZATION

The following table sets forth our capitalization as of December 31, 2006:

- on an actual basis;
- on a pro forma basis to give effect, as of December 31, 2006, to our issuance on March 12, 2007 of 14,823,985 shares of series D redeemable convertible preferred stock, the automatic exercise for cash upon the completion of this offering of all outstanding warrants to purchase 447,583 shares of series B redeemable convertible preferred stock, and the automatic conversion of all shares of our redeemable convertible preferred stock into an aggregate of 120,987,335 shares of common stock outstanding upon the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ 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.

The pro forma information below is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and the related notes appearing at the end of this prospectus.

	As of December 31, 2006		
	Actual (audited)	Pro Forma (unaudited)	Pro Forma As Adjusted (unaudited)
		(in thousands)	
Capital lease obligations	$ 3,564	$ 3,564	
Series A redeemable convertible preferred stock, par value $0.01 per share; 3,333,334 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	2,476		
Series B redeemable convertible preferred stock, par value $0.01 per share; 37,025,594 shares authorized, actual, 36,470,591 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	30,869		
Series C redeemable convertible preferred stock, par value $0.01 per share; 43,650,262 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	54,869		
Series D redeemable convertible preferred stock, par value $0.01 per share; 36,978,145 shares authorized, 22,154,160 issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro	35,877		

forma as adjusted		
Stockholders equity:		
Common stock, par value $0.01 per share; 160,000,000 shares authorized, actual and pro forma; 7,428,854 shares issued and outstanding, actual; 128,416,189 shares issued and outstanding, pro forma; shares authorized and shares issued and outstanding, pro forma as adjusted	70	1,280
Additional paid-in capital[1]	6,067	153,989
Accumulated other comprehensive income	15	15
Deficit accumulated during the development stage	(83,667)	(83,667)
Total stockholders (deficiency) equity[1]	$ (77,515)	$ 71,616
Total capitalization[1]	$ (50,139)	$ 75,180

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) each of cash, and cash equivalents and short-term investments, additional paid-in capital, total stockholders equity and total capitalization by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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The table above does not include:

14,013,659 shares of common stock issuable upon exercise of options outstanding as of December 31, 2006 at a weighted average exercise price of $0.57 per share;

40,000 shares of common stock issuable upon exercise of a warrant to purchase common stock at an exercise price of $0.75 per share; and

an aggregate of shares of common stock reserved for future issuance under our 2007 equity incentive plan as of the closing of this offering.

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DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the pro forma net tangible book value per share of our common stock after this offering.

The historical net tangible book value of our common stock as of December 31, 2006 was approximately $ million or $ per share, based on shares of common stock outstanding, as adjusted to reflect the one-for- reverse split of our common stock to be effected prior to the completion of this offering. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of common stock outstanding. Our pro forma net tangible book value as of December 31, 2006 was approximately $ million, or $ per share of common stock. Pro forma net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the pro forma number of shares of common stock outstanding after giving effect, as of December 31, 2006, to the issuance on March 12, 2007 of 14,823,985 shares of our series D redeemable convertible preferred stock, the automatic exercise for cash upon completion of this offering of all outstanding warrants to purchase 447,583 shares of series B redeemable convertible preferred stock, and the automatic conversion of all shares of our redeemable convertible preferred stock into an aggregate of 120,987,335 shares of common stock outstanding upon completion of this offering.

After giving effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus) less the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of December 31, 2006, would have been approximately $ million, or $ per share of our common stock. This represents an immediate increase in pro forma net tangible book value of $ per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of $ per share to new investors purchasing shares in this offering at the initial public offering price. Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by a new investor.

The following table illustrates this per share dilution:

Assumed initial public offering price per share	$
Historical net tangible book value per shares as of December 31, 2006	$
Increase attributable to the conversion of outstanding preferred stock	
Pro forma net tangible book value per share before this offering	
Increase per share attributable to new investors	
Pro forma net tangible book value per share after this offering	
Dilution per share to new investors	$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) our pro forma net tangible book value after this offering by approximately $ million, our pro forma net tangible book value per share after this offering by approximately $ per share and dilution per share to new investors in this offering by approximately $ assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions.

If the underwriters exercise their over-allotment option in full to purchase additional shares of common stock in this offering, the proforma as adjusted net tangible book value per share after the offering would be $ per share, the increase in net tangible book value per share to existing stockholders would be

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$ per share and the dilution to new investors, calculated before deduction of the estimated underwriting discounts and commissions and offering expenses payable by us:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of December 31, 2006	$	
Increase attributable to the conversion of outstanding redeemable convertible preferred stock	$	
Pro forma net tangible book value per share as of December 31, 2006	$	
Increase per share attributable to new investors	$	
Pro forma as adjusted net tangible book value per share after this offering	$	
Dilution per share to new investors		$

The following table sets forth, as of December 31, 2006, on a pro forma basis to give effect to our issuance on March 12, 2006 of 14,823,985 shares of series D redeemable convertible preferred stock, the automatic exercise for cash upon completion of this offering of outstanding warrants to purchase 447,583 shares of series B redeemable convertible preferred stock, and the automatic conversion of all shares of our redeemable convertible preferred stock into an aggregate of 120,987,335 shares of common stock outstanding upon the closing of this offering, the total consideration paid investors in this offering and the average price per share paid, or to be paid, to us by existing stockholders and by new investors in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%		%	$
New investors[1]					
Total		100%		100%	

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the total consideration paid by new investors by $ million and increase (decrease) the percentage of total consideration paid by new investors by approximately %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The discussion and tables above exclude:

- 14,013,659 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2006 at a weighted average exercise price of $0.57 per share;

40,000 shares of common stock issuable upon exercise of a warrant to purchase common stock at an exercise price of $0.75 per share; and

an aggregate of shares of common stock reserved for future issuance under our 2007 equity incentive plan as of the closing of this offering.

If the underwriters exercise their over-allotment option in full, the following will occur:

the percentage of shares of common stock held by existing stockholders will decrease to approximately % of the total number of shares of our common stock outstanding after this offering; and

the pro forma as adjusted number of shares held by new investors will be increased to , or approximately %, of the total pro forma as adjusted number of shares of our common stock outstanding after this offering.

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SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this prospectus. We have derived the statements of operations data for the years ended December 31, 2004, 2005 and 2006 and the period from February 4, 2002 (inception) to December 31, 2006 and the balance sheet data at December 31, 2005 and 2006 from our audited financial statements, which are included in this prospectus. We have derived the statement of operations for the period of February 4, 2002 (inception) to December 31, 2002, the year ended December 31, 2003, and the balance sheet data at December 31, 2002, 2003 and 2004, from our audited financial statements, which are not included in this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected for any future period.

	Period from February 4, 2002 (Inception) to December 31, 2002	Year Ended December 31, 2003	2004	2005	2006	Period from February 4, 2002 (Inception) to December 31, 2006
	(in thousands, except shares and per share data)					
Statement of Operations Data:						
Operating expenses:						
Research and development	$ 788	$ 4,433	$ 6,301	$ 13,652	$ 33,630	$ 58,804
General and administrative	552	1,005	2,081	6,877	12,277	22,792
Impairment of leasehold improvements		1,030				1,030
Depreciation and amortization	24	132	146	303	952	1,557
In-process research and development	418					418
Total operating expenses	1,783	6,600	8,528	20,831	46,859	84,601
Loss from operations	(1,783)	(6,600)	(8,528)	(20,831)	(46,859)	(84,601)
Other income (expenses):						
Interest income	13	5	190	610	1,991	2,808

Interest expense	(6)	(172)	(550)	(82)	(273)	(1,083)
Change in fair value of warrant liability			(2)	(280)	(22)	(304)
Other expense					(1,182)	(1,182)
Loss before tax benefit	(1,776)	(6,768)	(8,890)	(20,584)	(46,345)	(84,362)
Income tax benefit			83	612		695
Net loss	(1,776)	(6,768)	(8,807)	(19,972)	(46,345)	(83,667)
Deemed dividend					(19,424)	(19,424)
Preferred stock accretion	(10)	(17)	(126)	(139)	(159)	(451)
Net loss attributable to common stockholders	$ (1,786)	$ (6,785)	$ (8,933)	$ (20,111)	$ (65,928)	$ (103,543)
Net loss attributable to common stockholders per common share basic and diluted		$ (2.94)	$ (3.87)	$ (6.54)	$ (11.94)	
Weighted-average common shares outstanding basic and diluted		2,306,541	2,306,541	3,076,649	5,519,749	
Unaudited pro forma net loss					$ (46,345)	
Unaudited pro forma basic and diluted net loss per share					$ (0.37)	
Unaudited shares used to compute pro forma basic and diluted net loss per share					126,507,084	

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	As of December 31,				
	2002	2003	2004	2005	2006
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents and marketable securities	$ 1,341	$ 15	$ 4,336	$ 24,418	$ 54,699
Working capital	947	(5,588)	3,569	22,267	44,814
Total assets	1,919	501	5,073	28,670	59,646
Total liabilities	752	5,776	1,346	4,031	13,071
Redeemable convertible preferred stock[(1)]	2,416	2,432	20,013	60,469	124,091
Deficit accumulated during the development stage	(1,775)	(8,503)	(17,351)	(37,322)	(83,667)
Total stockholders deficiency	$ (1,249)	$ (7,708)	$ (16,287)	$ (35,830)	$ (77,515)

(1) In March 2007, we issued an additional 14,823,985 shares of series D redeemable convertible preferred stock for proceeds of $24.1 million.

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MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

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. 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. Misfolded proteins are often recognized by cells as having defects and, as a result, may be eliminated prior to reaching their intended location in the cell. The reduced biological activity of these proteins leads to impaired cellular function and ultimately to 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. We are currently conducting Phase II clinical trials of Amigal for Fabry disease, Phase II clinical trials of Plicera for Gaucher disease, and Phase I clinical trials of AT2220 for Pompe disease.

We have generated significant losses to date and expect to continue to generate losses as we continue the clinical development of Amigal, Plicera, and AT2220. From our inception in February 2002 through December 31, 2006, we have accumulated a deficit of $83.7 million. Because we do not generate revenue from any of our product candidates, our losses will continue as we conduct our research and development activities. These activities are budgeted to expand over time and will require further resources if we are to be successful. As a result, our operating losses are likely to be substantial over the next several years. We will need to obtain additional funds to further develop our research and development programs.

Financial Operations Overview

Revenue

We have not generated any revenue since our inception. To date, we have funded our operations primarily through the sale of equity securities and equipment financings through capital leases. If our development efforts result in clinical success, regulatory approval and successful commercialization of any of our products, we could generate revenue from sales of any of our products.

Research and Development Expense

We expect our research and development expense to increase as we continue to develop our product candidates. Research and development expense consists of:

- internal costs associated with our research activities;
- payments we make to third party contract research organizations, contract manufacturers, investigative sites, and consultants;
- manufacturing development costs;

personnel related expenses, including salaries, benefits, travel, and related costs for the personnel involved in drug discovery and development;

activities relating to regulatory filings and the advancement of our product candidates through preclinical studies and clinical trials; and

facilities and other allocated expenses, which include direct and allocated expenses for rent, facility maintenance, as well as laboratory and other supplies.

We have multiple research and development projects ongoing at any one time. We utilize our internal resources, employees and infrastructure across multiple projects. We do not believe that allocating internal

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costs on the basis of estimates of time spent by our employees would accurately reflect the actual costs of a project. We do, however, record and maintain information regarding external, out-of-pocket research and development expenses on a project-specific basis.

We expense research and development costs as incurred, including payments made to date under our license agreements. We believe that significant investment in product development is a competitive necessity and plan to continue these investments in order to realize the potential of our product candidates. From our inception in February 2002 through December 31, 2006, we have incurred research and development expense in the aggregate of $58.8 million, including stock-based compensation expense of approximately $2.0 million.

The following table summarizes our principal product development programs, including the related stages of development for each product candidate in development, and the out-of-pocket, third party expenses incurred with respect to each product candidate (in thousands).

	Year Ended December 31,			Period from February 4, 2002 (Inception) to December 31,
Product Candidate	**2004**	**2005**	**2006**	**2006**
Third party direct project expenses				
Amigal (Fabry Disease Phase II)	$ 4,547	$ 5,579	$ 3,215	$ 16,382
Plicera (Gaucher Disease Phase II)	26	2,164	9,595	11,785
AT2220 (Pompe Disease Phase I)		374	4,389	4,763
Total third party direct project expenses	4,573	8,117	17,199	32,930
Internal project costs[1]				
Personnel related costs	1,363	4,031	8,187	15,160
Other internal costs	365	1,504	8,244	10,714
Total internal project costs	1,728	5,535	16,431	25,874
Total research and development costs	$ 6,301	$ 13,652	$ 33,630	$ 58,804

(1) We utilize our internal resources across multiple projects.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of, or the period, if any, in which material net cash inflows may commence from Amigal, Plicera, AT2220 or any of our other preclinical product candidates. This uncertainty is due to the numerous risks and uncertainties associated with the duration and cost of clinical trials which vary significantly over the life of a project as a result of differences arising during clinical development, including:

- the number of clinical sites included in the trials;

the length of time required to enroll suitable patients;

the number of patients that ultimately participate in the trials; and

the results of our clinical trials.

Our expenditures are subject to additional uncertainties, including the terms and timing of regulatory approvals, and the expense of filing, prosecuting, defending and enforcing any patent claims or other intellectual property rights. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of the foregoing variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those

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which we currently anticipate, or if we experience significant delays in enrollment in any our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Drug development may take several years and millions of dollars in development costs.

General and Administrative Expense

General and administrative expense consists primarily of salaries and other related costs, including stock-based compensation expense, for persons serving in our executive, finance, accounting, information technology and human resource functions. Other general and administrative expense includes facility-related costs not otherwise included in research and development expense, promotional expenses, costs associated with industry and trade shows, and professional fees for legal services, including patent-related expense, and accounting services. We expect that our general and administrative expenses will increase as we add personnel and become subject to the reporting obligations applicable to public companies. From our inception in February 2002 through December 31, 2006, we spent $22.8 million, including stock-based compensation expense of approximately $2.0 million, on general and administrative expense.

Beneficial Conversion Charges

When we issue debt or equity securities which are convertible into common stock at a discount from the common stock fair value at the date the debt or equity is issued, a beneficial conversion charge for the difference between the closing price and the conversion price multiplied by the number of shares issuable upon conversion is recognized. The beneficial conversion charge for our debt instruments is presented as a discount to the related debt, with an offsetting amount increasing additional paid-in capital. We recorded a beneficial conversion charge for a bridge loan financing of $0.1 million which was initially recorded as debt discount and amortized to interest expense through May 2004. We also recorded a beneficial conversion charge (deemed dividend) during the second quarter of 2006 of approximately $19.4 million related to the issuance of certain shares of series C redeemable convertible preferred stock. The beneficial conversion charge for our equity instruments is recorded with offsetting charges and credits to additional paid in capital with no effect on total shareholder equity. The beneficial conversion charge (deemed dividend) increases the loss applicable to our common stockholders in the calculation of basic net loss per share for the year ended December 31, 2006. The estimated fair value of the common stock was approximately $2.15 per share at the measurement date for the second tranche of series C redeemable convertible preferred stock.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and cash equivalents and marketable securities. Interest expense consists of interest incurred on our capital lease facility.

Other income and expenses

During the second and third quarter of 2006, we deferred and capitalized $1.2 million of costs directly attributable to the planned initial public offering of our common stock as other non-current assets. These costs were recorded as non-operating expenses when the planned offering was withdrawn during the third quarter of 2006.

Change in Warrant Liability

We account for warrants to purchase shares of our series B redeemable convertible preferred stock in accordance with FASB statement No. 150, Accounting for Certain financial instruments with Characteristics of both Liabilities and Equity, or SFAS 150. SFAS 150 requires that a financial instrument, other than an outstanding share, that, at inception, is indexed to an obligation to repurchase the issuer s equity shares, regardless of the timing of the

redemption feature, and may require the issuer to settle the obligation by transferring assets shall be classified as a liability. We recognize changes in the fair value of the warrants in the statements of operations as non-operating income or expense.

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Critical Accounting Policies and Significant Judgments and Estimates

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our financial statements appearing at the end of this filing, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

fees owed to contract research organizations in connection with preclinical and toxicology studies and clinical trials;

fees paid to investigative sites in connection with clinical trials;

fees owed to contract manufacturers in connection with the production of clinical trial materials;

fees owed for professional services, and

unpaid salaries, wages, and benefits.

Adoption of SFAS No. 123(R)

Effective January 1, 2006, we adopted the fair value recognition provisions of FASB Statement No. 123(R), *Share-Based Payment,* or SFAS No. 123(R), using the prospective transition method. Under the prospective transition method, compensation expense is recognized in the financial statements on a prospective basis for all share-based payments granted subsequent to December 31, 2005, based upon the grant-date fair value estimated in accordance with the provisions of SFAS 123(R). Options granted prior to January 1, 2006, as a non-public company and accounted for using the intrinsic value method, will continue to be expensed over the vesting period. The fair value of awards expected to vest, as measured at grant date, is expensed on a straight-line basis over the vesting period of the related awards. Under the prospective transition method, results for prior periods are not restated.

Stock-Based Compensation

At December 31, 2006, we had one stock-based employee compensation plan, which is described more fully in Note 7 to our financial statements appearing at the end of this prospectus. Prior to January 1, 2006, we accounted for this plan under the recognition and measurement provisions of Accounting Principles Board Opinion No 25, *Accounting for Stock Issued to Employees*, or APB 25, and related interpretations, as permitted by SFAS 123. Stock-based employee compensation cost was recognized in the statement of operations for periods prior to January 1, 2006, to the extent options granted under the plan had an exercise price that was less than the fair market value of the underlying common stock on the date of grant. Under the prospective

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transition method, compensation cost recognized for all stock-based payments granted subsequent to January 1, 2006 is based on the grant-date fair value estimated in accordance with the provisions of SFAS 123(R). Results for prior periods have not been restated. As a result of adopting SFAS 123(R) on January 1, 2006, our net income for the year ended December 31, 2006 was less than it would have been had we continued to account for stock-based compensation under APB 25.

Prior to the adoption of SFAS 123(R), we presented our unamortized portion of deferred compensation cost for nonvested stock options in the statement of changes in shareholders deficiency with a corresponding credit to additional paid-in capital. Upon the adoption of SFAS 123(R), these amounts were offset against each other as SFAS 123(R) prohibits the gross-up of stockholders equity. Under SFAS 123(R), an equity instrument is not considered to be issued until the instrument vests. As a result, compensation cost is recognized over the requisite service period with an offsetting credit to additional paid-in capital.

We recognized employee stock-based compensation expense of $0.1 million, $0.4 million, and $2.8 million for the years ended 2004, 2005 and 2006, respectively.

During the year ended December 31, 2006, we recorded incremental compensation expense of approximately $2.2 million ($0.40 per basic and diluted share) related to the expensing of our options under SFAS 123(R) during the year. The compensation expense had no impact on our cash flows from operations and financing activities. The total unrecognized compensation cost related to non-vested stock option awards as of December 31, 2006 was approximately $8.1 million. This expense will be recorded on a straight-line basis over approximately 2.7 years.

Upon adoption of SFAS 123(R), we selected the Black-Scholes option pricing model as the most appropriate model for determining the estimated fair value for stock-based awards. The fair value of stock option awards subsequent to December 31, 2005 is amortized on a straight-line basis over the requisite service periods of the awards, which is generally the vesting period. Use of a valuation model requires management to make certain assumptions with respect to selected model inputs. Expected volatility was calculated based on a blended weighted average of historical information of our stock and the weighted average of historical information of similar public entities for which historical information was available. We will continue to use a blended weighted average approach using our own historical volatility and other similar public entity volatility information until our historical volatility is relevant to measure expected volatility for future option grants. The average expected life was determined according to the SEC shortcut approach as described in Staff Accounting Bulletin, or SAB, 107, *Disclosure about Fair Value of Financial Instruments*, which is the mid-point between the vesting date and the end of the contractual term. The risk-free interest rate is based on U.S. Treasury, zero-coupon issues with a remaining term equal to the expected life assumed at the date of grant. Forfeitures are estimated based on voluntary termination behavior, as well as a historical analysis of actual option forfeitures. The weighted average assumptions used in the Black-Scholes option pricing model are as follows:

	Year Ended December 31, 2006
Expected stock price volatility	74.8%
Risk free interest rate	4.7%
Expected life of options (years)	6.25
Expected annual dividend per share	$ 0.00

The weighted-average fair value (as of the date of grant) of the options granted during the year ended December 31, 2006 is $1.36.

The exercise prices for options granted were set by our board of directors, the members of which have extensive experience in the life sciences industry and all but one of whom are non-employee directors, with input from our management, based on our board s determination of the fair market value of our common stock at the time of the grants. In connection with the preparation of the financial statements for a public offering, we performed a retrospective determination of fair value for financial reporting purposes of our common stock

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underlying stock option grants in 2005 and the first quarter of 2006 utilizing a combination of valuation methods described in the AICPA *Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid. We utilized the same combination of valuation methods to perform contemporaneous valuations of our common stock for each quarter subsequent to March 31, 2006. Information on stock option grants during 2005 and 2006 are as follows:

Date of 2005 Issuance	Number of Options Granted	Average Exercise Price	Retrospective Fair Value Estimate per Common Share	Intrinsic Value per Share
January - May	3,037,037	$ 0.09	$ 0.31	$ 0.22
June - July	1,768,748	0.09	0.77	0.68
August - September	315,500	0.22	0.95	0.73
October - November	2,351,000	0.71	1.14	0.43
December	104,500	0.71	1.44	0.73
	7,576,785			

Date of 2006 Issuance	Number of Options Granted	Average Exercise Price	Average Fair Value Estimate per Common Share	Average Intrinsic Value per Share
January - March	5,895,000	$ 0.71	$ 1.83(1)	$ 1.12
April - June	899,500	1.09	1.09	
July - August	405,000	1.09	1.09	
September - December	339,000	1.22	1.22	
	7,538,500			

(1) Retrospectively determined fair value for financial reporting purposes.

Determining the fair value of the common stock of a private enterprise requires complex and subjective judgments. Our retrospective and contemporaneous estimates of enterprise value at each of the grant dates during 2005 and 2006 used results from both the income approach and the market approach.

Under the income approach, our enterprise value was based on the present value of our forecasted operating results. Our revenue forecasts were based on our estimates of expected annual growth rates following the anticipated commercial launch of our product candidates Amigal, Plicera and AT2220. Estimated operating expenses were based on our internal assumptions, including continuing research and development activities for Amigal, Plicera, AT2220 and other preclinical candidates, and preparation and ongoing support for the commercialization of our lead product

candidates. The assumptions underlying the estimates are consistent with our business plan. The risks associated with achieving our forecasts were assessed in selecting the appropriate discount rates, which were approximately 25% to 35%.

Under the market approach, our estimated enterprise value was developed based on a comparison of pre-money initial public offering, or IPO, values of recent biotechnology and emerging pharmaceutical companies at a similar stage of development to ours. When we achieved or exceeded a significant milestone, we reduced the discount rate applied to determine our enterprise value.

Once our enterprise value was established, an allocation method was used to allocate the enterprise value to the different classes of equity instruments. During our retrospective and contemporaneous reviews, we used

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the probability weighted expected returns, or PWER, method to allocate our enterprise value to our common stock. Under the PWER method, the value of common stock is estimated based upon an analysis of future values for the enterprise assuming various future outcomes. In our retrospective review, the future outcomes included two scenarios: (i) we become a public company and; (ii) we remain a private company. In our contemporaneous review, the future outcomes included three scenarios: (i) we become a public company, (ii) we merge or are acquired by another company, and; (iii) we remain a private company. In general, the closer a company gets to an IPO, the higher the probability assessment weighting is for that scenario. We used a low probability assumption for our January 2005 grants and this percentage increased over time as significant milestones were achieved and as discussions with our investment bankers began and continued to increase as we prepared for our IPO process. An increase in the probability assessment for an IPO increases the value ascribed to our common stock while a decrease in that probability has the opposite effect on the value ascribed to our common stock.

For each of the scenarios, estimated future and present value for the common shares were calculated using assumptions including:

- our expected pre-IPO valuation;
- a risk-adjusted discount rate associated with the IPO scenario;
- the liquidation preferences of our redeemable convertible preferred stock;
- appropriate discount for lack of marketability assuming we remained a private company;
- the expected probability of completing an IPO versus remaining a private company or completing a merger or acquisition; and
- the estimated timing of a potential IPO.

The increase in the fair value of our common stock for financial reporting purposes during 2005 and the 2006 principally reflects increases resulting from achieving significant clinical milestones and a significant increase in our probability weighting for the IPO scenario until we withdrew our offering in the third quarter of 2006. The following is a summary of the significant factors that resulted in changes in the fair value of our common stock for the two years ended December 31, 2006:

- The reassessed fair value for financial reporting purposes of common stock underlying 3,037,037 options granted to employees during the period from January 2005 through May 2005 was $0.31 per share. This valuation was attributable to the hiring of our President and Chief Executive Officer and other members of executive management and a relatively low probability estimate for the IPO scenario under the PWER method.
- The reassessed fair value for financial reporting purposes of common stock underlying 1,768,748 options granted to employees during the period from June 2005 through July 2005 was determined to be $0.77 per share based on the ongoing clinical trial of Amigal, additional development of our preclinical programs, and an increased probability estimate for the IPO scenario under the PWER method.
- The reassessed fair value for financial reporting purposes of common stock underlying 315,500 options granted to employees during the period from August 2005 through September 2005 was determined to be $0.95 per share. This increase in valuation was based on the completion of Phase I clinical trials for Amigal and completion of our series C redeemable convertible preferred stock financing of $55 million.

The reassessed fair value for financial reporting purposes of common stock underlying 2,351,000 options granted to employees during the period from October 2005 through November 2005 was determined to be $1.14 per share. This increase was primarily based on positive developments in the capital markets for early stage life science companies, the start of Phase II clinical trials for Amigal, and further preclinical development of our other programs.

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The reassessed fair value for financial reporting purposes of common stock underlying 104,500 options granted to employees in December 2005 and 92,500 options granted to employees in the period from January 1, 2006 to February 22, 2006 was determined to be $1.44 per share. This increase was primarily based on preclinical development of Plicera and AT2220, as well as an acceleration of our IPO planning.

The reassessed fair value for financial reporting purposes of common stock underlying 5,802,500 options granted to employees and directors in the period from February 28, 2006 to March 27, 2006 was determined to be $1.84 per share. This increase was primarily based on initial data from our Phase II studies in Fabry disease and a further acceleration of our IPO timeline.

The fair value of common stock underlying 1,304,500 options granted to employees during the second and third quarters of 2006 was determined to be $1.09 per share. This decrease was primarily based on a comparison of then current pre-money IPO values of biotechnology and emerging pharmaceutical companies at a similar stage of development to ours, a decreased probability estimate for the IPO scenario under the PWER method due to the withdrawal of our planned IPO, and an increased the estimate of the period prior to a potential IPO under that scenario.

The fair value of common stock underlying 339,000 options granted to employees during the fourth quarter of 2006 was determined to be $1.22 per share. This increase was primarily based on a comparison to improved pre-money IPO values of biotechnology and emerging pharmaceutical companies at a similar stage of development to ours and an increased probability estimate for the IPO scenario under the PWER method subsequent to the completion of our Series D financing.

The intrinsic value of all outstanding vested and unvested options based on the estimated IPO price of $ was $ based on 14,013,659 options outstanding at December 31, 2006.

Basic and Diluted Net Loss Attributable to Common Stockholders per Common Share

We calculated net loss per share in accordance with SFAS No. 128, *Earnings Per Share*. We have determined that the series A, B, C, and D redeemable convertible preferred stock represent participating securities in accordance with Emerging Issue Task Force, or EITF, 03-6 *Participating Securities and the Two Class Method under FASB Statement No. 128*. However, since we operate at a loss, and losses are not allocated to the redeemable convertible preferred stock, the two class method does not affect our calculation of earnings per share. We had a net loss for all periods presented; accordingly, the inclusion of common stock options and warrants would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same.

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The following table provides a reconciliation of the numerator and denominator used in computing basic and diluted net loss attributable to common stockholders per common share and pro forma net loss attributable to common stockholders per common share:

	Years Ended December 31,		
	2004	2005	2006
Historical			
Numerator:			
Net loss	$ (8,807,102)	$ (19,972,289)	$ (46,344,910)
Deemed dividend			(19,424,367)
Accretion of redeemable convertible preferred stock	(125,733)	(138,743)	(158,802)
Net loss attributable to common stockholders	$ (8,932,835)	$ (20,111,032)	$ (65,928,079)
Denominator:			
Weighted average common shares outstanding basic and diluted	2,306,541	3,076,649	5,519,749

Dilutive common stock equivalents would include the dilutive effect of convertible securities, common stock options and warrants for common stock equivalents. Potentially dilutive common stock equivalents totaled approximately 28,749,798, 70,948,031 and 131,007,390 for the years ended December 31, 2004, 2005 and 2006, respectively. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect.

Results of Operations

Year Ended December 31, 2006 Compared to Year Ended December 31, 2005

Research and Development Expense. Research and development expense was $33.6 million in 2006, an increase of $19.9 million, or 145%, from $13.7 million in 2005. The increase was primarily attributable to increased contract research and manufacturing costs for Amigal, Plicera and AT2220 of $11.1 million, an increase in personnel costs of $4.6 million, and costs associated with licenses totaling $2.5 million. The increase in personnel costs was due to headcount and salary increases in our research, clinical, and regulatory functions and the impact of adopting SFAS 123(R).

General and Administrative Expense. General and administrative expense was $12.3 million in 2006, an increase of $5.4 million, or 78%, from $6.9 million in 2005. The increase resulted principally from an increase in personnel costs of $3.7 million attributable to increased headcount, a rise in salaries, and the impact of adopting SFAS 123(R).

Depreciation and Amortization. Depreciation and amortization expense was $1.0 million in 2006, and increase of $0.7 million or 233%, from $0.3 million in 2005. The increase is primarily due to leasehold improvements completed in late 2005 and early 2006 as well as purchases of equipment during 2006.

Interest Income and Interest Expense. Interest income was $2.0 million in 2006, compared to $0.6 million in 2005. The increase in interest income resulted from higher average cash and cash equivalents balances and higher average interest rates in 2006. Interest expense was $0.3 million in 2006, compared to $0.1 million in 2005. The increase in

interest expense resulted from additional capital lease borrowings during 2006.

Other Expense. During 2006, we capitalized $1.2 million of costs directly attributable to the planned offering of our anticipated IPO. These costs were expensed when we withdrew our offering in the third quarter of 2006.

Tax Benefit. In 2005, we recognized tax benefits related to our sale of net operating losses in the New Jersey Tax Transfer Program. Our tax benefit was $0.6 million in 2005. We sold $6.7 million of net operating

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losses in 2005. We did not sell net operating losses in the New Jersey Tax Transfer Program in 2006 and therefore we did not recognize any tax benefits in 2006.

Year Ended December 31, 2005 Compared to Year Ended December 31, 2004

Research and Development Expense. Research and development expense was $13.7 million in 2005, an increase of $7.4 million, or 117%, from $6.3 million in 2004. The increase resulted primarily from an increase in contract research costs for Amigal, Plicera, and AT2220 of $3.5 million during 2005, and a rise in personnel related costs of $2.7 million.

General and Administrative Expense. General and administrative expense was $6.9 million in 2005, an increase of $4.8 million, or 228%, from $2.1 million in 2004. This increase is primarily attributable to a rise in salaries, as well as an increase in headcount in finance, human resources, information technology and general management, including the hiring of many of our current senior executives.

Interest Income and Interest Expense. Interest income was $0.6 million in 2005, compared to $0.2 million in 2004. Interest expense was $0.1 million in 2005, compared to $0.6 million in 2004. The increase in interest income resulted from higher average cash and cash equivalents balances and higher average interest rates in 2005. The reduction in interest expense resulted from the conversion of our bridge loans into series B redeemable convertible preferred stock during 2004.

Tax Benefit. In 2005 and 2004, we recognized tax benefits related to our sale of net operating losses in the New Jersey Tax Transfer Program. Our tax benefit was $0.6 million in 2005 and $0.1 million in 2004. We sold $6.7 million and $1.1 million of net operating losses in 2005 and 2004, respectively.

Liquidity and Capital Resources

Source of Liquidity

As a result of our significant research and development expenditures and the lack of any approved products to generate product sales revenue, we have not been profitable and have generated operating losses since we were incorporated in 2002. We have funded our operations principally with $124.5 million of gross proceeds from redeemable convertible preferred stock offerings through December 31, 2006. We received an additional $24.1 million of proceeds from a second tranche of Series D redeemable convertible preferred stock issuance in March 2007. The following table summarizes our funding sources as of December 31, 2006:

Issue	Year	No. Shares	Approximate Amount[(1)]
Series A Redeemable Convertible Preferred Stock	2002	3,333,334	$ 2,500,000
Series B Redeemable Convertible Preferred Stock	2004, 2005, 2006	36,578,011	31,091,307
Series C Redeemable Convertible Preferred Stock	2005, 2006	43,650,262	54,999,332
Series D Redeemable Convertible Preferred Stock	2006	22,154,160	35,946,897
		105,715,767	$ 124,537,536

(1) Represents gross proceeds.

As of December 31, 2006, we had cash and cash equivalents and marketable securities of $54.7 million. We hold our cash and investment balances in a variety of high quality interest-bearing instruments, including obligations of U.S. government agencies and money market accounts. We invest cash in excess of our immediate requirements with regard to liquidity and capital preservation. Wherever possible, we seek to minimize the potential effects of concentration and degrees of risk.

Also, we maintain cash balances with financial institutions in excess of insured limits. We do not anticipate any losses with respect to such cash balances.

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Net Cash Used in Operating Activities

Net cash used in operations was $33.9 million for the year ended December 31, 2006. The net loss for the year ended December 31, 2006 of $46.3 million was offset primarily by non-cash charges for depreciation and amortization of $1.0 million, stock-based compensation of $3.3 million, stock-based license payment of $1.2 million and changes in operating assets and liabilities of $7.0 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was $26.6 million for the year ended December 31, 2006. Net cash used in investing activities reflects $62.0 million for the purchase of marketable securities and $2.0 million for the acquisition of property and equipment, partially offset by $37.4 million for the sale and redemption of marketable securities.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $66.2 million for the year ended December 31, 2006. Net cash provided by financing activities mainly reflects $27.5 million of proceeds from the issuance of our series C redeemable convertible preferred stock, $35.9 million of proceeds from the issuance of our series D redeemable convertible preferred stock, and $3.4 million of proceeds from our capital asset financing arrangement, partially offset by $0.9 million of payments of capital lease obligations.

Funding Requirements

We expect to incur losses from operations for the foreseeable future. We expect to incur increasing research and development expenses, including expenses related to the hiring of personnel and additional clinical trials. We expect that our general and administrative expenses will also increase as we expand our finance and administrative staff, add infrastructure, and incur additional costs related to being a public company, including directors and officers insurance, investor relations programs, and increased professional fees. Our future capital requirements will depend on a number of factors, including the continued progress of our research and development of products, the timing and outcome of clinical trials and regulatory approvals, the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims and other intellectual property rights, the acquisition of licenses to new products or compounds, the status of competitive products, the availability of financing, and our success in developing markets for our product candidates.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least until . We believe that if we sell the shares of our common stock in this offering at an initial public offering price of $ per share ($1.00 lower than the mid-point of the price range set forth on the cover page of this prospectus), the resultant reduction in proceeds we receive from the offering would cause us to require additional capital earlier. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials.

Our future capital requirements will depend on many factors, including the progress and results of our clinical trials, the duration and cost of discovery and preclinical development and laboratory testing and clinical trials for our product candidates, the timing and outcome of regulatory review of our product candidates, the number and development requirements of other product candidates that we pursue, and the costs of commercialization activities,

including product marketing, sales and distribution.

We do not anticipate that we will generate product revenue for at least the next several years. In the absence of additional funding, we expect our continuing operating losses to result in increases in our cash used in operations over the next several quarters and years.

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We will need to finance our future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. We do not currently have any commitments for future external funding. We may need to raise additional funds more quickly if one or more of our assumptions prove to be incorrect or if we choose to expand our product development efforts more rapidly than we presently anticipate, and we may decide to raise additional funds even before we need them if the conditions for raising capital are favorable. We may seek to sell additional equity or debt securities or obtain a bank credit facility. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations.

Additional equity or debt financing, grants, or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2006 and the effects such obligations are expected to have on our liquidity and cash flows in future periods.

	Total	Less than 1 Year	1-3 Years	3-5 Years	Over 5 Years
Operating lease obligations	$ 7,631,820	$ 1,629,181	$ 4,477,324	$ 1,525,315	
Capital lease obligations	4,113,425	1,624,727	2,488,698		
Employment agreement	1,850,669	1,388,002	462,667		
Total fixed contractual obligations	$ 13,595,914	$ 4,641,910	$ 7,428,689	$ 1,525,315	

In May 2005, we entered into a seven-year, non-cancelable operating sublease agreement for office and laboratory space in Cranbury, New Jersey. The operating sublease will expire by its terms in February 2012. In August 2006, we entered into a sublease agreement for office space in an adjacent building. This sublease will expire by its terms in August 2009.

In August 2002, we entered into capital lease agreements that provide for up to $1.0 million of equipment financing through August 2004. The facility was increased to $3.0 million in May 2005 and to $5.0 million in November 2005. These financing arrangements include interest of approximately 9-12%, and lease terms of 36 or 48 months. Eligible assets under the lease lines include laboratory and scientific equipment, computer hardware and software, general office equipment, furniture, and tenant improvements. Upon termination of the lease agreements, we may renew the lease or purchase the leased equipment for $1.00. We also have the option to purchase the equipment at set prices before termination of the lease. In addition, at lease inception, we issued a warrant to the equipment financing lender to purchase 40,000 shares of common stock. The warrant was valued at $8,000 using a Black-Scholes option pricing model and this value was amortized to interest.

On April 28, 2006, we entered into an employment agreement with our president and chief executive officer that provides for an annual base salary of $400,000, a cash bonus of up to 50% of base salary, an executive medical

reimbursement contract, annual reimbursement up to $220,000 for medical expenses not covered by the executive medical reimbursement contract or our medical or health insurance policies, and gross up for federal and state income taxes of income tax incurred in connection with medical reimbursement. The agreement will continue for successive one-year terms until either party provides written notice of termination to the other in accordance with the terms of the agreement. The table above includes costs

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associated with the remainder of the first one-year term and second one-year term ending April 28, 2008. The cost of the executive medical reimbursement contract is estimated based on current premiums. This employment agreement is more fully described in the Compensation Discussion and Analysis section of this prospectus.

We have entered into agreements with clinical research organizations and other outside contractors who will be partially responsible for conducting and monitoring our clinical trials for Amigal, Plicera and AT2220. These contractual obligations are not reflected in the table above because we may terminate them without penalty.

Except for the capital lease agreements described above, we have no other lines of credit or other committed sources of capital. To the extent our capital resources are insufficient to meet future capital requirements, we will need to raise additional capital or incur indebtedness to fund our operations. We cannot assure you that additional debt or equity financing will be available on acceptable terms, if at all.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during 2004, 2005 or 2006.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements as of December 31, 2005 and 2006.

Recent Accounting Pronouncements

In July 2006, FASB issued FSAB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an Interpretation of FASB Statement No. 109*, or FIN No. 48, which clarifies the accounting for uncertainty in tax positions. This Interpretation prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. It also provides guidance on derecognition, clarification, interest and penalties, accounting in interim periods, disclosures and transitions. The provision of FIN 48 are effective as of the beginning of our 2007 fiscal year, with the cumulative effect, if any, of the change in accounting principle recorded as an adjustment to opening retained earnings. We do not expect that FIN 48 will impact our financial statements.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measures*, or SFAS No. 157. SFAS No. 157 defines fair value, establishes a framework for measuring fair value and enhances disclosures about fair value measures required under other accounting pronouncements, but does not change existing guidance as to whether or not an instrument is carried at fair value. SFAS No. 157 is effective as of the beginning of our 2008 fiscal year. We are currently reviewing the provisions of SFAS No. 157 to determine the impact. We do not expect this will have a significant impact on our financial statements.

Quantitative and Qualitative Disclosures about Market Risk

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. As of December 31, 2006, we had cash and cash equivalents and investments in marketable securities of $54.7 million. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our investments are short-term in duration, we believe that our exposure to interest rate risk is not significant and a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio.

We actively monitor changes in interest rates.

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BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of a new class of orally-administered, small molecule 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. We have completed enrollment of our Phase II clinical trials of Amigal, and are currently conducting Phase II clinical trials of Plicera and Phase I clinical trials of AT2220. 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 were 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.

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. Misfolded proteins are often recognized by cells as having defects and, as a result, may be eliminated prior to reaching their intended location in the cell. The reduced biological activity of these proteins leads to impaired cellular function and ultimately to 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.

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.

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. Our initial clinical efforts are currently focused on developing pharmacological chaperones for the treatment of lysosomal storage disorders, which are chronic genetic diseases, such as Fabry, Gaucher and Pompe, that frequently result in severe symptoms. We believe our technology also 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. Each of these disorders results from the deficiency of a single enzyme.

Amigal for Fabry disease. We are developing Amigal for the treatment of Fabry disease and are currently conducting multiple Phase II clinical trials of Amigal. We expect to complete these trials by the end of 2007.

Plicera for Gaucher disease. We are developing Plicera for the treatment of Gaucher disease and 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.

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AT2220 for Pompe disease. We are developing AT2220 for the treatment of Pompe disease, and are currently conducting Phase I clinical trials of AT2220. We expect to initiate a Phase II clinical trial of AT2220 by the end of 2007.

Our Pharmacological Chaperone Technology

In the human body, proteins are involved in almost every aspect of cellular function. Proteins are linear strings of amino acids that fold and twist into specific three-dimensional shapes in order to function properly. Certain human diseases result from mutations that cause changes in the amino acid sequence of a protein which reduce its stability and may prevent it from folding properly. The majority of genetic mutations that lead to the production of less stable or misfolded proteins are called missense mutations. These mutations result in the substitution of a single amino acid for another in the protein. Because of this error, missense mutations often result in proteins that have a reduced level of biological activity. In addition to missense mutations, there are also other types of mutations that can result in proteins with reduced biological activity.

Proteins generally fold in a specific region of the cell known as the endoplasmic reticulum, or ER. The cell has quality control mechanisms that ensure that proteins are folded into their correct three-dimensional shape before they can move from the ER to the appropriate destination in the cell, a process generally referred to as protein trafficking. Misfolded proteins are often eliminated by the quality control mechanisms after initially being retained in the ER. In certain instances, misfolded proteins can accumulate in the ER before being eliminated.

The retention of misfolded proteins in the ER interrupts their proper trafficking, and the resulting reduced biological activity can lead to impaired cellular function and ultimately to disease. In addition, the accumulation of misfolded proteins in the ER may lead to various types of stress on cells, which may also contribute to cellular dysfunction and disease.

At Amicus, we have developed a novel approach to address human genetic diseases. We use small molecule drugs, which are called pharmacological chaperones, to selectively bind to a target protein and increase its stability. The binding of the chaperone molecule helps the protein fold into its correct three-dimensional shape. This allows the protein to be trafficked from the ER to the appropriate location in the cell, thereby increasing protein activity, improving cellular function and potentially reducing cell stress.

Pharmacological chaperones represent a new way of increasing the levels of specific proteins to improve cellular function and treat disease. Our proprietary approach to the discovery of pharmacological chaperone drug candidates involves the use of rapid molecular and cell-based screening methods combined with our understanding of the intended biological function of proteins implicated in disease. We use this knowledge to select and develop compounds with desirable properties. In many cases, we are able to start with specific molecules and classes of compounds already known to interact with the target protein but not used previously as therapies. This can greatly reduce the time and cost of the early stages of drug discovery and development.

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. We are also exploring other applications in which the ability of pharmacological chaperones to increase the activity of normal proteins may provide a therapeutic benefit.

Potential Advantages of Pharmacological Chaperones for the Treatment of Lysosomal Storage Disorders

To date, we have focused on developing pharmacological chaperones for the treatment of lysosomal storage disorders. Lysosomal storage disorders are a type of metabolic disorder characterized by mutations in lysosomal enzymes, which are specialized proteins that break down cellular substrates in a part of the cell called the lysosome.

The current therapeutic standard of care for the most common lysosomal storage disorders is enzyme replacement therapy. Enzyme replacement therapy involves regular infusions of recombinant human enzyme to compensate for the deficient lysosomal enzyme. We believe that pharmacological chaperone therapy may have

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advantages relative to enzyme replacement therapy for the treatment of lysosomal storage disorders. The following table compares some features of enzyme replacement therapy to pharmacological chaperone therapy.

Product Characteristic	Enzyme Replacement Therapy	Pharmacological Chaperone Therapy
Biodistribution	Variable tissue distribution	Broad tissue distribution, including brain
Ease of Use	Weekly or every other week intravenous infusion	Oral administration
Manufacturing	Recombinant protein manufacturing	Chemical synthesis

An additional therapeutic approach to the treatment of certain lysosomal storage disorders is called substrate reduction therapy. We believe our pharmacological chaperone therapies may have advantages relative to substrate reduction therapy. Substrate reduction therapy uses orally-administered small molecules; however, the underlying mechanism of action is very different than for pharmacological chaperones. Substrate reduction therapies are designed to prevent the production of the substrate that accumulates in disease by inhibiting an enzyme required to make the substrate in cells. This is not the same enzyme that is deficient in the disease. Importantly, if synthesis of the substrate is inhibited it cannot perform its normal biological functions. Additionally, the enzyme that is inhibited is needed to make other molecules that are used in other biological processes. As a result, inhibiting this enzyme may have adverse effects that are difficult to predict. By contrast, our pharmacological chaperones are designed to bind directly to the enzyme deficient in the disease, increasing its stability and helping it fold into its correct three-dimensional shape. This in turn enables proper trafficking to the lysosome where the enzyme can directly decrease substrate accumulation.

To date, one substrate reduction therapy product has received regulatory approval in the United States and the European Union for the treatment of one lysosomal storage disorder. Zavesca, a substrate reduction therapy product commercialized by Actelion, Ltd., is approved for the treatment of Gaucher disease in the United States, the European Union and other countries.

Our Lead Product Candidates

The following table summarizes key information about our product candidates. All of our current product candidates are orally-administered, small molecules based on our pharmacological chaperone technology.

Product Candidate	Indication	Stage of Development	Worldwide Commercial Rights
Amigal	Fabry Disease	Phase II	Amicus
Plicera	Gaucher Disease	Phase II	Amicus
AT2220	Pompe Disease	Phase I	Amicus

Amigal for Fabry Disease

Overview

Our most advanced product candidate, Amigal, is an orally-administered, small molecule pharmacological chaperone for the treatment of 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 who 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 alpha-galactosidase A, or -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.

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Globotriaosylceramide, or 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 two patients treated in our Phase II clinical trials and were assessed by a blinded independent expert using light and electron microscopy. A decrease of GL-3 levels was observed in multiple cell types of the kidney of one patient after 12 weeks of treatment. A second patient also showed a decrease of GL-3 levels in these 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. These initial results are consistent with the GL-3 reductions we have observed after oral administration of Amigal to mice that produce a form of human -GAL found in some Fabry patients.

We expect to complete our Phase II clinical trials of Amigal by the end of 2007. In February 2004, the FDA granted orphan drug designation to Amigal for the treatment of Fabry disease and in March 2006, the European Medicines Agency, or EMEA, recommended orphan medicinal product designation for Amigal.

Causes of Fabry Disease and Rationale for Use of Amigal

Fabry disease is a lysosomal storage disorder resulting from a deficiency in -GAL. Symptoms can be severe and debilitating, including kidney failure and increased risk of heart attack and stroke. The deficiency of -GAL in Fabry patients is caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of -GAL that may result in the production of -GAL with reduced stability that does not fold into its correct three-dimensional shape. Although -GAL produced in patient cells often retains the potential for some level of biological activity, the cell s quality control mechanisms recognize and retain misfolded -GAL in the endoplasmic reticulum, or ER, until it is ultimately moved to another part of the cell for degradation and elimination. Consequently, little or no -GAL moves to the lysosome, where it normally breaks down GL-3. This leads to accumulation of GL-3 in cells, which is believed to be the cause of the symptoms of Fabry disease. In addition, accumulation of the misfolded -GAL enzyme in the ER may lead to stress on cells and inflammatory-like responses, which may contribute to cellular dysfunction and disease.

Amigal is designed to act as a pharmacological chaperone for -GAL by selectively binding to the enzyme, which increases its stability and helps the enzyme fold into its correct three-dimensional shape. This stabilization of -GAL allows the cell s quality control mechanisms to recognize the enzyme as properly folded so that trafficking of the enzyme to the lysosome is increased, enabling it to carry out its intended biological function, the metabolism of GL-3. As a result of restoring the proper trafficking of -GAL from the ER to the lysosome, Amigal also reduces the accumulation of misfolded protein in the ER, which may alleviate stress on cells and some inflammatory-like responses that may be contributing factors in Fabry disease.

Because Amigal increases levels of a patient s naturally produced -GAL, those Fabry disease patients with a missense mutation or other genetic mutations that result in production of -GAL that is less stable but with some residual enzyme activity are the ones most likely to respond to treatment with Amigal. We estimate that the majority of patients with Fabry disease may respond to pharmacological chaperone therapy. Patients with genetic mutations leading to a partially made -GAL enzyme or -GAL enzyme with an irreversible loss of activity are less likely to respond to treatment with Amigal.

Fabry Disease Background

The clinical manifestations of Fabry disease span a broad spectrum of severity and roughly correlate with a patient s residual -GAL levels. The majority of currently treated patients are referred to as classic Fabry disease patients, most

of whom are males. These patients experience disease of various organs, including the kidneys, heart and brain, with disease symptoms first appearing in adolescence and typically progressing in severity until death in the fourth or fifth decade of life. A number of recent studies suggest that there are a large number of undiagnosed males and females that have a range of Fabry disease symptoms, such as impaired cardiac or renal function and strokes, that usually first appear in adulthood. Individuals with this type

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of Fabry disease, referred to as later-onset Fabry disease, tend to have higher residual -GAL levels than classic Fabry disease patients. Although the symptoms of Fabry disease span a spectrum of severity, it is useful to classify patients as having classic or later-onset Fabry disease when discussing the disease and the associated treatable population.

Classic Fabry Disease

Individuals with classic Fabry disease are in most instances males. They have little or no detectable -GAL levels and are the most severely affected. These patients first experience disease symptoms in adolescence, including pain and tingling in the extremities, skin lesions, a decreased ability to sweat and clouded eye lenses. If these patients are not treated, their life expectancy is reduced and death usually occurs in the fourth or fifth decade of life from renal failure, cardiac dysfunction or stroke. Studies reported in JAMA (January 1999) and The Metabolic and Molecular Bases of Inherited Disease (8th edition 2001) suggest the annual incidence of Fabry disease in newborn males is 1:40,000-1:60,000. Current estimates from the University of Iowa and the National Kidney Foundation suggest that there are a total of approximately 5,000 classic Fabry disease patients worldwide.

Later-onset Fabry Disease

Individuals with later-onset Fabry disease can be male or female. They typically first experience disease symptoms in adulthood, and often have disease symptoms focused on a single organ. For example, many males and females with later-onset Fabry disease have enlargement of the left ventricle of the heart. As the patients advance in age, the cardiac complications of the disease progress and can lead to death. Studies reported in Circulation and Journal of the American Heart Association (March 2002 and August 2004), estimated that 6-12% of patients between 40 and 60 years of age with an unexplained enlargement of the left ventricle of the heart, a condition referred to as left ventricular hypertrophy, have Fabry disease.

A number of males and females also have later-onset Fabry disease with disease symptoms focused on the kidney that progress to end stage renal failure and eventually death. Studies reported in Nephrology Dialysis Transplant (2003), Clinical and Experimental Nephrology (2005) and Nephrology Clinical Practice (2005) estimate that 0.20% to 0.94% of patients on dialysis have Fabry disease.

In addition, later-onset Fabry disease may also present in the form of strokes of unknown cause. A recent study reported in The Lancet (November 2005) found that approximately 4% of 721 male and female patients in Germany between the ages of 18 to 55 with stroke of unknown cause have Fabry disease.

It was previously believed to be rare for female Fabry disease patients to develop overt clinical manifestations of Fabry disease. Fabry disease is known as an X-linked disease because the inherited -GAL gene mutation is located only on the X chromosome. Females inherit an X chromosome from each parent and therefore can inherit a Fabry mutation from either parent. By contrast, males inherit an X chromosome (and potentially a Fabry mutation) only from their mothers. For this reason, there are expected to be roughly twice as many females as males that have Fabry disease mutations. Recently, several studies reported in the Journal of Medical Genetics (2001), the Internal Medicine Journal (2002) and the Journal of Inherited Metabolic Disease (2001), each of which is summarized on the website of the Mount Sinai School of Medicine, Department of Genetics and Genomic Sciences, report that, while the majority of females with Fabry disease mutations have mild symptoms, many have severe symptoms, including enlargement of the left ventricle of the heart and/or renal failure.

In a recent study reported in the American Journal of Human Genetics, more than thirty-seven thousand newborn males in Italy were screened for -GAL activity and mutations. The incidence of Fabry mutations in this study was 1:3100, over ten times higher than previous estimates. This high incidence was attributed to a large number of newborn males with -GAL mutations often associated with later-onset Fabry disease, which may not have been

identified in previous screening studies that relied on diagnosis based on development of symptoms of classic Fabry disease.

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Fabry Disease Market Opportunity

Fabry disease is a relatively rare disorder. The current estimates of approximately 5,000 patients worldwide are generally based on a small number of studies in single ethnic populations in which people were screened for classic Fabry disease. The results of these studies were subsequently extrapolated to the broader world population assuming similar prevalence rates across populations. We believe these previously reported studies did not account for the prevalence of later-onset Fabry disease and, as described above, a number of recent studies suggest that the prevalence of Fabry disease could be many times higher than previously reported.

We expect that as awareness of later-onset Fabry disease grows, the number of patients diagnosed with the disease will increase. Increased awareness of all forms of Fabry disease, particularly for specialists not accustomed to treating Fabry disease patients, may lead to increased testing and diagnosis of patients with the disease. We intend to develop and launch educational and awareness campaigns targeting cardiologists, nephrologists and neurologists regarding Fabry disease and its diagnosis. Assuming we receive regulatory approval, we expect these educational and awareness campaigns would continue as a part of the marketing of Amigal. In order to facilitate the proper diagnosis of Fabry disease patients seen by specialist physicians, we intend to provide support for testing for the disease, which is performed using a simple blood test for the level of -GAL activity.

Based on published data from the Human Gene Mutation Database and our experience in the field, we believe the majority of the known genetic mutations that cause Fabry disease are missense mutations. There are few widely-occurring genetic mutations reported for Fabry disease, suggesting that the frequency of a specific genetic mutation reported in the Human Gene Mutation Database reflects the approximate frequency of that mutation in the general Fabry patient population. In addition, data presented at the 11th International Conference on Health Problems Related to the Chinese (2002) suggest that the vast majority of newly diagnosed patients with later-onset Fabry disease also have missense mutations. Because missense mutations often result in less stable, misfolded -GAL with some residual enzyme activity, we believe patients with these mutations may benefit from treatment with Amigal. We also believe that other types of genetic mutations may result in misfolded -GAL and therefore may respond to treatment with Amigal. Based on this, we believe that a majority of the Fabry disease patient population may benefit from treatment with Amigal.

Existing Products for the Treatment of Fabry Disease and Potential Advantages of Amigal

The current standard of treatment for Fabry disease is enzyme replacement therapy. There are currently two products approved for the treatment of Fabry disease. One of the products is Fabrazyme, a product approved globally and commercialized by Genzyme Corporation. Fabrazyme was approved in the United States in 2003 and has orphan drug exclusivity in the United States until 2010. It was approved in the European Union in 2001 and has orphan drug exclusivity in the European Union until 2011. The other product approved for treatment of Fabry disease is Replagal, a product approved in the European Union and other countries but not in the United States, commercialized by Shire PLC. Replagal was approved in the European Union in August 2001 and has orphan drug exclusivity in the European Union until 2011. The net product sales of Fabrazyme and Replagal for 2006 were approximately $359 million and $118 million, respectively, as publicly reported by Genzyme Corporation and Shire PLC, respectively.

Prior to the availability of enzyme replacement therapy, treatments for Fabry disease were directed at ameliorating symptoms without treating the underlying disease. Some of these treatments include opiates, anticonvulsants, antipsychotics and antidepressants to control pain and other symptoms, and beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin receptor antagonists and other agents to treat blood pressure and vascular disease.

For Fabry disease patients who respond to Amigal, we believe that the use of Amigal may have advantages relative to the use of Fabrazyme and Replagal. Published data for patients treated with Fabrazyme and Replagal for periods of up to five years demonstrate that these drugs can lead to the reduction of GL-3 in multiple cell types in the skin, heart and kidney. However, because they are large protein molecules, Fabrazyme and Replagal are believed to have difficulty penetrating some tissues and cell types. In particular,

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it is widely believed that Fabrazyme and Replagal are unable to cross the blood-brain barrier and thus are unlikely to address the neurological symptoms of Fabry disease. As a small molecule therapy that has demonstrated high oral bioavailability and good biodistribution properties in preclinical testing, Amigal has the potential to reach cells of all the target tissues of Fabry disease. Furthermore, treatment with Fabrazyme and Replagal requires intravenous infusions every other week, frequently on-site at health care facilities, presenting an inconvenience to Fabry patients. Oral treatment with Amigal may be much more convenient for patients and may not have the safety risks associated with intravenous infusions. See Potential Advantages of Pharmacological Chaperones in the Treatment of Lysosomal Storage Disorders .

In February 2004, Amigal was granted orphan drug designation by the FDA for the treatment of Fabry disease and in March 2006 the EMEA recommended orphan medicinal product designation for Amigal. We believe that orphan drug designation of Fabrazyme in the United States and of Fabrazyme and Replagal in the European Union will not prevent us from obtaining marketing approval of Amigal in either geography. See Government Regulation .

Amigal Development Activities

Preclinical Activities

We have completed experiments in collaboration with researchers in the field to better understand the mechanism of action of Amigal. In one experiment we crystallized -GAL both alone and with Amigal. These data demonstrate that Amigal binds directly to the active site of -GAL. See Figure 1 below.

Figure 1: Crystal Structure of -GAL with Amigal

We have conducted multiple in vitro and in vivo preclinical studies of Amigal. Key findings of our studies include:

- Amigal increased -GAL enzyme levels in cells derived from a variety of different Fabry disease patients. Over 60 different -GAL missense mutations have been examined in cell culture assays with approximately 65% showing an increase in -GAL enzyme levels after incubation with Amigal for several days.

- Treatment of normal mice and mice that produce a form of human -GAL resulted in a dose-dependent increase in -GAL enzyme levels in a variety of tissues including skin, liver, heart, kidney and spleen.

- Treatment of mice that produce a form of human -GAL resulted in both an increase of -GAL enzyme levels and a decrease in GL-3 levels in skin, heart and kidney.

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Amigal had an acceptable toxicity profile when tested at high exposure levels in rats, dogs and monkeys. Amigal showed no signs of systemic toxicity in two-week studies in rats, dogs and monkeys, in six-month studies in rats and in nine-month studies in monkeys when tested at levels that were well above those that we are studying in our current Phase II clinical trials. In the nine-month monkey study, all doses were well tolerated and showed no signs of toxicity.

Some treatment-related effects on reproduction and fertility have been observed in rabbit and rat studies. At high exposure levels that were well above those that we are studying in our current Phase II clinical trials, maternal toxicity studies in rabbits showed a dose-related increase in embryonic death, a reduction in fetal weight, delayed bone development and slightly increased incidences of other minor skeletal abnormalities. These effects were not seen in rats. At exposure levels within the range of those we are studying in our current Phase II clinical trials, male rats experienced infertility, which was completely reversible within four weeks after discontinuation of treatment. No treatment-related changes have been detected in the male rat reproductive organs or sperm to account for the infertility and no mechanism of action has been established to explain this effect. The implications for humans, if any, of these treatment-related reproductive and fertility effects in rabbit and rat studies are unknown at this time. We are currently planning additional reproductive toxicity and carcinogenicity studies with Amigal in accordance with standard regulatory guidelines.

Phase I Clinical Trials

We have completed Phase I clinical trials of Amigal in a total of 48 healthy volunteers, of which 36 were treated with Amigal and 12 were given placebo.

Single Dose Phase I Trial. Our single-dose Phase I trial was a single center, randomized, dose ranging study in healthy volunteers. The clinical phase began in July 2004 and was completed in November 2004. The study consisted of a total of 32 healthy volunteers divided into four groups of eight subjects. Six subjects in each group received Amigal and two subjects received placebo. All subjects received single doses of placebo or 25 mg, 75 mg, 225 mg or 675 mg of Amigal and were evaluated on Day 1 and on Day 8. The objectives of the study were to evaluate the safety and pharmacokinetics of Amigal in healthy volunteers.

Multiple-Dose Phase I Trial. Our multiple-dose Phase I trial was a single center, randomized, dose ranging study in healthy volunteers. The clinical phase began in December 2004 and was completed in January 2005. The study consisted of a total of 16 healthy volunteers divided into two groups of eight subjects. Six subjects in each group received Amigal and two subjects received placebo. All subjects in one group received placebo or 50 mg twice a day for seven days, and all subjects in the other group received placebo or 150 mg twice a day for seven days. Subjects were evaluated at the beginning of the study, on Day 7 after seven days of treatment and on Day 14 after a seven day washout period. The objectives of the study were to evaluate the safety and pharmacokinetics of Amigal in healthy volunteers and to measure -GAL enzyme levels in white blood cells of healthy volunteers treated with Amigal.

The data from our Phase I clinical trials in healthy volunteers showed that Amigal 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 studies also demonstrate that Amigal has high oral bioavailability with a terminal half-life in plasma of approximately three to four hours.

In addition, the data from the multiple-dose Phase I trial showed a dose-related increase in the level of -GAL in the white blood cells of healthy volunteers administered Amigal for seven days. At the highest dose level there was approximately a 2-fold increase in levels of -GAL, and this increase was maintained for at least seven days after the last dose. We believe normal enzyme levels can be increased because some fraction of normal protein molecules can

also misfold and fail to pass the cell s quality control mechanisms. Normal -GAL is stabilized by binding to the pharmacological chaperone, which results in an increase in the amount successfully trafficked to the lysosome. We believe the sustained elevation of enzyme levels following discontinuation of treatment occurs because the enzyme is stable for many days once it reaches the lysosome.

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We believe these Phase I results are the first demonstration of an increase in enzyme levels in humans following oral administration of a pharmacological chaperone.

Phase II Clinical Trials

We have completed enrollment of our four open-label Phase II clinical trials of Amigal with a target aggregate enrollment for all four trials of between 20 and 25 patients, and have obtained initial results for the first eleven patients who have completed at least 12 weeks of treatment. These studies were open to male and female patients with all forms of Fabry disease, including both classic and later-onset Fabry disease.

In order to qualify for these clinical studies, patients must have a confirmed diagnosis of Fabry disease with a documented missense mutation in -GAL and a positive result in either an in vitro or in vivo test of the effect of Amigal on -GAL enzyme levels. The in vitro test requires a simple blood draw and consists of incubation of a patient s cells derived from white blood cells, with and without Amigal for a period of time followed by measurement of -GAL enzyme activity. The in vivo test involves measuring -GAL enzyme activity from white blood cells before and after 2 weeks of treatment to assess response. For entry into the Phase II clinical trials, enzyme activity from a patient s white blood cells must show a relative increase of at least 20% to 100% after treatment in the in vitro or in vivo screen, depending on the amount of baseline -GAL activity.

We have four ongoing Phase II clinical trials.

Phase II Study 201. Eight patients have been treated in this study and an additional patient is in screening. Enrollment is complete and the study is expected to be finished by the end of 2007. The study consists of treatment with Amigal for a period of twelve weeks with a possible extension up to 48 weeks in male Fabry disease patients that are naïve to enzyme replacement therapy or have not had enzyme replacement therapy for at least one month. These eight patients received 25 mg of Amigal twice a day for two weeks, followed by 100 mg of Amigal twice a day for two weeks, followed by 250 mg of Amigal twice a day for two weeks and followed by 25 mg of Amigal twice a day for six weeks. All eight patients are currently in the extension phase and are now receiving 50 mg of Amigal once a day.

Phase II Study 202. Two patients have been treated in this study and additional patients are in screening. Enrollment is complete and the study is expected to be finished by the end of 2007. The study consists of treatment with Amigal for a period of 24 weeks with a possible extension to 48 weeks in male Fabry disease patients that are naïve to enzyme replacement therapy or have not had enzyme replacement therapy for at least one month. All patients will receive 150 mg of Amigal every other day during the duration of the study.

Phase II Study 203. Four patients have been treated in this study and additional patients are in screening. Enrollment is complete and the study is expected to be finished by the end of 2007. The study consists of treatment with Amigal for a period of 12 weeks with a possible extension to 48 weeks in male Fabry disease patients that are naïve to enzyme replacement therapy or have not had enzyme replacement therapy for at least one month. All patients will receive 150 mg of Amigal every other day during the duration of the study.

Phase II Study 204. Five patients have been treated in this study and additional patients are in screening. Enrollment is complete and the study is expected to be finished by the end of 2007. The study consists of treatment with Amigal for a period of 12 weeks with a possible extension to 48 weeks in female Fabry disease patients that are naïve to enzyme replacement therapy or have not had enzyme replacement therapy for at least one month. Patients will receive 50 mg, 150 mg or 250 mg doses of Amigal every other day for 12 weeks. If the patient participates in the extension phase, the dose during the extension will be determined based on data from the first 12 weeks.

The primary objective of the Phase II clinical trials is to evaluate the safety and tolerability of Amigal in patients with Fabry disease. The secondary objective is to evaluate certain pharmacodynamic measures of treatment with Amigal including effects on -GAL activity and GL-3 levels. GL-3 levels are measured from skin biopsies,

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kidney biopsies, plasma and urine of patients in all four ongoing Phase II clinical studies of Amigal except Study 201 which does not include kidney biopsies. An additional objective of the Phase II clinical trials is the preliminary assessment of Amigal s effect on cardiac, renal and central nervous system function in Fabry disease patients.

Preliminary Data From Our Ongoing Phase II Clinical Trials

We have obtained initial results for the first eleven patients who have completed at least 12 weeks of treatment in our Phase II clinical trials of 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.

Initial results for the first eleven patients suggest that treatment with Amigal causes an increase in the level of -GAL that we believe is likely to be clinically meaningful for a wide range of Fabry patients. Figure 2 below summarizes the available white blood cell -GAL data for all eleven patients that have completed at least 12 weeks of treatment.

Figure 2: Enzyme Activity Response to Treatment with Amigal

Patients in the 202, 203 and 204 studies received 150 mg of Amigal every other day throughout the study.
For purposes of calculating the percentage of normal in the table, the level of -GAL that is normal was derived by using the average of the levels of -GAL in white blood cells of 15 healthy volunteers from the multiple-dose Phase I trial.

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A summary of the preliminary data displayed in Figure 2 is provided below.

The eleven patients represent ten different genetic mutations.

The eleven patients consist of ten males and one female.

The eleven patients have baseline levels of -GAL enzyme activity in white blood cells that range from 0% to 30% of normal.

Patients have been treated with various doses and regimens of Amigal for various periods of time in accordance with relevant protocols of our Phase II clinical trials.

An increase in the level of -GAL in white blood cells was observed in ten out of eleven patients.

The results suggest a dose dependence particularly in several patients in Study 201, which included ascending doses through Week 6 and then a significantly decreased dose thereafter.

We believe the -GAL responses observed are likely to be therapeutically meaningful because it is generally believed that even small increases in lysosomal enzyme levels may have clinical benefits.

We believe that these results provide the first evidence in patients of an effect of an orally administered pharmacological chaperone on its intended protein target.

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 cells of the interstitial capillaries of the kidney was the basis of prior regulatory approval by the FDA of an enzyme replacement therapy for the treatment of Fabry disease. Initial data on kidney GL-3 levels before and after treatment with Amigal are available for two patients in our Phase II clinical trials.

Kidney GL-3 levels were assessed by an independent expert using light and electron microscopy. The expert was blinded to sample identification, including patient information and whether the sample came from a patient before or after treatment. GL-3 accumulation in each cell type was scored using a scale of 0-3 units, with 3 indicating severe GL-3, 2 indicating moderate GL-3, 1 indicating mild GL-3, and 0 indicating no GL-3. When the level of GL-3 in a cell was assessed to be in between scoring units, half point scores were used. For example, a score of 0.5 designates a cell with detectable GL-3, but at levels that are not as high as in a cell scored as 1. A change in GL-3 of at least 1 unit is considered conclusive. This same scoring system was used for the prior regulatory approval by the FDA of an enzyme replacement therapy for the treatment of Fabry disease.

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Figure 3: GL-3 Response to Treatment with Amigal in Various Kidney Cell Types

A summary of the preliminary data displayed in Figure 3 is provided below.

A decrease in GL-3 of at least 1 unit was observed in the kidney of one patient after 12 weeks of treatment in mesangial cells and the cells of the glomerular endothelium and distal tubules.

A second patient also showed a decrease of GL-3 levels in these same kidney cell types. In this patient, some of the scores were zero after treatment, but the decreases cannot be considered conclusive on their own because they involved a change of less than 1 full unit due to the lower levels of GL-3 observed at baseline.

Both patients showed a decrease of GL-3 levels in other kidney cell types including cells of the interstitial capillaries, but the decreases were less than 1 unit and, thus, even though the post-treatment GL-3 score was zero, cannot be considered independently conclusive.

Some kidney cell types such as podocyte cells did not show signs of GL-3 reduction.

Results are presented as determined by electron microscopy, however light and electron microscopy values were generally consistent with one another.

These initial results are consistent with the GL-3 reductions observed after oral administration of Amigal to mice that produce a form of human -GAL.

We believe that these data are the first evidence in patients of treatment with a pharmacological chaperone resulting in an effect on the biological activity of the intended protein target.

A summary of additional preliminary data from the first eleven patients that have completed 12 weeks of treatment is provided below.

Skin GL-3 levels at baseline and after treatment as assessed by light and electron microscopy are available for 10 patients. Seven patients had skin GL-3 levels that were normal or near normal both before and after treatment. Results for the three other patients were difficult to interpret because they showed evidence of a decrease in GL-3 in some skin cell types and an increase in GL-3 in other skin cell types, with variability over time.

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Urine and plasma GL-3 levels at baseline and after treatment as assessed by liquid chromatography mass spectrometry are available for 10 patients. Most patients had GL-3 levels in urine and plasma that were normal or near normal both before and after treatment. For the few patients that had elevated levels of GL-3 in urine or plasma at baseline, the results were difficult to interpret due to high intra-patient variability.

Most patients in these studies had normal or near normal cardiac, renal and central nervous system function before treatment, and no clinically meaningful changes have been observed after 12 to 48 weeks of treatment.

The available data from the first eleven patients suggest that treatment with Amigal causes an increase in the level of -GAL for a wide range of Fabry patients. 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. We also believe the initial kidney GL-3 data suggest that the increased level of -GAL that occurs after treatment with Amigal may result in a decrease in the substrate believed to be the cause of the symptoms of Fabry disease. Reduction of the level of GL-3 in cells of the interstitial capillaries 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 believe the preliminary results from the first eleven Fabry patients support the continuation of our current Phase II clinical trials.

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 trials or additional data from these first eleven patients may cause the assessment of our Phase II trials to differ from or be less favorable than the assessment based on the initial results presented above. We cannot guarantee that our Phase II clinical trials will ultimately be successful.

Plicera for Gaucher Disease

Overview

Our second most advanced clinical product candidate, Plicera, is an orally-administered, small molecule, pharmacological chaperone for the treatment of Gaucher disease. We completed Phase I clinical trials which demonstrated that Plicera was safe and well tolerated in healthy subjects at all doses tested. We are currently conducting Phase II clinical trials of Plicera in Type I Gaucher patients. We expect to complete enrollment and obtain preliminary results of our Phase II trials in 2007. In February 2006, the FDA granted orphan drug designation for Plicera for the treatment of Gaucher disease in the United States.

Causes of Gaucher Disease and Rationale for Use of Plicera

Gaucher disease is a lysosomal storage disorder resulting from a deficiency in the enzyme, -glucocerebrosidase, or GCase. Signs and symptoms can be severe and debilitating, including an enlarged liver and spleen, abnormally low levels of red blood cells and platelets, and skeletal complications. In some forms of the disease there is also significant impairment of the central nervous system. The deficiency of GCase in Gaucher patients is caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of GCase that may result in the production of GCase with reduced stability that does not fold into its correct three-dimensional shape. Although GCase produced in patient cells often retains the potential for some level of biological activity, the cell s quality control mechanisms recognize and retain misfolded GCase in the ER until it is ultimately moved to another part of the cell for degradation and elimination. Consequently, little or no GCase moves to the lysosome, where it normally breaks down its substrate, a complex lipid called glucocerebroside. This leads to accumulation of glucocerebroside in cells, which is believed to result in the clinical manifestations of Gaucher disease. In addition, the accumulation of the misfolded GCase enzyme in the ER may lead to cellular stress and inflammatory-like responses, which may contribute to cellular dysfunction and disease.

Plicera is designed to act as a pharmacological chaperone for GCase by selectively binding to the enzyme, which increases the stability of the enzyme and helps it fold into its correct three-dimensional shape. This stabilization of GCase allows the cell s quality control mechanisms to recognize the enzyme as properly

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folded so that trafficking of the enzyme to the lysosome is increased, enabling it to carry out its intended biological function, the metabolism of glucocerebroside. As a result of restoring proper trafficking of GCase from the ER to lysosomes, Plicera reduces the accumulation of misfolded GCase in the ER, which may alleviate cellular stress and inflammatory-like responses that may be contributing factors in Gaucher disease.

Because Plicera increases the cellular levels of a patient s naturally produced GCase, those Gaucher disease patients with a missense mutation or other genetic mutation that results in production of GCase that is less stable but with some residual enzyme activity are the ones most likely to respond to treatment with Plicera. We estimate that the substantial majority of patients with Gaucher disease may respond to pharmacological chaperone therapy. Patients with genetic mutations leading to a partially made GCase enzyme or GCase enzyme with an irreversible loss of activity are less likely to respond to treatment with Plicera.

Gaucher Disease Background

Gaucher disease is often described in terms of the following three clinical subtypes:

Type I Chronic Nonneuronopathic Gaucher Disease. Type I Gaucher disease is the most common subtype affecting more than 90% of patients and symptoms usually first appear in adulthood. Type I Gaucher disease is characterized by the occurrence of an enlarged spleen and liver, anemia, low platelet counts and fractures and bone pain. Patients with Type I Gaucher disease do not experience the neurological features associated with Types II and III Gaucher disease. The clinical severity of Type I Gaucher disease is extremely variable with some patients experiencing the full range of symptoms, while others are asymptomatic throughout most of their lives.

Type II Acute Neuronopathic Gaucher Disease. Type II Gaucher disease symptoms typically appear in infancy with an average age of onset of about three months. Type II Gaucher disease involves rapid neurodegeneration with extensive visceral involvement that usually results in death before two years of age, typically due to respiratory complications. The clinical presentation in Type II Gaucher disease is typically more uniform than Type I Gaucher disease.

Type III Subacute Neuronopathic Gaucher Disease. Type III Gaucher disease symptoms typically first appear in infancy or early childhood and involve some neurological symptoms, along with visceral and bone complications. Age of onset and disease severity can vary widely. Disease progression in Type III Gaucher disease is typically slower than in Type II Gaucher disease.

Gaucher Disease Market Opportunity

Gaucher disease is a relatively rare disorder. According to estimates reported by the American Society of Health-System Pharmacists (August 2003) and the National Institute of Neurological Disorders and Stroke (updated as of January 2006) there are approximately 10,000 patients worldwide. Type I Gaucher disease is, by far, the most common of the subtypes.

Published data, including data from the Human Gene Mutation Database, suggest that the substantial majority of patients with Gaucher disease have a missense mutation in at least one copy of the gene. The majority of the Type I Gaucher patients in the United States, Europe and Israel have at least one copy of either the N370S or the L444P mutation, both of which are missense mutations. Based on our experience in the field and studies we have completed, including a Gaucher Ex Vivo Response Study, we believe that the substantial majority of individuals with Gaucher disease may benefit from treatment with Plicera. In addition, we believe that Plicera may also benefit some patients with the neuronopathic forms of Gaucher disease (Type II and Type III) because of the ability of the small molecule to

cross the blood-brain barrier.

Existing Products for the Treatment of Gaucher Disease and Potential Advantages of Plicera

The current standard of treatment for Gaucher patients is enzyme replacement therapy. There are currently two products approved for the treatment of Gaucher disease, one of which is an enzyme replacement therapy. One of the products is Cerezyme, an enzyme replacement therapy approved globally and commercialized by Genzyme Corporation. Cerezyme was approved in the United States in 1994 and in the European Union in

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1997 and no longer has orphan drug exclusivity in the United States. In the United States, Cerezyme is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type I Gaucher disease. In the European Union, it is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type I Gaucher disease and for Type III Gaucher disease patients who exhibit clinically significant non-neurological manifestations. The other product approved for treatment of Gaucher disease is Zavesca, a substrate reduction therapy product approved in the United States, the European Union and other countries and commercialized by Actelion, Ltd. Zavesca was approved in the United States in 2003 and has orphan drug exclusivity in the United States until 2010. It was approved in the European Union in 2002 and has orphan drug exclusivity in the European Union until 2012. It is indicated for adults with mild to moderate Type I Gaucher disease for whom enzyme replacement therapy is not an option. The net product sales of Cerezyme and Zavesca for the year 2006 were approximately $1.0 billion and $20 million, respectively, as publicly reported by Genzyme Corporation and Actelion Ltd. respectively.

For Gaucher disease patients who respond to Plicera, we believe that the use of Plicera may have advantages relative to the use of Cerezyme. Published data demonstrate that treatment with Cerezyme can lead to the reduction of glucocerebroside in multiple tissue types, especially the liver and spleen, and to increased levels of red blood cells and platelets. However, because it is a large protein molecule, Cerezyme is believed to have difficulty penetrating some tissues and cell types. In particular, it is widely believed that Cerezyme is unable to cross the blood-brain barrier and thus unlikely to address the neurological symptoms of Type II and Type III Gaucher disease. Studies in animals show that Plicera distributes throughout the body. In particular, studies show that Plicera crosses the blood-brain barrier, suggesting that it may provide a clinical benefit to patients with Type II and Type III Gaucher disease. Additionally, treatment with Cerezyme requires intravenous infusions every other week, presenting an inconvenience to Gaucher disease patients. Oral treatment with Plicera may be more convenient for patients and may not have the safety risks associated with intravenous infusions. See Potential Advantages of Pharmacological Chaperones in the Treatment of Lysosomal Storage Disorders .

We also believe that Plicera may have advantages over the use of Zavesca, a substrate reduction therapy. Zavesca is an orally-administered small molecule; however, the underlying mechanism of action is very different than for pharmacological chaperones. Substrate reduction therapies are designed to prevent the production of the substrate that accumulates in disease by inhibiting an enzyme required to make the substrate in cells. This is not the same enzyme that is deficient in Gaucher disease. Importantly, the enzyme that is inhibited is needed to make molecules that are used for many types of biological processes. As a result, inhibiting this enzyme may have adverse effects that are difficult to predict. By contrast, Plicera is designed to bind directly to GCase, increasing its stability and helping it fold into its correct three-dimensional shape. This in turn enables proper trafficking to the lysosome where it can directly decrease substrate accumulation. Several side effects were reported by Actelion, Ltd. in clinical trials of Zavesca, including diarrhea, which was observed in more than 85% of patients who received the drug. Other side effects included hand tremors and numbness and tingling in the hands, arms, legs or feet. Plicera s mechanism of action is very different from Zavesca s, and we do not expect it to have the same side-effect profile.

In February 2006, the FDA granted orphan drug designation for the active ingredient in Plicera for the treatment of Gaucher disease in the United States. We believe that the orphan drug designation of Zavesca in the United States and the European Union will not prevent us from obtaining marketing approval of Plicera in either geography. See Government Regulation .

Plicera Development Activities

Preclinical Activities

We have conducted experiments in collaboration with researchers in the field to better understand the mechanism of action of Plicera. The primary conclusions of these experiments are summarized below.

We have crystallized GCase both alone and with Plicera. These structural data demonstrate that Plicera binds directly to the active site of GCase. See Figure 4 below.

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In vitro exposure to Plicera increased transport of GCase to the lysosome in cells derived from a patient with the N370S mutation. Once in the lysosome, the enzyme was stable and active for more than 3 days after Plicera was removed. The N370S is the most common mutation associated with Gaucher disease in the western world.

Figure 4: Crystal Structure of GCase with Plicera

We have conducted several in vitro and in vivo preclinical studies of Plicera. Key findings of our studies are listed below.

Oral administration of Plicera to both normal mice and mice expressing the L444P mutation resulted in a dose-dependent increase in GCase levels in the liver, spleen, brain and lungs. The L444P is one of the most common mutations associated with Gaucher disease.

Oral administration of Plicera to L444P mice resulted in decreased spleen and liver weights and reduced plasma IgG and chitin III levels, which are biomarkers related to Gaucher disease.

Oral administration of Plicera resulted in increased GCase levels in cells from hard bone and bone marrow in mice.

In 14-day, short-term, repeat dose, oral administration studies in rats and monkeys, no mortality or morbidity was observed at dose levels up to 1,500 mg/kg of Plicera. This dose was significantly higher than the human equivalent doses being considered for our future clinical studies. All toxicities were found to be reversible or showed a trend toward reversibility. The clinical implications of these preclinical observations are unknown at this time. The primary treatment-related toxicities were thickening of the lining of the forestomach of rats and mild reddening of the skin of monkeys. The forestomach is a region of the stomach that is only present in rodents and its lining is structurally similar to skin.

Six-month data from 9-month, repeat dose, oral administration studies in rats and monkeys showed that there was no mortality or morbidity at dose levels up to 200 mg/kg of Plicera. As in the 14-day toxicology studies, the primary treatment-related toxicities were thickening of the lining of the forestomach of rats and mild reddening of the skin of monkeys. All toxicities were found to be dose related and reversible or showed a trend toward reversibility. The clinical implications of these preclinical observations are unknown at this time. While the toxicities were observed at exposures comparable to the projected human exposure, the effect on the skin of the monkeys was very mild and any potential effect on the skin of humans could be readily monitored. In our 7-day, multiple-dose Phase I clinical trial of Plicera, no comparable effects on skin were observed.

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Plicera has been tested for genotoxicity in a battery of both in vitro and in vivo genotoxicity assays. The results of these studies suggest that Plicera has an acceptable safety profile. We are currently conducting standard reproductive toxicity studies of Plicera and planning standard carcinogenicity studies.

Gaucher Ex Vivo Response Study

We have completed a study that corroborates our belief that a substantial majority of Gaucher patients may benefit from treatment with Plicera. The study evaluated and characterized the effects of Plicera in cells derived from patients with Gaucher disease. In this study, patients did not receive Plicera directly but provided blood samples from which certain cell types were isolated. We measured GCase levels in these cells before treatment and after incubation with Plicera for several days. We also measured biomarkers associated with Gaucher disease and other exploratory biomarkers. Preliminary data are available from 40 of the 53 patients who were enrolled in this study. These 40 patients included 21 males and 18 females with Type I Gaucher disease, the most common subtype of Gaucher disease which accounts for more than 90% of cases. In addition, preliminary data are available from one male with type III Gaucher disease. Out of these 40 patients, 34 (85%) had at least one copy of the GCase gene with the N370S mutation, the most common mutation in Type I Gaucher disease in the western world, found in more than 80% of the patient population. Patients ranged in age from 7 to 83 years, 38 of 40 patients were receiving enzyme replacement therapy and blood was drawn prior to infusion. We were able to derive usable cells from 34 of 40 subjects. A summary of the preliminary findings from the study is given below.

Plicera increased GCase levels in cells derived from 32 of 34 patients (94%).

Plicera increased GCase levels in cells derived from 28 of 29 patients (97%) with an N370S mutation and from 4 of 5 patients with mutations other than N370S.

Phase I Clinical Trials

We have completed two Phase I clinical trials of Plicera in a total of 72 healthy volunteers, of which 54 were treated with Plicera and 18 were given placebo.

Single-Dose Phase I Trial. Our single-dose Phase I trial was a single center, randomized, dose ranging study in healthy volunteers. The clinical phase began in June 2006 and was completed in September 2006. The study consisted of a total of 48 healthy volunteers divided into six groups of eight subjects. Six subjects in each group received oral administration of Plicera and two subjects received placebo. All subjects received single doses of placebo or 8 mg, 25 mg, 75 mg, 150 mg, 150 mg (repeat) or 300 mg of Plicera and were evaluated on Days 1 to 3 and on Day 7. The objectives of the study were to evaluate the safety and pharmacokinetics of Plicera in healthy volunteers.

Multiple-Dose Phase I Trial. Our multiple-dose Phase I trial was a single center, randomized, dose ranging study in healthy volunteers. The clinical phase began in August 2006 and was completed in October 2006. The study consisted of a total of 24 healthy volunteers divided into three groups of eight subjects. Six subjects in each group received oral administration of Plicera and two subjects received placebo. All subjects received placebo or 25 mg, 75 mg or 225 mg of Plicera once a day for seven days. Subjects were evaluated on Days 1 to 7 and Days 9, 14 and 21. The objectives of the study were to evaluate the safety and pharmacokinetics of Plicera in healthy volunteers and to measure the level of GCase enzyme levels in white blood cells of healthy volunteers who received Plicera.

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. In these studies, Plicera was shown to have 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 trial showed a statistically significant, dose-related increase in GCase levels in the white blood cells of normal, healthy volunteers who received oral administration of Plicera for seven days. The results are summarized below in Figure 5.

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Figure 5: GCase Response to Plicera in Normal Volunteers

GCase activity was measured in white blood cells isolated from subjects receiving Plicera in daily oral doses for 7 days. Compared to placebo, GCase activity was significantly higher and increased over time in all treatment groups. GCase activity also increased with dose with the most marked increase, in absolute terms, between 25 and 75 mg. Relative percent increases at day 7 (time of maximal increase) compared to baseline were 147%, 209% and 279% at 25, 75 and 225 mg, respectively. Upon discontinuation of Plicera, GCase activity declined, returning to or near to baseline by day 21 (14 days of wash-out). The terminal half-life for decline of GCase activity upon removal of Plicera is about 4 to 5 days.

In addition to our findings in the Fabry disease studies, we believe these Phase I results are the only other demonstration of an increase in enzyme levels in humans following oral administration of a pharmacological chaperone. We believe normal enzyme levels can be increased because some fraction of normal protein molecules can also misfold and fail to pass the cell s quality control mechanisms. Normal GCase is stabilized by binding to the pharmacological chaperone, which results in an increase in the amount of enzyme successfully trafficked to the lysosome.

Phase II Clinical Trials

We are conducting two open-label Phase II clinical trials in up to 48 adult male and female patients with Type I Gaucher disease. In order to qualify for these clinical studies, patients must have a confirmed diagnosis of Type I Gaucher disease with a documented missense mutation in GCase. We expect to obtain preliminary results from the first of these two Phase II trials by the end of 2007.

Phase II Study 201. We are conducting a Phase II trial in which we are seeking to enroll 32 patients with Type I Gaucher disease who are currently receiving enzyme replacement therapy and have agreed to discontinue their enzyme replacement therapy for a total of 7 weeks. The study is designed to assess the safety and pharmacodynamic effects of Plicera, particularly its effect on GCase levels. We will also monitor the effect of Plicera on parameters that are commonly abnormal in Gaucher disease including levels of red blood cells and platelets, although we do not expect to observe a change in these parameters in this 4-week trial because of its short duration. Patients will be assigned to one of four treatment arms and will receive Plicera for 4 weeks.

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Phase II Study 202. We are conducting a Phase II trial in which we are seeking to enroll 16 patients with Type I Gaucher disease who are naïve to enzyme replacement therapy and substrate reduction therapy. The study is designed to evaluate the safety of Plicera and its effect on parameters that are commonly abnormal in Gaucher disease including levels of red blood cells, platelets, liver and spleen volumes and other biomarkers related to Gaucher disease. Patients will be assigned to one of two treatment arms and will receive treatment with Plicera for approximately 6 months.

AT2220 for Pompe Disease

Overview

Our third most advanced product candidate, AT2220, is an orally-administered small molecule pharmacological chaperone for the treatment of Pompe disease. We are currently conducting Phase I clinical trials of AT2220 for Pompe disease.

Causes of Pompe Disease and Rationale for Use of AT2220

Pompe disease is a neuromuscular and lysosomal storage disorder caused by a deficiency in the enzyme -glucosidase, or Gaa. Symptoms can be severe and debilitating, including progressive muscle weakness throughout the body, particularly the heart and skeletal muscles. The deficiency of Gaa in Pompe patients is caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of Gaa that may result in the production of Gaa with reduced stability that does not fold into its correct three-dimensional shape. Although Gaa produced in patient cells often retains the potential for biological activity, the cell s quality control mechanisms recognize and retain misfolded Gaa in the ER, until it is ultimately moved to another part of the cell for degradation and elimination. Certain other mutations cause changes in RNA processing that lead to the production of normal Gaa, but at levels that are much lower than in an unaffected individual. In either case, little or no Gaa moves to the lysosome, where it normally breaks down its substrate, glycogen. This leads to accumulation of glycogen in cells, which is believed to result in the majority of clinical manifestations of Pompe disease. In addition, the accumulation and mistrafficking of Gaa may lead to stress on cells and inflammatory-like responses, which may contribute to cellular dysfunction and disease.

AT2220 is designed to act as a pharmacological chaperone for Gaa by selectively binding to Gaa and increasing its stability which helps the enzyme fold into its correct three-dimensional shape. We believe this stabilization of Gaa allows the cell s quality control mechanisms to recognize the protein as properly folded so that trafficking of the enzyme to the lysosome is increased, enabling it to carry out its intended biological function, the metabolism of glycogen. We believe AT2220 may increase proper trafficking of Gaa in patients that produce unstable misfolded Gaa, and in patients that produce low levels of normal Gaa because some fraction of normal Gaa can also fail to pass the cell s quality control system. In addition, as a result of increasing the proper trafficking of unstable misfolded Gaa to the lysosome, AT2220 may reduce the accumulation of misfolded Gaa in the ER, which may alleviate cellular stress and inflammatory-like responses that may be contributing factors in Pompe disease.

Because AT2220 is believed to increase the activity of a patient s naturally produced Gaa, those Pompe disease patients with a mutation that results in production of Gaa with some residual enzyme activity are the ones most likely to respond to treatment with AT2220. We estimate that the majority of patients with Pompe disease may respond to pharmacological chaperone therapy. Patients with genetic mutations leading to a partially made Gaa enzyme or Gaa enzyme with an irreversible loss of activity are less likely to respond to treatment with AT2220.

Pompe Disease Background

Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency, is a relatively rare disorder caused by mutations in Gaa. The mutations in Gaa result in the accumulation of lysosomal glycogen, especially in skeletal, cardiac and smooth muscle tissues. According to reported estimates of the

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Acid Maltase Deficiency Association, the United Pompe Foundation and the Lysosomal Disease Program at Massachusetts General Hospital, there are 5,000-10,000 patients with Pompe disease worldwide.

Pompe disease ranges from a rapidly fatal infantile form with severe cardiac involvement to a more slowly progressive, later-onset form primarily affecting skeletal muscle. All forms are characterized by severe muscle weakness that worsens over time. In the rapid onset form, patients are usually diagnosed shortly after birth and often experience enlargement of the heart and severe muscle weakness. In later-onset Pompe disease, symptoms may not appear until late childhood or adulthood and patients often experience progressive muscle weakness.

Pompe Disease Market Opportunity

Pompe disease is a relatively rare disorder. Most reported estimates project that there are 5,000 to 10,000 patients worldwide, the majority of whom have later-onset Pompe disease.

Based on published data from the Human Gene Mutation Database and our experience in the field, we believe that many of the known genetic mutations that cause Pompe disease are mutations that result in measurable residual enzyme activity. The majority of Pompe patients have either juvenile or adult-onset disease, and both types of patients generally have measurable levels of residual enzyme activity. Because pharmacological chaperone therapy is most likely to benefit patients with some residual enzyme activity, we believe that a majority of the Pompe patient population may benefit from treatment with AT2220. There are a few mutations reported in Pompe disease that are more common in specific ethnic populations, including a splice-site mutation common in Caucasians with adult-onset disease. Studies published in the Journal of Medical Genetics, Human Mutation, and the Journal of Neurology suggest that over 70% of all Caucasians with adult-onset Pompe disease have at least one copy of this splice-site mutation. Because this splice-site mutation results in the production of normal Gaa protein, albeit at a level lower than in a non-affected individual, we believe patients with this mutation may be addressable with pharmacological chaperone therapy.

Existing Products for the Treatment of Pompe Disease and Potential Advantages of AT2220

The current standard of treatment for Pompe patients is enzyme replacement therapy. There is currently one product approved for the treatment of Pompe disease, Myozyme, approved in the United States and the European Union and commercialized by Genzyme Corporation. Myozyme was approved in the United States in April 2006 and has orphan drug exclusivity in the United States until 2013. It was approved in the European Union in March 2006 and has orphan drug exclusivity in the European Union until 2016. Although Myozyme is approved for use in all Pompe patients, studies have only been reported in infantile-onset disease. No data have been reported on the safety or efficacy of Myozyme in later-onset disease. The net product sales of Myozyme for 2006 were approximately $59 million as publicly reported by Genzyme Corporation.

For Pompe disease patients who respond to AT2220, we believe that the use of AT2220 may have advantages relative to the use of Myozyme. Available data demonstrate that treatment with Myozyme can improve survival in patients with the infantile form of the disease. Because it is a large protein molecule, Myozyme is believed to have difficulty penetrating many tissues and cell types. Because AT2220 is a small molecule that has demonstrated high oral bioavailability and good biodistribution properties in preclinical testing, it has the potential to reach all cells of the target tissues of Pompe disease patients. Furthermore, treatment with Myozyme requires intravenous infusions every other week, frequently on site at health care facilities, presenting an inconvenience to Pompe disease patients. The label for Myozyme also indicates that the infusion has safety concerns, with infusion reactions observed in 51% of patients, and severe infusion-related reactions observed in 14% of patients. Oral treatment with AT2220 may be more convenient for patients and may not have the safety risks associated with intravenous infusions. See Potential Advantages of Pharmacological Chaperones in the Treatment of Lysosomal Storage Disorders.

We believe that the orphan drug designation of Myozyme in the United States and in the European Union will not prevent us from obtaining marketing approval of AT2220 in either geography. See Government Regulation.

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AT2220 Development Activities

Preclinical Activities

We have conducted multiple in vitro and in vivo preclinical studies of AT2220. Key findings of our studies include:

AT2220 increased levels of the active, mature form of Gaa in cells engineered to express different human Gaa missense mutations and in cells derived from patients with Pompe disease.

Oral administration of AT2220 to normal mice resulted in an approximately 5-fold increase in the level of Gaa activity in most tissues examined, including heart, brain, diaphragm, soleus, tongue, and gastocnemius muscle. This increase in Gaa was assessed using a lysed cell enzyme activity assay and was correlated with increased levels of the mature form of Gaa in heart and gastrocnemius.

AT2220 demonstrated a favorable pharmacokinetic profile when tested in rats and monkeys, including good oral bioavailability and a terminal half-life of approximately 5 hours in rats, and 3 hours in monkeys. No mortality or morbidity was observed in the 14-day repeat dose, oral administration studies in rats and monkeys at dose levels up to 2,000 mg/kg of AT2220 in rats and up to 1,000 mg/kg of AT2220 in monkeys. The primary treatment-related toxicity observed in rats was decreased body weight gain which was correlated with decreased food consumption. These findings were modest and only occurred at the highest dose level. The primary treatment-related toxicities observed in monkeys were red blood cell, hemoglobin and hematocrit counts that were slightly lower relative to control. These toxicities were considered to be minimal and were observed in male and female monkeys at the highest dose, and male monkeys at the second highest dose. All of the observed toxicities in rats and monkeys were found to be reversible or showed a trend toward reversibility, and occurred only at doses that are significantly higher than the human equivalent doses being considered for clinical studies. The clinical implications of these preclinical observations are unknown at this time. Chronic toxicity testing of AT2220 is ongoing in 6-month rat studies and 9-month monkey studies. We are currently planning reproductive toxicity and carcinogenicity studies of AT2220.

Phase I Clinical Trials

We have completed a single-dose Phase I clinical trial of AT2220 and plan to initiate a multiple-dose Phase I clinical trial. Our single-dose Phase I study was a single center, randomized, dose-ranging study in healthy volunteers. The clinical phase began in December 2006 and was completed in February 2007. The study consisted of a total of 32 healthy volunteers divided into four groups of eight subjects. Six subjects in each group received AT2220 and two subjects received placebo. All subjects received single doses of placebo or 50 mg, 150 mg, 300 mg or 600 mg of AT2220 and were evaluated on Day 1 and on Day 8. The objectives of the study was to evaluate the safety and pharmacokinetics of AT2220 in healthy volunteers. The data from our single-dose Phase I clinical trial in healthy volunteers showed that AT2220 was well tolerated. The study also demonstrated that AT2220 has high oral bioavailability with a terminal half-life in plasma of approximately seven to eight hours.

If our Phase I trials are successful, we plan to initiate a Phase II trial by the end of 2007, and intend to develop AT2220 for the treatment of all forms of Pompe disease.

Other Programs

We believe that our pharmacological chaperone technology is applicable to the development of drugs for the treatment of a wide range of human genetic and other diseases. We are currently researching the use of pharmacological chaperones for the treatment of diseases other than lysosomal storage disorders, including neurological diseases such

as Parkinson s disease. We have an ongoing research program in Parkinson s disease and in January 2007, we received a grant from The Michael J. Fox Foundation for Parkinson s Research to further support this research program. Parkinson s disease is a chronic, progressive, degenerative disorder of the central nervous system. The disease affects an estimated 1 million people in the United States.

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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. To achieve this objective, we intend to:

Focus our initial efforts on developing pharmacological chaperones for severe genetic diseases called lysosomal storage disorders. Our most advanced programs are for the treatment of Fabry, Gaucher and Pompe disease. We identify the compounds for these diseases using our proprietary approach. We believe our pharmacological chaperone therapy may have advantages over current therapies. We have focused initially on lysosomal storage disorders for a number of reasons:

- the therapeutic targets involved in these diseases are amenable to rapid drug discovery and development using our pharmacological chaperone technology;
- the novel mechanism of action of our product candidates may allow us to better address unmet medical needs in these very debilitating diseases;
- the severity of these diseases may permit smaller and more expedited clinical studies; and
- the specialized nature of these markets allows for small, targeted sales and marketing efforts that we can pursue independently.

Rapidly advance our lead programs. We are devoting a significant portion of our resources and business efforts to completing the development of our most advanced product candidates. We are currently conducting multiple Phase II clinical trials of Amigal for the treatment of Fabry disease. We expect to complete our current Phase II trials for Amigal by the end of 2007. We completed Phase I trials for Plicera in 2006 and are currently conducting Phase II trials for the treatment of Gaucher disease. We are currently conducting Phase I clinical trials of AT2220 for the treatment of Pompe disease. To accomplish these goals, we are building an appropriate medical, clinical and regulatory operations infrastructure. In addition, we are collaborating with physicians, patient advocacy groups, foundations and government agencies in order to assist with the development of our products. We plan to pursue similar activities in future programs.

Leverage our proprietary approach to the discovery and development of additional small molecules. We are focused on the discovery and development of small molecules designed to exert therapeutic effects by acting as pharmacological chaperones. We have steadily advanced these proprietary technologies and built an intellectual property position protecting our discoveries over a number of years. Our technologies span the disciplines of biology, chemistry and pharmacology. 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. We are also exploring other applications in which the ability of pharmacological chaperones to increase the activity of normal proteins may provide a therapeutic benefit. We plan to continue to apply our technologies to the discovery and development of treatments for genetic diseases as well as other conditions.

Build a targeted sales and marketing infrastructure. We plan to establish our own sales and marketing capabilities in the U.S. and potentially in other major markets. We believe that because our current clinical pipeline is focused on relatively rare genetic disorders, we will be able to access the market through a focused, targeted sales force. For example, for Amigal and Plicera, we believe that the clinical geneticists who are the

key specialists in treating Fabry and Gaucher disease are sufficiently concentrated that we will be able to effectively promote the product with our own targeted sales force.

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Intellectual Property

Patents and Trade Secrets

Our success depends in part on our ability to maintain proprietary protection surrounding our product candidates, technology and know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by filing U.S. and foreign patent applications related to our proprietary technology, including both new inventions and improvements of existing technology, that are important to the development of our business, unless this proprietary position would be better protected using trade secrets. Our patent strategy includes obtaining patent protection, where possible, on compositions of matter, methods of manufacture, methods of use, combination therapies, dosing and administration regimens, formulations, therapeutic monitoring, screening methods and assays. We also rely on trade secrets, know-how, continuing technological innovation, in-licensing and partnership opportunities to develop and maintain our proprietary position. Lastly, we monitor third parties for activities that may infringe our proprietary rights, as well as the progression of third party patent applications that may have the potential to create blocks to our products or otherwise interfere with the development of our business. We are aware, for example, of U.S. patents, and corresponding international counterparts, owned by third parties that contain claims related to treating protein misfolding. If any of these patents were to be asserted against us we do not believe that our proposed products would be found to infringe any valid claim of these patents. There is no assurance that a court would find in our favor or that, if we choose or are required to seek a license, a license to any of these patents would be available to us on acceptable terms or at all.

As of the date of this prospectus, we own or license rights to a total of 10 patents issued in the United States, 5 issued in current member states of the European Patent Convention and 34 pending foreign applications, which are foreign counterparts of many of our U.S. patents. We also own or license rights to 26 pending U.S. applications, 13 of which are provisional. Our patent portfolio includes patents and patent applications with claims relating to methods of increasing deficient enzyme activity to treat genetic diseases. The patent positions for our three leading product candidates are described below and include both patents and patent applications we own or exclusively license:

We have an exclusive license to five U.S. patents and three pending U.S. applications that cover use of Amigal, as well as corresponding foreign applications. U.S. patents relating to Amigal expire in 2018, while the foreign counterpart patents, if granted, would expire in 2019. The patents and the pending applications include claims covering methods of increasing the activity of and preventing the degradation of -GAL, and methods for the treatment of Fabry disease using Amigal and other specific competitive inhibitors of -GAL. In addition, we own a pending U.S. application directed to specific treatment and monitoring regimens with Amigal, which, if granted, may result in a patent that expires in 2028; three pending U.S. applications directed to synthetic steps related to the commercial process for preparing Amigal, which may result in patents that expire in 2026; and two pending U.S. applications for diagnosis of Fabry patients that will respond to treatment with Amigal, which, if granted, will expire in 2027. We have filed, or plan to file, foreign counterparts of these applications, where appropriate, by the applicable deadlines.

We have an exclusive license to seven U.S. patents and two pending U.S. applications, and five foreign patents and a pending foreign application, that cover Plicera or its use. Two of the U.S. patents relating to Plicera compositions of matter expire in 2015 and 2016; the five composition of matter foreign patents and one pending foreign application, if granted, expire in 2015. The other five U.S. patents and two pending applications, which claim methods of increasing the activity of and preventing the degradation of GCase, and methods for the treatment of Gaucher disease using Plicera and other specific competitive inhibitors of GCase, expire in 2018. We own two pending U.S. applications directed to the particular form of the active agent in

Plicera, which, if granted, will expire in 2027. We have filed, or plan to file, foreign counterparts of these applications, where appropriate, by the applicable deadlines.

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We have an exclusive license to three U.S. patents that cover use of AT2220, two pending U.S. applications, as well as corresponding foreign applications. The U.S. patents relating to AT2220 expire in 2018, while the foreign counterpart patents, if granted, would expire in 2019. The patents and the pending applications include claims covering methods of increasing the activity of and preventing the degradation of Gaa, and methods for the treatment of Pompe disease using AT2220 and other specific competitive inhibitors of Gaa.

Our patent estate includes patent applications relating to combination uses for our product candidates or new potential product candidates. Some of these applications are pending in the United States and foreign patent offices, and include one family of patents licensed from Mt. Sinai School of Medicine and one U.S. patent application and international application jointly owned with the Université of Montréal. Others have to date only been filed as provisional applications in the United States. We expect to file some of these as non-provisional applications in United States and in other countries at the appropriate time. These patent applications, assuming they issue as patents, would expire in the United States between 2023 and 2028.

Individual patents extend for varying periods depending on the effective date of filing of the patent application or the date of patent issuance, and the legal term of the patents in the countries in which they are obtained. Generally, patents issued in the United States are effective for:

the longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent application was filed prior to June 8, 1995; and

20 years from the earliest effective filing date, if the patent application was filed on or after June 8, 1995.

The term of foreign patents varies in accordance with provisions of applicable local law, but typically is 20 years from the earliest effective filing date.

The United States Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, provides for an extension of patent protection for drug compounds for a period of up to five years to compensate for time spent in regulatory review. Similar provisions are available in European countries, Japan and other countries. However, we will not know what, if any, extensions are available until a drug is approved. In addition, in the U.S. we may be entitled to an additional six month period of patent exclusivity for pediatric clinical studies.

The patent positions of companies like ours are generally uncertain and involve complex legal, technical, scientific and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in promptly filing patent applications on new discoveries, and in obtaining effective claims and enforcing those claims once granted. We focus special attention on filing patent applications for formulations and delivery regimens for our products in development to further enhance our patent exclusivity for those products. We seek to protect our proprietary technology and processes, in part, by contracting with our employees, collaborators, scientific advisors and our commercial consultants to ensure that any inventions resulting from the relationship are disclosed promptly, maintained in confidence until a patent application is filed and preferably until publication of the patent application, and assigned to us or subject to a right to obtain a license. We do not know whether any of our own patent applications or those patent applications that are licensed to us will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, invalidated or circumvented or be found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products and reduce the term of patent protection that we may have for our products. Neither we nor our licensors can be certain that we were the first to invent the inventions claimed in our owned or licensed patents or patent applications. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us and the rights granted under any issued patents may not provide us with any meaningful

competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to or shortly after commencing commercialization, thereby reducing the advantage of the patent to our business and products.

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We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our trade secret technology and processes, in part, by entering into confidentiality agreements with commercial partners, collaborators, employees, consultants, scientific advisors and other contractors, and by contracting with our employees and some of our commercial consultants to ensure that any trade secrets resulting from such employment or consulting are owned by us. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be discovered independently by others. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License Agreements

We have acquired rights to develop and commercialize our product candidates through licenses granted by various parties. The following summarizes our material rights and obligations under those licenses:

Mt. Sinai School of Medicine We have acquired exclusive worldwide patent rights to develop and commercialize Amigal, Plicera and AT2220 and other pharmacological chaperones for the prevention or treatment of human diseases or clinical conditions by increasing the activity of wild-type and mutant enzymes pursuant to a license agreement with Mt. Sinai School of Medicine of New York University. Under this agreement, to date we have paid no upfront or annual license fees and we have no milestone or future payments other than royalties on net sales. In connection with this agreement, we issued 1,742,000 shares of our common stock to Mt. Sinai School of Medicine in April 2002. In October 2006 we issued Mt. Sinai School of Medicine an additional 1,000,000 shares of common stock and made a payment of $1,000,000 in consideration of an expanded field of use under that license. This agreement expires upon expiration of the last of the licensed patent rights, which will be in 2019 if a foreign patent is granted and 2018 otherwise, or later subject to any patent term extension that may be granted.

University of Maryland, Baltimore County We have acquired exclusive U.S. patent rights to develop and commercialize Plicera for the treatment of Gaucher disease from the University of Maryland, Baltimore County. Under this agreement, to date we have paid aggregate upfront and annual license fees of $29,500. Upon the satisfaction of certain milestones and assuming successful development of Plicera, we could be required to make up to $175,000 in aggregate payments. We are also required to pay royalties on net sales. This agreement expires upon expiration of the last of the licensed patent rights in 2015.

Novo Nordisk A/S We have acquired exclusive patent rights to develop and commercialize Plicera for all human indications. Under this agreement, to date we have paid an aggregate of $400,000 in license fees. Upon the satisfaction of certain milestones and assuming successful development of Plicera worldwide, we could be required to make up to $7,750,000 in aggregate payments. We are also required to pay royalties on net sales. This license will terminate in 2016.

Under our license agreements, if we owe royalties on net sales for one of our products to more than one of the above licensors, then we have the right to reduce the royalties owed to one licensor for royalties paid to another. The amount of royalties to be offset is generally limited in each license and can vary under each agreement. For Amigal and AT2220, we will owe royalties only to Mt. Sinai School of Medicine and will owe no milestone payments. We expect to pay royalties to all three licensors with respect to Plicera.

Our rights with respect to these agreements to develop and commercialize Amigal, Plicera and AT2220 may terminate, in whole or in part, if we fail to meet certain development or commercialization requirements or if we do not meet our obligations to make royalty payments.

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Trademarks

In addition to our patents and trade secrets, we have filed applications to register certain trademarks in the U.S. and abroad, including AMICUS, AMICUS THERAPEUTICS (and design), AMIGAL and PLICERA. At present we have allowances as intent-to-use in the U.S., and some allowances or issued foreign registrations for all of these marks except PLICERA. In addition, we have filed an application in the United States to register PLICERA. We have not yet obtained allowance for this mark. Our ability to obtain and maintain trademark registrations will in certain instances depend on making use of the mark in commerce on or in connection with our products. For the allowed marks for our candidate products, it may be necessary to re-apply for registration if it becomes apparent that we will not use the mark in commerce within the prescribed time period.

Manufacturing

We rely on contract manufacturers to supply the active pharmaceutical ingredients for Amigal, Plicera and AT2220. The active pharmaceutical ingredients for all three products are manufactured under current good manufacturing practices, or cGMP, at kilogram scale initiated with commercially available starting materials. We also rely on a separate contract manufacturer to formulate the active pharmaceutical ingredients into hard gelatin capsules that are also made under cGMP. The components in the final formulation for each product are commonly used in other encapsulated products and are well characterized ingredients. We have implemented appropriate controls for assuring the quality of both active pharmaceutical ingredients and the formulated capsules. Product specifications will be established in concurrence with regulatory bodies at the time of product registration.

Competition

Overview

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical studies, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than products that we may develop. In addition, our ability to compete may be affected because in some cases insurers or other third party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive to buyers.

Major Competitors

Our major competitors include pharmaceutical and biotechnology companies in the United States and abroad that have approved therapies or therapies in development for lysosomal storage disorders within our core programs. Other competitors are pharmaceutical and biotechnology companies that have approved therapies or therapies in development for genetic diseases for which pharmacological chaperone technology may be applicable. Additionally, we are aware of several early-stage, niche pharmaceutical and biotechnology

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companies whose core business revolves around protein misfolding; however, we are not aware that any of these companies is currently working to develop products that would directly compete with ours. The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, convenience and price.

Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. The following table lists our principal competitors and publicly available information on the status of their product offerings:

Competitor	Indication	Product	Class of Product	Status	2006 Sales (in millions)
Genzyme Corporation	Fabry disease	Fabrazyme	Enzyme Replacement Therapy	Marketed	$ 359
	Gaucher disease	Cerezyme	Enzyme Replacement Therapy	Marketed	$ 1,007
	Pompe disease	Myozyme	Enzyme Replacement Therapy	Marketed	$ 59
	Gaucher disease	Genz-112638	Substrate Reduction Therapy	Phase II	N/A
Shire PLC	Fabry disease	Replagal	Enzyme Replacement Therapy	Marketed	$ 118
	Gaucher disease	GA-GCB	Enzyme Replacement Therapy	Phase III	N/A
Actelion, Ltd.	Gaucher disease	Zavesca	Substrate Reduction Therapy	Marketed	$ 20

We are aware of other companies that are conducting preclinical development activities for enzyme replacement therapies to treat Gaucher disease and Pompe disease.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications or NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development in the U.S. typically involves preclinical laboratory and animal tests, the submission to the FDA of a notice of claimed investigational exemption or an investigational new drug application or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of

reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not commented on or questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, good clinical practices or GCP, as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol

involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase II usually involves trials in a limited patient population, to determine the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage, and identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II evaluations, Phase III trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees. These fees are typically increased annually.

The FDA has 60 days from its receipt of a NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of new drug applications. Most such applications for non-priority drug products are reviewed within ten months. The review process may be extended by FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues an approval letter, an approvable letter or a not-approvable letter. Both approvable and not-approvable letters generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in 2 or 6 months depending on the type

of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling restrictions which can materially affect the potential market and profitability of the drug. Once granted,

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product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The Hatch-Waxman Act

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant s product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. ANDA applicants are not required to conduct or submit results of pre-clinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product s listed patents or that such patents are invalid is called a Paragraph 4 certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph 4 certification to the FDA, the applicant must also send notice of the Paragraph 4 certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph 4 certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph 4 certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph 4 challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which FDA cannot grant effective approval of an ANDA based on that listed drug for the same new dosage form, route of administration or combination, or new use.

Other Regulatory Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval

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of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to current good manufacturing practices, or cGMPs, after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the agency inspects manufacturing facilities to access compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first NDA applicant with FDA orphan drug designation for a particular active ingredient to receive FDA approval of the designated drug for the disease for which it has such designation, is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Pediatric Information

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Fast Track Designation

Under the fast track program, the sponsor of a new drug candidate may request FDA to designate the drug candidate as a fast track drug concurrent with or after the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor s request. Once FDA designates a drug as a fast track candidate, it is required to facilitate the development and expedite the review of that drug.

In addition to other benefits such as the ability to use surrogate endpoints and have greater interactions with FDA, FDA may initiate review of sections of a fast track drug s NDA before the application is complete. This rolling review is available if the applicant provides and FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA s time period goal for

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reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the fast track designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review

Under FDA policies, a drug candidate is eligible for priority review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. A fast track designated drug candidate would ordinarily meet FDA s criteria for priority review.

Accelerated Approval

Under FDA s accelerated approval regulations, FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by FDA.

Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the safety and efficacy data of an existing product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon certain preclinical or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Thus approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph 4 certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Anti-Kickback, False Claims Laws & The Prescription Drug Marketing Act

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving

remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Physician Drug Samples

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act, or the PDMA, imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

Regulation Outside the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing clinical studies and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the United States before we can commence clinical studies or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval.

To obtain regulatory approval of a drug under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state s assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public

health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

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We have obtained an orphan medicinal product designation in the European Union from the EMEA for Amigal for the treatment of Fabry disease and we anticipate filing for orphan medicinal product designation from the EMEA for Plicera for the treatment of Gaucher disease and for AT2220 for the treatment of Pompe disease. The EMEA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation provides opportunities for free protocol assistance and fee reductions for access to the centralized regulatory procedures before and during the first year after marketing approval, which reductions are not limited to the first year after marketing approval for small and medium enterprises. In addition, if a product which has an orphan drug designation subsequently receives EMEA marketing approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the EMEA may not approve any other application to market the same drug for the same indication for a period of ten years. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Competitors may receive marketing approval of different drugs or biologics for the indications for which the orphan product has exclusivity. In order to do so, however, they must demonstrate that the new drugs or biologics provide a significant benefit over the existing orphan product. This demonstration of significant benefit may be done at the time of initial approval or in post-approval studies, depending on the type of marketing authorization granted.

As described in the section of this prospectus entitled Amigal for Fabry Disease Existing Products for the Treatment of Fabry Disease and Potential Advantages of Amigal, we believe that the orphan designation of Fabrazyme and Replagal in the European Union will not prevent us from obtaining marketing approval of Amigal in the European Union for the treatment of Fabry disease because Amigal will provide significant benefits over Fabrazyme and Replagal. Similarly, we believe the orphan drug designation of Zavesca in the European Union will not prevent us from obtaining marketing approval of Plicera in the European Union for the treatment of Gaucher disease because Plicera will provide significant benefits over Zavesca.

Pharmaceutical Pricing and Reimbursement

In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third party payors. Third party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. These third party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare product candidates. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the United States government enacted legislation providing a partial prescription drug benefit for Medicare recipients, that began in 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through managed care organizations and other health care

delivery systems operating pursuant to this legislation. These organizations would negotiate prices for our products, which are likely to be lower than we might otherwise obtain. Federal, state and local governments in the United States continue to consider legislation to limit the growth of

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healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as the drug candidates that we are developing.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on pharmaceutical pricing.

Scientific Advisory Board

Our scientific advisory board consists of scientific advisors who are leading experts in the fields of lysosomal enzymes, protein folding and structures, protein trafficking, sugar and carbohydrate biochemistry, post-transcriptional regulation and the underlying pathology, clinical diagnosis and treatment of lysosomal storage disorders. Our scientific advisory board consults with us regularly on matters relating to:

- our research and development programs;
- the design, implementation of basic science and mechanistic studies;
- the design, implementation and interpretation of animal model studies;
- market opportunities from a clinical perspective;
- new ideas, science and technologies relevant to our research and development programs; and
- scientific, technical and medical issues relevant to our business.

Our current scientific advisory board members are:

Name	Professional Affiliation
Michel Bouvier, Ph.D.	Professor and Director, University Research Group on Drug Discovery, Department of Biochemistry, Institute for Research in Immunology and Cancer, Faculty of Medicine, Université de Montréal; Canada Research Chair in Signal Transduction and Molecular Pharmacology
Barry J. Byrne, M.D., Ph.D.	Director, UF Powell Gene Therapy Center; Professor, Molecular Genetics & Microbiology; Associate chair of Pediatrics, Department of Pediatrics/Powell Gene Therapy Center
Gregory A. Grabowski, M.D.	The A. Graeme Mitchell Chair in Human Genetics, Professor of Pediatrics, and Molecular Genetics, Biochemistry and Microbiology, University of Cincinnati College of Medicine; Director of Human Genetics, Children s Hospital Medical Center, Cincinnati, Ohio
Arthur L. Horwich, M.D.	Professor of Genetics and Pediatrics, Yale University School of Medicine; Investigator, Howard Hughes Medical Institute
Stuart A. Kornfeld, M.D.	

Gregory A. Petsko, D.Phil., Ph.D.	Professor, Department of Medicine, Hematology Division; Professor, Department of Biochemistry & Molecular Biophysics, Washington University Medical School Gyula and Katica Tauber Professor, Department of Biochemistry and Department of Chemistry and Director, Rosenstiel Basic Medical Sciences Research Center, Brandeis University; Adjunct Professor, Department of Neurology and Center for Neurologic Diseases, Harvard Medical School

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Medical Advisory Board

Our medical advisory board consists of physician scientists who are leading experts in the diagnosis, understanding and treatment of Gaucher disease, Fabry disease and Pompe disease. The members of the board are well-published and perform clinical and basic science research in lysosomal storage disease; they are recognized as opinion-leaders in the field of genetic medicine and metabolic disorders. Our medical advisory board consults with us periodically on matters relating to:

- our research and clinical development programs;
- the design and implementation of our clinical studies;
- market opportunities from a medical perspective;
- leading medical understanding of lysosomal diseases; and
- current therapeutic paradigms in our target medical areas.

Name	Professional Affiliation
Dominique Germain, M.D., Ph.D.	Assistant Professor, Department of Genetics; Director, Centre de référence de la maladie de Fabry et des maladies héréditaires du tissu conjonctif, Assistance Publique, Hopitaux de Paris, Paris, France
Pramod K. Mistry M.D., Ph.D., FRCP	Professor and Chief, Section of Pediatric Hepatology and Gastroenterology, Yale University School of Medicine; Director, National Gaucher Disease Program; Director, Inherited Metabolic Liver Disease Clinic, Yale University School of Medicine
Marc Patterson, M.D., FRACP	Professor of Clinical Neurology and Pediatrics and Director, Division of Pediatric Neurology, Departments of Neurology and Pediatrics, College of Physicians & Surgeons of Columbia University; Director of Pediatric Neurology and Child Neurology Training Program Director, Morgan Stanley Children s Hospital of New York-Presbyterian Columbia University Medical Center
Thomas Voit, M.D., Ph.D.	Medical and Scientific Director, Institut de Myologic, Groupe Hospitalier Pitié-Salpétrière; Assistant Professor, University Pierre et Marie Curie Paris VI, Paris, France

Employees

As of March 15, 2007, we had 77 full-time employees, 54 of whom were primarily engaged in research and development activities and 23 of whom provide administrative services. A total of 30 employees have an M.D. or Ph.D. degree. None of our employees are represented by a labor union. We have not experienced any work stoppages and consider our employee relations to be good.

Property

Our headquarters are located in Cranbury, New Jersey, consisting of approximately 32,000 square feet of subleased office and laboratory space. In May 2005, we entered into a seven-year non-cancelable operating sublease agreement for this office and laboratory space. This operating sublease will expire by its terms in February 2012. In August 2006, we entered into a 3-year non-cancellable operating sublease agreement for additional office and laboratory space at a second facility located in Cranbury, New Jersey, consisting of 17,000 square feet. This operating sublease will expire by its terms in August 2009.

Legal Proceedings

We are not currently a party to any material legal proceedings.

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MANAGEMENT

Our executive officers and directors and their respective ages and positions as of March 15, 2007 are as follows:

Name	Age	Position
John F. Crowley	39	President and Chief Executive Officer and Director
Matthew R. Patterson	35	Chief Operating Officer
James E. Dentzer	40	Chief Financial Officer
David J. Lockhart, Ph.D.	45	Chief Scientific Officer
David Palling, Ph.D.	53	Senior Vice President, Drug Development
Karin Ludwig, M.D.	45	Senior Vice President, Clinical Research
Mark Simon	45	Senior Vice President, Business Development
Douglas A. Branch	50	Vice President, General Counsel and Secretary
Gregory P. Licholai, M.D.	42	Vice President, Medical Affairs
S. Nicole Schaeffer	38	Vice President, Human Resources and Leadership Development
Donald J. Hayden[3]	51	Chairman and Director
Alexander E. Barkas, Ph.D.[3]	59	Director