

AMICUS THERAPEUTICS INC

Form 10-K

February 08, 2008

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

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2007  
Commission File Number 001-33497

Amicus Therapeutics, Inc.  
(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

20-0422823  
(IRS Employer  
Identification No.)

6 Cedar Brook Drive, Cranbury, NJ 08512  
(Address of principal executive offices)  
Telephone: (609) 662-2000

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, par value \$0.01 per share	The NASDAQ Stock Market LLC
Securities registered pursuant to Section 12(g) of the Act: None	

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer  Accelerated filer  Non-accelerated filer

Indicate by check mark if the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the 8,713,683 shares of voting common equity held by non-affiliates of the registrant, computed by reference to the closing price as reported on the NASDAQ, as of the last business day

of the registrant's most recently completed second fiscal quarter (June 29, 2007) was approximately \$100,207,355. Shares of voting and non-voting stock held by executive officers, directors and holders of more than 5% of the outstanding stock have been excluded from this calculation because such persons or institutions may be deemed affiliates. This determination of affiliate status is not a conclusive determination for other purposes.

As of January 31, 2008, there were 22,431,817 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE:** Portions of the Proxy Statement for the registrant's 2008 Annual Meeting of Stockholders which is to be filed subsequent to the date hereof are incorporated by reference into Part III of this Annual Report on Form 10-K.

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License and Collaboration Agreement

Consent of Independent Registered Public Accounting Firm

Certification of Principal Executive Officer

Certification of Principal Financial Officer

Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350

Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350

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**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This annual report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this annual report on Form 10-K 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, in may, plan, predict, project, will, 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 annual report on Form 10-K, particularly in Part I, Item 1A Risk Factors, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments we may make.

You should read this annual report on Form 10-K and the documents that we incorporate by reference in this annual report on Form 10-K 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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**PART I**

**Item 1. 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 (migalastat hydrochloride) for Fabry disease, Plicera (isofagomine tartrate) for Gaucher disease and AT2220 for Pompe disease. We completed our Phase 2 clinical trials of Amigal, are currently conducting Phase 2 clinical trials of Plicera and completed Phase 1 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 currently approved therapeutics to treat Fabry, Gaucher and Pompe disease were approximately \$1.9 billion in 2007, as publicly reported by the companies that market these therapeutics.

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 bio-distribution 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.

In November 2007, we entered into a strategic collaboration with Shire Pharmaceuticals Ireland Ltd. (Shire), a subsidiary of Shire plc, to jointly develop our three lead pharmacological chaperone compounds for lysosomal storage disorders. Shire will receive rights to commercialize these products outside of the United States (U.S.). We retain all rights to commercialize these products in the U.S.

**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 have completed four Phase 2 clinical trials. Based on the results of these Phase 2 clinical trials, we plan to meet with U.S. and European regulatory authorities to discuss the design of a Phase 3 clinical trial.

*Plicera for Gaucher disease.* We are developing Plicera for the treatment of Gaucher disease and are currently conducting two Phase 2 clinical trials of Plicera in Type I Gaucher patients. The first of these trials has completed enrollment and we expect to receive data to be presented in the first half of 2008. The second of these trials is currently underway.





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*AT2220 for Pompe disease.* We are developing AT2220 for the treatment of Pompe disease, and have completed three Phase 1 clinical trials. We plan to initiate a Phase 2 clinical trial in 2008.

### **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 (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 advantages relative to enzyme replacement therapy for the treatment of lysosomal storage disorders.

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The following table compares some features of enzyme replacement therapy to pharmacological chaperone therapy.

<b>Product Characteristic</b>	<b>Enzyme Replacement Therapy</b>	<b>Pharmacological Chaperone Therapy</b>
<i>Biodistribution</i>	Variable tissue distribution	Broad tissue distribution, including brain
<i>Ease of Use</i>	Weekly or every other week intravenous infusion	Oral administration
<i>Manufacturing</i>	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 U.S. and the European Union (EU) 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 U.S., the EU 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.

<b>Product Candidate</b>	<b>Indication</b>	<b>Stage of Development</b>	<b>Worldwide Commercial Rights</b>
<b>Amigal</b> (migalastat hydrochloride)	Fabry Disease	Phase 2 Complete	Amicus U.S., Shire ex-U.S.
<b>Plicera</b> (isofagomine tartrate)	Gaucher Disease	Phase 2 Ongoing	Amicus U.S., Shire ex-U.S.
<b>AT2220</b>	Pompe Disease	Phase 1 Complete	Amicus U.S., Shire ex-U.S.

**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. As of November 2007, we are developing Amigal in partnership with Shire.

We completed four Phase 2 clinical trials of Amigal in 2007. The primary objective of the Phase 2 trials was to evaluate the safety and tolerability of treatment with Amigal. The secondary objective was to evaluate certain pharmacodynamic measures of treatment, including effects on -GAL (the target enzyme deficient in Fabry patients)

and levels of GL-3 (the substrate that builds up in the cells of patients) in cells and tissues affected by the disease. An additional objective was the preliminary assessment of cardiac and renal function. The four open-label, multi-national Phase 2 trials of Amigal enrolled 18 men and 9 women with Fabry disease between the ages of 17 and 65. The four studies examined various dose levels and frequencies of Amigal administration and had 12 or 24 week primary treatment arms with an optional treatment extension.

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Twenty-six patients completed the primary treatment arms and all entered the optional treatment extension. The 26 patients had 21 different missense genetic mutations that cause Fabry disease. The mutations represented the full spectrum of Fabry patients, including those with both early-onset and late-onset forms of the disease. Twenty-three patients are currently being treated with Amigal under the treatment extension, including 8 who have been treated for more than a year and 4 who have been treated for almost 2 years.

The key findings in the Phase 2 studies were:

Amigal was generally safe and well-tolerated at all doses evaluated and no drug-related serious adverse events were reported.

Amigal increased the level of the enzyme deficient in Fabry patients in 24 of 26 study subjects.

Amigal was shown to reduce the accumulated substrate in a majority of study subjects.

Renal and cardiac function results were encouraging, including those seen in patients treated for nearly two years.

Responses in patients with different Fabry mutations were consistent with the results of in vitro testing, thus confirming the ability to use pharmacogenetics to select likely responders for future studies.

Twenty-three patients have elected to continue Amigal treatment in an extension protocol.

Based on the results of these Phase 2 clinical trials, Amicus and Shire plan to meet with U.S. and European regulatory authorities to discuss the design of a Phase 3 clinical trial for Amigal. In February 2004, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to Amigal for the treatment of Fabry disease and in March 2006, the European Medicines Agency (EMA), 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  $\alpha$ -GAL. Symptoms can be severe and debilitating, including kidney failure and increased risk of heart attack and stroke. The deficiency of  $\alpha$ -GAL in Fabry patients is caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of  $\alpha$ -GAL that may result in the production of  $\alpha$ -GAL with reduced stability that does not fold into its correct three-dimensional shape. Although  $\alpha$ -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  $\alpha$ -GAL in the ER, until it is ultimately moved to another part of the cell for degradation and elimination. Consequently, little or no  $\alpha$ -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  $\alpha$ -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  $\alpha$ -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  $\alpha$ -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  $\alpha$ -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  $\alpha$ -GAL, those Fabry disease patients with a missense mutation or other genetic mutations that result in production of  $\alpha$ -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  $\alpha$ -GAL enzyme or  $\alpha$ -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  $\alpha$ -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 of Fabry disease, referred to as later-onset Fabry disease, tend to have higher residual  $\alpha$ -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.

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### ***Classic Fabry Disease***

Individuals with classic Fabry disease are in most instances males. They have little or no detectable  $\alpha$ -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  $\alpha$ -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. Several studies reported in the Journal of Medical Genetics (2001), the Internal Medicine Journal (2002) and the Journal of Inherited Metabolic Disease (2001) 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  $\alpha$ -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  $\alpha$ -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.

### ***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

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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 U.S. in 2003 and has orphan drug exclusivity in the U.S. until 2010. It was approved in the EU in 2001 and has orphan drug exclusivity in the EU until 2011. The other product approved for treatment of Fabry disease is Replagal, a product approved in the EU and other countries but not in the U.S., commercialized by Shire. Replagal was approved in the EU in August 2001 and has orphan drug exclusivity in the EU until 2011. The net product sales of Fabrazyme for 2007 were approximately \$424 million as publicly reported by Genzyme Corporation. The net product sales for Replagal for the nine months ended September 30, 2007 were approximately \$105 million as publicly reported by Shire.

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, 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.

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 U.S. and of Fabrazyme and Replagal in the EU will not prevent us from obtaining marketing approval of Amigal in either geography. See Government Regulation.

**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. As of November 2007, Plicera is being developed in partnership with Shire.



We completed Phase 1 clinical trials which demonstrated that Plicera was safe and well tolerated in healthy subjects at all doses tested. We are currently conducting two Phase 2 clinical trials of Plicera in Type I Gaucher patients.

The first study, GAU-CL-201, involves subjects with Type I Gaucher disease who were currently receiving enzyme replacement therapy and agreed to discontinue their enzyme replacement therapy for a total of 7 weeks. The study was designed to assess the safety and pharmacodynamic effects of Plicera, particularly its effect on GCase levels.

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We also monitored 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 were assigned to one of four treatment arms which include: 25 mg once per day, 150 mg once per day, 150 mg every four days, or 150 mg every seven days. Thirty individuals were enrolled in this study and enrollment is complete. Data are expected to be available in the first half of 2008.

The second study, GAU-CL-202, involves subjects 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. This trial is currently underway.

### ***Causes of Gaucher Disease and Rationale for Use of Plicera***

Gaucher disease is a lysosomal storage disorder resulting from a deficiency in the enzyme,  $\beta$ -glucocerebrosidase (GCCase). 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 GCCase in Gaucher patients is caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of GCCase that may result in the production of GCCase with reduced stability that does not fold into its correct three-dimensional shape. Although GCCase produced in patient cells often retains the potential for some level of biological activity, the cell's quality control mechanisms recognize and retain misfolded GCCase in the ER until it is ultimately moved to another part of the cell for degradation and elimination. Consequently, little or no GCCase 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 GCCase 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 GCCase 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 GCCase 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 glucocerebroside. As a result of restoring proper trafficking of GCCase from the ER to lysosomes, Plicera reduces the accumulation of misfolded GCCase 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 GCCase, those Gaucher disease patients with a missense mutation or other genetic mutation that results in production of GCCase 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 GCCase enzyme or GCCase 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

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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 U.S., 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 U.S. in 1994 and in the EU in 1997 and no longer has orphan drug exclusivity in the U.S. In the U.S., 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 EU, 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 U.S., the EU and other countries and commercialized by Actelion, Ltd. Zavesca was approved in the U.S. in 2003 and has orphan drug exclusivity in the U.S. until 2010. It was approved in the EU in 2002 and has orphan drug exclusivity in the EU 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 for the year 2007 were approximately \$1.1 billion as publicly reported by Genzyme Corporation. The net product sales for Zavesca for the year ended 2007 were approximately \$29 million as publicly reported by Actelion Ltd.

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.

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 U.S. We believe that the orphan drug designation of Zavesca in the U.S. and the EU will not prevent us from obtaining marketing approval of Plicera in either geography. See Government Regulation.

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### **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. As of November 2007, AT2220 is being developed in partnership with Shire.

We completed three Phase 1 clinical trials of AT2220 for Pompe disease in 2007. Three double-blind, placebo-controlled, dose escalation Phase 1 studies in healthy volunteers were completed. These studies were designed to evaluate the safety, tolerability and pharmacokinetics of AT2220. In a single ascending dose study, 32 individuals received oral doses of 50, 150, 300, or 600 mg AT2220 or placebo. In a multiple ascending dose study, 24 individuals received oral doses of 50, 150, or 450 mg/day AT2220 or placebo for 7 days. In a second multiple ascending dose study, 16 individuals received oral doses of 1000 or 2000 mg/day or placebo for 14 days. In all three studies, AT2220 was generally safe and well-tolerated at all doses and was orally bioavailable with a plasma half-life of 4 to 5 hours. There were no drug-related serious adverse events and no adverse events were considered to be definitely or probably related to study treatment. In the multiple ascending dose studies, all possibly-related adverse events were mild or moderate in severity and resolved spontaneously.

We expect to initiate a Phase 2 clinical trial of AT2220 for Pompe disease in the first half of 2008. The FDA's Office of Orphan Products Development has granted orphan drug designation for the active ingredient in AT2220 in the U.S.

#### ***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  $\alpha$ -glucosidase (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. AT2220 has been shown to increase Gaa levels in cell lines derived from Pompe patients, in transfected cells expressing mutant forms of Gaa and in healthy mice and monkeys. 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 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.

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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 U.S. and the EU and commercialized by Genzyme Corporation. Myozyme was approved in the U.S. in April 2006 and has orphan drug exclusivity in the U.S. until 2013. It was approved in the EU in March 2006 and has orphan drug exclusivity in the EU until 2016. Although Myozyme is approved for use in all Pompe patients, studies currently reported on the label included only patients with infantile-onset disease. Data from a study looking at Myozyme in patients with later-onset disease was reported in late 2007 and is currently under review by various regulatory authorities. This study reportedly achieved the primary endpoint of demonstrating an improvement in motor and pulmonary function. The net product sales of Myozyme for the first full year of sales in 2007 were approximately \$201 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 and may slow the decline in motor and pulmonary function in patients with the later onset 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.

We believe that the orphan drug designation of Myozyme in the U.S. and in the EU will not prevent us from obtaining marketing approval of AT2220 in either geography. See Government Regulation.

***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. An epidemiological and biochemical link between Gaucher and



Parkinson's disease has been established. Furthermore, in 2007, we generated data showing that treatment with Plicera led to reduction in a-synuclein in the brains of animal model for Parkinson's disease.

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**Table of Contents****Strategic Alliances and Arrangements**

We intend to form strategic alliances to gain access to the financial, technical, clinical and commercial resources necessary to develop and market pharmacological chaperone therapeutics. We expect these alliances to provide us with financial support in the form of equity investments, research and development funding, license fees, milestone payments and royalties or profit-sharing based on sales of pharmacological chaperone therapeutics. We currently have one strategic alliance with Shire.

On November 7, 2007, we entered into a License and Collaboration Agreement with Shire. Under the agreement, Amicus and Shire will jointly develop Amicus three lead pharmacological chaperone compounds for lysosomal storage disorders: Amigal, Plicera and AT2220. We granted Shire the rights to commercialize these products outside the U.S. We will retain all rights to our other programs and to develop and commercialize Amigal, Plicera and AT2220 in the U.S.

We received an initial, non-refundable license fee payment of \$50 million from Shire. Joint development costs toward global approval of the three compounds will be shared 50/50 going forward. In addition, we are eligible to receive, for all three drug product candidates, aggregate potential milestone payments of up to \$150 million if certain clinical and regulatory milestones are achieved for all three of the programs, and \$240 million in sales-based milestones for all three of the programs. We will also be eligible to receive tiered double-digit royalties on net sales of the products which are marketed outside of the U.S. Not including royalties and cost-sharing, the deal is valued at up to U.S. \$440 million.

**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.

We own or license rights to several issued patents in the U.S., current member states of the European Patent Convention and numerous pending foreign applications, which are foreign counterparts of many of our U.S. patents. We also own or license rights to several pending U.S. applications. 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 issued U.S. patents and several pending U.S. applications that cover use of Amigal, as well as corresponding foreign applications. U.S. patents relating to Amigal expire in 2018 (not including the Hatch-Waxman statutory extension, which is described below), while the foreign counterpart patents, if granted, would expire in 2019 (not including the Supplemental Protection Certificates or SPC extensions, which are described below). The patents and the pending applications include claims covering methods of increasing the activity of and preventing the degradation of  $\beta$ -GAL, and methods for the treatment of

Fabry disease using Amigal and other specific competitive inhibitors of  $\alpha$ -GAL. In addition, we own pending U.S. applications directed to specific treatment and monitoring regimens with Amigal as well as to dosing regimens with Amigal, which, if granted, may result in patents that expire in 2028. Further, we have several 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. Lastly, we jointly own one pending U.S. application covering methods of diagnosing Fabry disease and determining whether Fabry patients 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.

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We have an exclusive license to seven U.S. patents and two pending U.S. applications, and five foreign patents and several pending foreign applications that cover Plicera or its use. Two of the U.S. patents relating to Plicera compositions of matter expire in 2015 and 2016 (not including the Hatch-Waxman statutory extension, which is described below); the five composition of matter foreign patents and one pending foreign application, if granted, expire in 2015 (not including the SPC extensions, which are described below). The other five U.S. patents and two pending applications, which claim methods of increasing the activity of and preventing the degradation of GCCase, and methods for the treatment of Gaucher disease using Plicera and other specific competitive inhibitors of GCCase, expire in 2018. We own a pending U.S. application directed to the particular form of the active agent in Plicera, which, if granted, will expire in 2027. We own one pending U.S. application directed to dosing regimens for Plicera, which if granted, will expire in 2028. We own one pending U.S. application directed to specific treatment and monitoring regimens with Plicera. If granted, this also will expire in 2028. Lastly, we own one pending U.S. application directed to methods of synthesis of Plicera, which if granted, will expire in 2028. We have filed, or plan to file, foreign counterparts of these applications, where appropriate, by the applicable deadlines.

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 (not including the Hatch-Waxman statutory extension, which is described below), while the foreign counterpart patents, if granted, would expire in 2019 (not including the SPC extensions, which are described below). 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 also includes patent applications we license or own relating to combination compositions or uses for our product candidates or new potential product candidates. Some of these applications are pending in the U.S. 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 U.S. We have filed or expect to file some of these as non-provisional applications in U.S. and in other countries at the appropriate time. These patent applications, assuming they issue as patents, would expire in the U.S. 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 U.S. 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 U.S. Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, provides for an extension of one patent, known as a Hatch-Waxman statutory extension, for each NCE to compensate for a portion of the time spent in clinical development and regulatory review. However, the maximum extension is five years and the extension cannot extend the patent beyond 14 years from New Drug Application (NDA) approval. Similar extensions are available in European countries, known as SPC extensions, 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., under provisions of the Best Pharmaceuticals for Children's Act, we may be entitled to an additional six month period of patent protection Market Exclusivity and Orphan Drug Exclusivity, for completing pediatric clinical studies in response to a FDA issued Pediatric Written Request before said exclusivities expire.

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

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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.

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 232,266 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 133,333 shares of common stock and made a payment of \$1.0 million 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. We are required to make a milestone payment upon the demonstration of safety and efficacy of Plicera for the treatment of Gaucher disease in a Phase 2 study, and another payment upon receiving FDA approval for Plicera for the treatment of Gaucher disease. We are also required to pay royalties on net sales. Upon satisfaction of both milestones, we could be required to make up to \$0.2 million in aggregate payments. 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 \$0.4 million in license fees. We are also required to make milestone payments based on clinical progress of Plicera, with a payment due after initiation of a Phase 2 clinical trial for Plicera for the treatment of Gaucher disease, and a payment due upon

each filing for regulatory approval of Plicera for the treatment of Gaucher disease in any of the U.S., Europe or Japan. An additional payment is due upon approval of Plicera for the treatment of Gaucher disease in the U.S. and a payment is also due upon each approval of Plicera for the treatment of Gaucher disease in either of Europe or Japan. Assuming successful development of Plicera for the treatment of Gaucher disease in the U.S., Europe and Japan, total milestone payments would be \$7.8 million. 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

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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.

### ***Trademarks***

In addition to our patents and trade secrets, we have filed applications to register certain trademarks in the U.S. and/or abroad, including AMICUS, AMICUS THERAPEUTICS (and design), AMIGAL and PLICERA. At present, all of the U.S. trademark applications for these marks, which are based on an intention to use these marks, have been approved by the U.S. Patent and Trademark Office and Notices of Allowances and have been issued. We have also received foreign allowances or issued foreign registrations for certain of these marks. 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 continue to rely on contract manufacturers to supply the active pharmaceutical ingredients and gelatin capsules for Amigal, Plicera and AT2220. The active pharmaceutical ingredients for all three products are manufactured under current good manufacturing practices (cGMP), at kilogram scale initiated with commercially available starting materials. 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 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 both existing and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise associated with research and development, regulatory approvals and marketing approved products. 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 U.S. 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 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.

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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 (U.S. dollars in millions):

<b>Competitor</b>	<b>Indication</b>	<b>Product</b>	<b>Class of Product</b>	<b>Status</b>	<b>2007 Sales (in millions)</b>
Genzyme Corporation	Fabry disease	Fabrazyme	Enzyme Replacement Therapy	Marketed	\$ 424
	Gaucher disease	Cerezyme	Enzyme Replacement Therapy	Marketed	\$ 1,100
	Pompe disease	Myozyme	Enzyme Replacement Therapy	Marketed	\$ 201
	Gaucher disease	Genz-112638	Substrate Reduction Therapy	Phase 2	N/A
Shire	Fabry disease	Replagal	Enzyme Replacement Therapy	Marketed	\$ 105*
	Gaucher disease	GA-GCB	Enzyme Replacement Therapy	Phase 3	N/A
Actelion, Ltd.	Gaucher disease	Zavesca	Substrate Reduction Therapy	Marketed	\$ 29
Protalix Biotherapeutics	Gaucher disease	prGCD	Enzyme Replacement Therapy	Phase 3	N/A

\* Nine Months Sales through September 30, 2007

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 U.S., pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic 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 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 (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 (GCP), as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety

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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 (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 1, 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 2 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 2 evaluations, Phase 2 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, 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 (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

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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 (New Chemical Entity Market Exclusivity). 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 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 assess 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

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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 indication for which it has such designation, is entitled to a seven-year exclusive marketing period (Orphan Drug Exclusivity) in the U.S. for that product, for that indication. During the seven-year period, the FDA may not finally 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 (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 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

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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 (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 U.S.***

In addition to regulations in the U.S., 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 U.S. 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 EU 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 EU 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

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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.

We have obtained an orphan medicinal product designation in the EU from the EMEA for Amigal for the treatment of Fabry disease and for Plicera for the treatment of Gaucher disease. We anticipate filing for orphan medicinal product designation from the EMEA 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 EU. 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 EU and that without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the EU 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 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 EU will not prevent us from obtaining marketing approval of Amigal in the EU 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 EU will not prevent us from obtaining marketing approval of Plicera in the EU for the treatment of Gaucher disease because Plicera will provide significant benefits over Zavesca.

**Pharmaceutical Pricing and Reimbursement**

In the U.S. 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 U.S. 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 U.S. continue to consider legislation to limit the growth of 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 U.S. has increased and will continue to increase the pressure on pharmaceutical pricing.

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**Employees**

As of December 31, 2007, we had 91 full-time employees, 60 of whom were primarily engaged in research and development activities and 31 of whom provide administrative services. A total of 32 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.

**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, NJ 08512 and our telephone number is (609) 662-2000. Our website address is [www.amicustherapeutics.com](http://www.amicustherapeutics.com). We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnishes such material to, the U.S. Securities and Exchange Commission.

Information relating to corporate governance at Amicus Therapeutics, including our Code of Business Conduct for Employees, Executive Officers and Directors, Corporate Governance Guidelines, and information concerning our senior management team, Board of Directors, including Board Committees and Committee charters, and transactions in our securities by directors and executive officers, is available on our website at [www.amicustherapeutics.com](http://www.amicustherapeutics.com) under the Investors Corporate Governance caption and in print to any stockholder upon request. Any waivers to the Codes by directors or executive officers and any material amendment to the Code of Business Conduct and Ethics for Employees, Executive Officers and Directors will be posted promptly on our website.

We have filed applications to register certain trademarks in the U.S. and abroad, including AMICUS , AMICUS THERAPEUTICS and design, AMIGAL and PLICERA . We plan to seek FDA approval of the trademarks Amigal and Plicera for migalastat hydrochloride and isofagomine tartrate, respectively. Fabrazyme®, Cerezyme®, Myozyme®, Replagal and Zavesca® are the property of their respective owners.

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**Item 1A. RISK FACTORS.**

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as other information in this report, before deciding to invest in shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects. In that case, the trading price of our common stock could decline, and you may lose all or part 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 \$41.5 million, \$65.9 million and \$20.1 million for the years ended 2007, 2006 and 2005 respectively. As of December 31, 2007, we had an accumulated deficit of \$124.8 million. To date, we have financed our operations primarily through private placements of our redeemable convertible preferred stock and through proceeds from our initial public offering. 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 2 extension study of Amigal (migalastat hydrochloride) for the treatment of Fabry disease and initiate a Phase 3 clinical trial of Amigal;

continue our ongoing Phase 2 clinical trials of Plicera (isofagomine tartrate) for the treatment of Gaucher disease and potentially conduct additional Phase 2 and later-stage clinical trials of Plicera;

initiate a Phase 2 clinical trial 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.

**We will need substantial 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 initiate a Phase 3 clinical trial of Amigal, continue our Phase 2 clinical trials of Plicera and initiate a

Phase 2 clinical trial 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 our initial public 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 early 2010. Capital may not be available when needed on terms that are acceptable to us, or at all. If adequate funds are not



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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 capital 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 capital 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 capital 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.

### **Our short operating history may make it difficult 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 generated any commercial sales for any of our 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 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;

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successful completion of preclinical studies and clinical trials;

obtaining marketing approvals from the United States Food and Drug Administration (FDA), and similar regulatory authorities outside the U.S.;

establishing commercial-scale manufacturing arrangements with third party manufacturers whose manufacturing facilities are operated in compliance with current good manufacturing practice (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 U.S. 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.

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 reflects 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-U.S. 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. We cannot be assured 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 who started dosing in March 2006 in the ongoing Phase 2 clinical trials for Amigal for the treatment of Fabry disease elected to withdraw from the study in March 2006, shortly after initial dosing. 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

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sell these product candidates from the FDA and regulatory authorities outside the U.S. 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 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 2 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 have completed Phase 2 clinical trials for Amigal and are currently conducting Phase 2 clinical trials for Plicera and have completed Phase 1 clinical trials for AT2220 but have not yet initiated a Phase 3 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-U.S. regulatory agencies. The requirements of our clinical testing mandate 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 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;

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conditions imposed on us by the FDA or any non-U.S. 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.

**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.

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**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 U.S. 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 payor's 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 that preclude payment for some uses that are approved by the FDA or non-U.S. 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 U.S. 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 U.S. 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 (EU) 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;

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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 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 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 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.

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**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 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.

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**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 non-renewal 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.

Our contract manufacturers will be required to adhere to FDA regulations setting forth 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 U.S. Our manufacturers are subject to unannounced inspections by the FDA, state regulators and similar regulators outside the U.S. 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.

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**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 and 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 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 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 U.S. 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

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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

- 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.

**Our collaboration with Shire Pharmaceuticals Ireland Ltd. (Shire) is important to our business. If this collaboration is unsuccessful or if Shire terminates this collaboration or its participation in individual programs, our business could be adversely affected.**

In November 2007, we entered into a license and collaboration agreement with Shire to jointly develop our three lead pharmacological chaperone compounds for lysosomal storage disorders: Amigal, Plicera and AT2220. Under this agreement, Shire will contribute 50% of joint development costs toward global approval, we are eligible to receive an additional \$150 million if certain clinical and regulatory milestones are met; and we are also eligible to receive up to \$240 million in sales-based milestones, as well as tiered double-digit royalties.

Shire may elect to terminate this collaboration or its participation in the development of individual programs under certain circumstances or in the event of a material uncured breach by us. We expect that a substantial amount of the funding for our operations will come from this collaboration. If this collaboration is unsuccessful, or if it is terminated in whole or in part, our business could be adversely affected and we could require additional financing earlier than we currently expect.

### **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 U.S. 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 U.S. 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.

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In addition, we cannot be assured 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 U.S. 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 U.S. and 2019 outside of the U.S., 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 U.S. and in 2015 outside of the U.S. for composition of matter, and in 2018 in the U.S. for methods of use. We currently have no issued patents or pending applications covering methods of using Plicera outside of the U.S. Patents and patent applications that we own or have licensed relating to the use of AT2220 expire in 2018 in the U.S. Further, we currently do not have composition of matter or method of use protection for AT2220 outside of the U.S. Where we lack patent protection outside of the U.S., we intend to seek orphan medicinal product designation and to rely on statutory data exclusivity provisions in jurisdictions outside the U.S. where such protections are available, including Europe. If we are unable to obtain such protection outside the U.S., our competitors may be free to use and sell Plicera and/or AT2220 outside of the U.S. 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 those 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 U.S. 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 U.S. 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 U.S. Patent and Trademark Office to determine priority of invention in the U.S. The costs of these proceedings could be substantial and it is possible that our efforts could be unsuccessful, resulting in a loss of our U.S. 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.

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**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 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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 or other intellectual property 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 declared by the U.S. 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.



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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 U.S. 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 is at least as effective as 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;

- 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-U.S. 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.**

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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 U.S. 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, for the active ingredient in Plicera for the treatment of Gaucher disease on January 10, 2006 and for AT2220 for the treatment of Pompe disease on June 18, 2007. We also obtained orphan medicinal product designation in the EU for Amigal on May 22, 2006 and for Plicera on October 23, 2007. We anticipate filing for orphan drug designation in the EU 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 7 years in the U.S. and 10 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;

finances;

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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.

**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 U.S. In order to market our products in the EU 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 U.S. may include all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., 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 U.S. 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 U.S. 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 John F. Crowley, our President and Chief Executive Officer, Matthew R. Patterson, our Chief Operating Officer, James E. Dentzer, our Chief Financial Officer, and David J. Lockhart, Ph.D., our Chief Scientific Officer. These executives each have significant pharmaceutical industry experience, including Mr. 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. We may terminate Mr. Crowley's employment without cause at any time, or we may decide not to extend Mr. Crowley's agreement at the end of any term, or he may terminate his employment for good reason at any time, in each case subject to certain severance payments and benefits.

Mr. Crowley is a commissioned officer in the U.S. Navy (Reserve). The U.S. 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 are also parties to employment agreements with each of Messrs. Patterson and Dentzer and Dr. Lockhart. These employment agreements each provide for an initial term of two years, and will continue thereafter for successive two-year periods until we provide the executive with written notice of the end of the agreement in accordance with its terms. We may terminate any of these executives without cause at any time, or one of these executives may quit for good reason within six months of the occurrence of certain corporate changes, in each case subject to certain severance payments and benefits. The loss of the services of any of these executives might impede the achievement of our research, development and commercialization objectives and 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.

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### **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 91 full-time employees as of December 31, 2007. Of these employees, 60 work primarily in research and development and 31 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 approximately 115 to 140 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, 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**

#### **Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to our stockholders for approval.**

Our executive officers, directors and principal stockholders beneficially own shares representing 74% 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 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 became effective upon our initial public 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 our stockholders might otherwise receive a premium for their 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

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

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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.

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

We completed our initial public offering of equity securities in June 2007, and prior to this offering, there was no public market for our common stock. Although we have been listed on The NASDAQ Global Market, an active trading market for our common stock may never develop or be sustained. If an active market for our common stock does not develop or is not sustained, it may be difficult for our stockholders to sell shares since our initial public 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 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. 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 U.S. 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;

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 potential purchasers of our common stock should consider an investment in our common stock as risky and invest only if they can withstand a significant loss and wide fluctuations in the marked value of their investment.

**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. If securities or industry analysts do not continue 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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**Item 1B. UNRESOLVED STAFF COMMENTS.**

None.

**Item 2. PROPERTIES.**

We currently lease approximately 49,000 square feet of subleased office and laboratory space in Cranbury, New Jersey under lease agreements that terminate in February 2012. We believe that our current office and laboratory facilities are adequate and suitable for our current and anticipated needs.

**Item 3. LEGAL PROCEEDINGS.**

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

**Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS.**

No matters were submitted to a vote of security holders during the fourth quarter of the year ended December 31, 2007.

**Table of Contents****PART II****Item 5. MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER****PURCHASES OF EQUITY SECURITIES.****Market For Our Common Stock**

Our common stock has been traded on the NASDAQ Global Market under the symbol FOLD since May 31, 2007. Prior to that time, there was no public market for our common stock. The following table sets forth, for the periods indicated, the range of high and low closing sales prices of our common stock as quoted on the NASDAQ Global Market for the period since our initial public offering on May 31, 2007.

		2007	
		High	Low
May 31, 2007	June 30, 2007	\$ 16.80	\$ 10.30
Third Quarter		16.75	10.00
Fourth Quarter		18.22	9.20

The closing price for our common stock as reported by the NASDAQ Global Market on January 31, 2008 was \$9.72 per share. As of January 31, 2008, there were 70 holders of record of our common stock.

**Dividends**

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.

**Recent Sales of Unregistered Securities**

None.

**Use of Proceeds from the Sale of Registered Securities**

Our initial public offering of common stock was effected through a Registration Statement on Form S-1 (File No. 333-141700) that was declared effective by the Securities and Exchange Commission (SEC) on May 30, 2007, which registered an aggregate of 5,750,000 shares of our common stock. On June 5, 2007, at the closing of the offering, 5,000,000 shares of common stock were sold on our behalf at an initial public offering price of \$15.00 per share, for aggregate offering proceeds of \$75.0 million. The initial public offering was underwritten and managed by Morgan Stanley, Merrill Lynch & Co., JPMorgan, Lazard Capital Markets and Pacific Growth Equities, LLC. Following the sale of the 5,000,000 shares, the public offering terminated.

We paid to the underwriters underwriting discounts totaling approximately \$5.3 million in connection with the offering. In addition, we incurred additional costs of approximately \$1.6 million in connection with the offering, which when added to the underwriting discounts paid by us, amounts to total expenses of approximately \$6.9 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and offering expenses, were approximately \$68.1 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of December 31, 2007, we had invested the \$68.1 million in net proceeds from the offering in money market funds and in investment-grade, interest bearing instruments, pending their use. Through December 31, 2007, we used these proceeds for clinical development of our drug candidates, for research and development activities relating to additional preclinical programs and to fund working capital and other general corporate purposes, which may include the acquisition or licensing of complementary technologies, products or businesses.

**Table of Contents****Performance Graph**

The following performance graph shows the total shareholder return of an investment of \$100 cash on May 30, 2007, the date our common stock first started trading on the NASDAQ Global Market, for (i) our common stock, (ii) the NASDAQ Composite Index (U.S.) and (iii) the NASDAQ Biotechnology Index as of December 31, 2007. Pursuant to applicable SEC rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder return shown on the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

\* \$100 invested on May 31, 2007 in Amicus Therapeutics, Inc. stock or in index-including reinvestment of dividends.

	May-07	Jun-07	Jul-07	Aug-07	Sep-07	Oct-07	Nov-07	Dec-07
<b>Amicus Therapeutics, Inc.</b>	100	80	78	82	116	114	106	74
<b>NASDAQ Composite</b>	100	100	98	100	104	110	102	102
<b>NASDAQ Biotechnology</b>	100	96	94	97	102	107	104	100

*The stock price performance included in this graph is not necessarily indicative of future stock price performance.*

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**Table of Contents****Issuer Purchases of Equity Securities**

The following table sets forth purchases of our common stock for the three months ended December 31, 2007:

<b>Period</b>	<b>(a) Total number of shares purchased</b>	<b>(b) Average Price Paid per Share</b>	<b>(c) Total number of shares purchased as part of publicly announced plans or programs</b>	<b>(d) Maximum number of shares that may yet be purchased under the plans or programs</b>
October 1, 2007 - October 31, 2007	2,645	\$ 17.10		10,580
November 1, 2007 - November 31, 2007	220	\$ 16.17		10,580
December 1, 2007 - December 31, 2007	220	\$ 15.30		10,580
<b>Total</b>	<b>3,085</b>			

Pursuant to a restricted stock award dated October 2, 2006 between Amicus Therapeutics and James E. Dentzer, Chief Financial Officer, Mr. Dentzer was granted 40,000 shares, 25% of which vested on October 2, 2007 and the remaining shares vest in a series of thirty-six successive equal monthly installments commencing on November 1, 2007, with the final installment vesting on November 1, 2010. In order to comply with the minimum statutory federal tax withholding rate of 25% plus 1.45% for Medicare, Mr. Dentzer surrenders a portion of his vested shares on each vesting date, representing 26.45% of the total value of the shares then vested, to Amicus Therapeutics in connection with his withholding obligations.

**Table of Contents****Item 6. SELECTED FINANCIAL DATA.****(in thousands except share and per share data)**

	Year Ended December 31					Period from February 4, 2002 (inception) to December 31, 2007
	2003	2004	2005	2006	2007	
<b>Statement of Operations Data:</b>						
Revenue:						
Research revenue	\$	\$	\$	\$	\$	\$ 1,375
Collaboration revenue						409
Total revenue					1,784	1,784
Operating expenses:						
Research and development	4,433	6,301	13,652	33,630	31,074	89,878
General and administrative	1,005	2,081	6,877	12,277	15,278	38,070
Impairment of leasehold improvements	1,030					1,030
Depreciation and amortization	132	146	303	952	1,237	2,794
In-process research and development						418
Total operating expenses	6,600	8,528	20,832	46,859	47,589	132,190
Loss from operations	(6,600)	(8,528)	(20,832)	(46,859)	(45,805)	(130,406)
Other income (expenses):						
Interest income	5	190	610	1,990	5,135	7,941
Interest expense	(172)	(550)	(82)	(273)	(348)	(1,430)
Change in fair value of warrant liability		(2)	(280)	(23)	(149)	(454)
Other expense				(1,180)		(1,180)
Loss before tax benefit	(6,768)	(8,890)	(20,584)	(46,345)	(41,167)	(125,529)
Income tax benefit		83	612			695

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Net loss	(6,768)	(8,807)	(19,972)	(46,345)	(41,167)	(124,834)
Deemed dividend				(19,424)		(19,424)
Preferred stock accretion	(17)	(126)	(139)	(159)	(351)	(802)
Net loss attributable to common stockholders	\$ (6,785)	\$ (8,933)	\$ (20,111)	\$ (65,928)	\$ (41,518)	(145,060)
Net loss attributable to common stockholders per common share basic and diluted	\$ (22.06)	\$ (29.05)	\$ (49.02)	\$ (89.58)	\$ (3.14)	
Weighted-average common shares outstanding basic and diluted	307,539	307,539	410,220	735,967	13,235,755	

	As of December 31,				
	2003	2004	2005	2006	2007
<b>Balance Sheet Data:</b>					
Cash and cash equivalents and marketable securities	\$ 15	\$ 4,336	\$ 24,418	\$ 54,699	\$ 161,527
Working capital	(5,588)	3,569	22,267	44,814	147,247
Total assets	501	5,073	28,670	59,645	167,097
Total liabilities	5,776	1,346	4,031	13,071	63,800
Redeemable convertible preferred stock	2,432	20,013	60,469	124,089	
Deficit accumulated during the development stage	(8,503)	(17,351)	(37,322)	(83,667)	(124,834)
Total stockholders (deficiency) equity	\$(7,708)	\$(16,287)	\$(35,830)	\$ (77,515)	\$ 103,297

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**Table of Contents****Item 7. 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 completed our Phase 2 clinical trials of Amigal (migalastat hydrochloride), are currently conducting Phase 2 clinical trials of Plicera (isofagomine tartrate) and completed Phase 1 clinical trials of AT2220.

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 and conduct research on other programs. From our inception in February 2002 through December 31, 2007, we have accumulated a deficit of \$124.8 million. As we have not yet generated commercial sales 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 may need to obtain additional funds to further develop our research and development programs and product candidates.

In June 2007, we completed our initial public offering (IPO) of 5,000,000 shares of common stock at a public offering price of \$15.00 per share. Net cash proceeds from the initial public offering were approximately \$68.1 million after deducting underwriting discounts, commissions and offering expenses payable by us. In connection with the closing of the initial public offering, all of the Company's shares of redeemable convertible preferred stock outstanding at the time of the offering were automatically converted into 16,112,721 shares of common stock.

***Collaboration with Shire Pharmaceuticals Ireland Ltd. (Shire)***

On November 7, 2007, we entered into a license and collaboration agreement with Shire. Under the agreement, Amicus and Shire will jointly develop Amicus' three lead pharmacological chaperone compounds for lysosomal storage disorders: Amigal, Plicera and AT2220. We granted Shire the rights to commercialize these products outside the United States (U.S.). We will retain all rights to our other programs and to develop and commercialize Amigal, Plicera and AT2220 in the U.S.

We received an initial, non-refundable license fee payment of \$50 million from Shire. Joint development costs toward global approval of the three compounds will be shared 50/50 going forward. In addition, we are eligible to receive, for all three drug product candidates, aggregate potential milestone payments of up to \$150 million if certain clinical and regulatory milestones are achieved for all three of the programs, and \$240 million in sales-based milestones for all three of the programs. We will also be eligible to receive tiered double-digit royalties on net sales of the products which are marketed outside of the U.S.

**Financial Operations Overview*****Revenue***

The collaboration agreement with Shire became effective in November 2007. Shire paid us an initial, non-refundable license fee of \$50 million in November 2007. At December 31, 2007, we recognized approximately \$0.4 million of the license fee in Collaboration Revenue and \$1.4 million of Research Revenue for reimbursed research and development fees. The license fee will be recognized as Collaboration Revenue over the 18 year performance obligation period. We have not generated any commercial sales revenue since our inception.



**Table of Contents****Research and Development Expenses**

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;

technology and intellectual property license costs;

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 costs on the basis of estimates of time spent by our employees would accurately represent 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, 2007, we have incurred research and development expense in the aggregate of \$89.9 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).

Product Candidate	Years Ended December 31,			Period from
	2005	2006	2007	February 4, 2002 (Inception) to December 31, 2007
Third party direct project expenses Amigal (Fabry Disease Phase 2)	\$ 5,579	\$ 3,361	\$ 4,648	\$ 21,030
Plicera (Gaucher Disease Phase 2)	2,109	9,905	4,378	16,108
AT2220 (Pompe Disease Phase 1)	374	4,427	3,426	8,188

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Total third party direct project expenses	8,062	17,693	12,452	45,326
Other project costs <sup>(1)</sup>				
Personnel costs	3,581	8,187	9,720	24,431
Other costs <sup>(2)</sup>	2,009	7,750	8,902	20,121
Total other project costs	5,590	15,937	18,622	44,552
Total research and development costs	\$ 13,652	\$ 33,630	\$ 31,074	\$ 89,878

(1) Other project costs are leveraged across multiple clinical and pre-clinical projects.

(2) Other costs include facility, supply, overhead, and licensing costs that support multiple clinical and preclinical 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

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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 U.S. Food and Drug Administration (FDA) or other regulatory authorities were to require us to conduct clinical trials beyond those which we currently anticipate, or if we experience significant delays in enrollment in any of 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 are subject to the reporting obligations applicable to public companies. From our inception in February 2002 through December 31, 2007, we spent \$38.1 million on general and administrative expense.

### ***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.

### **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. We believe that the following discussion represents our critical accounting policies.

### ***Revenue Recognition***

We recognize revenue in accordance with the Securities and Exchange Commission (SEC) Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition in Financial Statements* (SAB 101), as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13* (SAB 104). Currently, we derive all of our revenues from our collaboration agreement with Shire and expect that we will continue to derive all, or at least a substantial portion of our revenues from collaboration agreements over the next several years.

Collaboration arrangements may contain multiple elements, including up front licensing fees, reimbursement payments for ongoing research and development, payments for achieving research and development and product approval milestones, sales-based milestones and royalties based on percentages of net product sales. When evaluating multiple element arrangements, we follow the provisions of Emerging Issues Task Force (EITF) Issue 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). EITF 00-21 provides guidance on determining if an arrangement involves a single unit of accounting or separate units of accounting and if the arrangement is determined to have separate units, how to allocate amounts received in the

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arrangement for revenue recognition purposes. If a collaboration agreement involves a single unit of accounting, the revenue recognition policy and the performance obligation period is determined for the entire arrangement while if separate units of accounting are involved, we determine a revenue recognition policy for each unit.

In November 2007, we entered into a collaboration agreement with Shire. We evaluated the multiple elements of this agreement in accordance with the guidance in EITF 00-21 and determined that the multiple deliverables did not have value on a stand alone basis and were unable to obtain verifiable objective evidence to determine the fair value of undelivered elements. As a result, we concluded that there was one single unit of accounting for this collaboration and determined that the period of our performance obligations under the agreement is 18 years. Upon execution of the agreement in November 2007, we received an initial upfront payment of \$50 million from Shire which will be amortized to Collaboration Revenue over the period of the performance obligations which is contractually defined at 18 years.

Additionally, under the agreement we are entitled to receive reimbursement of up to 50% of research and development costs incurred in the development of the products covered by the agreement. We recognize revenue for reimbursed research and development costs in accordance with EITF Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* (EITF 99-19). We will record the revenue associated with these reimbursable amounts to Research Revenue while the costs associated with these reimbursable amounts will be recorded in research and development expenses.

**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 owed 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.

**Stock-Based Compensation**

Effective January 1, 2006, we adopted the fair value recognition provisions of Financial Accounting Standards Board (FASB) Statement of Financial Accounting Standards (SFAS) No. 123(R), *Share-Based Payment*, (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 No. 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.

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We recognized employee stock-based compensation expense of \$0.5 million, \$3.3 million, and \$4.0 million for the years ended 2005, 2006 and 2007, respectively.

Upon adoption of SFAS No. 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 SAB 107, *Disclosure about Fair Value of Financial Instruments* (SAB 107), 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:

	<b>Years Ended December</b>	
	<b>31,</b>	
	<b>2006</b>	<b>2007</b>
Expected stock price volatility	74.8%	78.3%
Risk free interest rate	4.7	4.5
Expected life of options (years)	6.25	6.25
Expected annual dividend per share	\$ 0.00	\$ 0.00

The weighted-average fair value (as of the date of grant) of the options granted during the years ended December 31, 2006 and 2007 was \$10.20 and \$9.45, respectively.

Prior to becoming a public company, 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 IPO, we performed a retrospective determination of fair value for financial reporting purposes of our common stock underlying stock option grants in 2005, 2006 and through April 2007, utilizing a combination of valuation methods described in the American Institute of Certified Public Accountants *Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, (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.

These assumptions and methods are more fully described in our Form S-1/A (333-141700) that was declared effective by the SEC in May 2007.



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**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 represented participating securities in accordance with EITF Issue No. 03-6 *Participating Securities and the Two Class Method under FASB Statement No. 128*. However, because 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. As a result of the IPO in May 2007, all outstanding redeemable convertible preferred stock was converted to common stock and were no longer outstanding as of December 31, 2007.

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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 (in thousands except share amounts):

	<b>Years Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
<b>Historical</b>			
Numerator:			
Net loss	\$ (19,972)	\$ (46,345)	\$ (41,167)
Deemed dividend		(19,424)	
Accretion of redeemable convertible preferred stock	(139)	(159)	(351)
Net loss attributable to common stockholders	\$ (20,111)	\$ (65,928)	\$ (41,518)
Denominator:			
Weighted average common shares outstanding basic and diluted	410,220	735,967	13,235,755

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 9.5 million, 17.5 million and 24.9 million for the years ended December 31, 2005, 2006 and 2007, 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, 2007 Compared to Year Ended December 31, 2006***

***Research and Development Expense.*** Research and development expense was \$31.1 million in 2007 representing a decrease of \$2.5 million or 7% from \$33.6 million in 2006. The variance was primarily attributable to a reduction in contract research and manufacturing costs due to the timing of studies of \$4.5 million, partially offset by higher personnel costs of \$1.6 million associated with headcount growth.

***General and Administrative Expense.*** General and administrative expense was \$15.3 million in 2007, an increase of \$3.0 million or 24% from \$12.3 million in 2006. The variance was primarily attributable to higher personnel costs of \$2.0 million associated with headcount growth and higher professional fees of \$0.3 million related primarily to finalizing the collaboration agreement with Shire.

***Depreciation and Amortization.*** Depreciation and amortization expense was \$1.2 million in 2007, and increase of \$0.2 million or 20%, from \$1.0 million in 2006. The increase is primarily due to assets acquired in the first nine months of 2007.

***Interest Income and Interest Expense.*** Interest income was \$5.1 million in 2007, compared to \$2.0 million in 2006. The increase of \$3.1 million or 155% was due to higher average cash and cash equivalents balances as a result of the issuance of the Series D redeemable convertible preferred stock, the \$68.1 million of proceeds from the IPO and the receipt of the \$50 million upfront licensing payment from Shire. Interest expense was \$0.3 million in 2007, compared to \$0.3 million in 2006.

***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 third party direct project expenses, including increased contract research and manufacturing costs for Plicera and AT2220 of \$9.6 million, an increase in personnel costs of \$4.6 million associated with headcount and salary increases in our research, clinical, and regulatory functions and the impact of adopting SFAS 123(R), and other costs associated with licenses totaling \$2.5 million as well as higher facility, supply, overhead, and non-program specific research.

*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).

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*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 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.

**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 \$148.7 million of proceeds from redeemable convertible preferred stock offerings, \$75.0 million of gross proceeds from our IPO in June 2007 and \$50.0 million from the non-refundable license fee from the Shire collaboration agreement in November 2007. The following table summarizes our significant funding sources as of December 31, 2007:

Funding	Year	No. Shares	Approximate Amount <sup>(1)</sup> (in thousands)
Series A Redeemable Convertible Preferred Stock	2002	444,443	\$ 2,500
	2004, 2005, 2006,	4,917,853	31,189
Series B Redeemable Convertible Preferred Stock	2007		
Series C Redeemable Convertible Preferred Stock	2005, 2006	5,820,020	54,999
Series D Redeemable Convertible Preferred Stock	2006, 2007	4,930,405	60,000
Common Stock	2007	5,000,000	75,000
Upfront License Fee from Shire	2007		50,000
		21,112,721	\$ 273,688

(1) Represents  
gross proceeds

In addition, in conjunction with the Shire collaboration agreement, we received reimbursement of research and development expenditures from the date of the agreement (November 7, 2007) through year-end 2007 of \$2.4 million.

As of December 31, 2007, we had cash and cash equivalents and marketable securities of \$161.5 million. We hold our cash and investment balances in a variety of 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.

***Net Cash Provided by and Used in Operating Activities***

Net cash provided by operations for the year ended December 31, 2007 was \$15.2 million due to the change in operating assets and liabilities of \$51.0 million, non-cash charges for depreciation and amortization of \$1.2 million, stock-based compensation of \$4.0 million and the change in fair value of warrant liability of \$0.2 million, offset by the net loss for the year ended December 31, 2007 of \$41.2 million. The change in operating assets and liabilities of \$51.0 million was due primarily to deferred revenue related to the \$50 million upfront licensing payment from Shire.

Net cash used in operations for the year ended December 31, 2006 was \$33.9 million. 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 and stock-based license payment of \$1.2 million and changes in operating assets and liabilities of \$7.0 million.

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**Table of Contents*****Net Cash Used in Investing Activities***

Net cash used in investing activities for the year ended December 31, 2007 was \$75.0 million. Net cash used in investing activities reflects \$200.7 million for the purchase of marketable securities and \$0.7 million for the acquisition of property and equipment, offset by \$126.4 million for the sale and redemption of marketable securities.

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 cash used for the purchase of marketable securities and \$2.0 million for the acquisition of property and equipment, offset by \$37.4 million of cash provided by the sale and redemption of marketable securities.

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities for the year ended December 31, 2007 was \$91.9 million, consisting primarily of \$24.1 million from the issuance of Series D redeemable convertible preferred stock, \$68.1 million from the issuance of common stock, \$0.5 million from asset financing arrangements, and \$0.6 million proceeds from exercise of stock options and warrants offset by payments of equipment debt financing obligations of \$1.4 million.

Net cash provided by financing activities for the year ended December 31, 2006 was \$66.2 million. 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, \$3.4 million of proceeds from our capital asset financing arrangement and \$0.3 million proceeds from the exercise of stock options and warrants, 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 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, 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, our success in developing markets for our product candidates and the costs of commercialization activities, including product marketing, sales and distribution.

We believe that our existing cash and cash equivalents and short-term investments, together with the expected reimbursement of research and development expenses and research milestones from our collaboration with Shire, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least until 2011.

We do not anticipate that we will generate revenue from commercial sales 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.

***Financial Uncertainties Related to Potential Future Milestone Payments***

We have acquired rights to develop and commercialize our product candidates through licenses granted by various parties. Two of these agreements contain milestone payments that are due with respect to Plicera only if certain specified pre-commercialization events occur. Amigal and AT2220 do not trigger such milestone payments. Upon the satisfaction of certain milestones and assuming successful development of Plicera, we may be obligated, under the agreements that we have in place, to make future milestone payments aggregating up to approximately \$7.9 million. In general, potential milestone payments for

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Plicera may or may not be triggered under these licenses, and may vary in size, depending on a number of variables, almost all of which are currently uncertain.

The events that trigger these payments include:

completion of Phase 2 clinical trials;

commencement of Phase 3 clinical trials;

submission of an NDA to the FDA or foreign equivalents; and

receipt of marketing approval from the FDA or foreign equivalents.

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 (MSSM). We expect to pay royalties to all three licensors with respect to Plicera. To date, we have not made any royalty payments on sales of our products and believe we are several years away from selling any products that would require us to make any such royalty payments. Whether we will be obligated to make milestone or royalty payments in the future is subject to the success of our product development efforts and, accordingly, is inherently uncertain. In conjunction with the \$50 million upfront payment from Shire in November 2007, we recorded an accrual for its best estimate of royalties due to MSSM on the upfront payment.

**Contractual Obligations**

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2007 and the effects such obligations are expected to have on our liquidity and cash flows in future periods (in thousands).

	<b>Total</b>	<b>Less than 1 Year</b>	<b>1-3 Years</b>	<b>3-5 Years</b>	<b>Over 5 Years</b>
Operating lease obligations	\$ 6,003	\$ 1,655	\$ 4,129	\$ 219	
Capital lease obligations	3,039	1,745	1,294		
Employment agreement	1,851	1,388	463		
<b>Total fixed contractual obligations (1)</b>	<b>\$ 10,893</b>	<b>\$ 4,788</b>	<b>\$ 5,886</b>	<b>\$ 219</b>	

(1) This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of

such payments are not known, (b) any royalty payments to third parties as the amounts of such payments, timing and/or the likelihood of such payments are not known, (c) amounts, if any, that may be committed in the future to construct additional facilities, and (d) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

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 million of equipment financing through August 2004. The facility was increased to \$3 million in May 2005 and to \$5 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 leasehold 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 5,333 shares of common stock. These warrants were outstanding at December 31, 2005 and 2006. The warrants have an exercise price of \$5.63 per share (adjusted for stock splits, stock dividends, etc.). The value of the warrants was calculated using the Black-Scholes option pricing model and was capitalized as debt issuance cost and amortized to interest expense over the term of the obligation. The value of the warrants and total charge to interest expense was not material for each of the years presented. The funding period of the facility expired by its own term in 2007.

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





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the other in accordance with the terms of the agreement. The table above includes costs associated with the remainder of the second one-year term and third one-year term ending April 28, 2009. The cost of the executive medical reimbursement contract is estimated based on current premiums.

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 Shire collaboration agreement 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.

**Off-Balance Sheet Arrangements**

We have no off-balance sheet arrangements as of December 31, 2006 and 2007.

**Recent Accounting Pronouncements**

In December 2007, the EITF of the FASB reached a consensus on Issue No. 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). The EITF concluded on the definition of a collaborative arrangement and that revenues and costs incurred with third parties in connection with collaborative arrangements would be presented gross or net based on the criteria in EITF 99-19 and other accounting literature. Based on the nature of the arrangement, payments to or from collaborators would be evaluated and its terms, the nature of the entity's business, and whether those payments are within the scope of other accounting literature would be presented. Companies are also required to disclose the nature and purpose of collaborative arrangements along with the accounting policies and the classification and amounts of significant financial-statement amounts related to the arrangements. Activities in the arrangement conducted in a separate legal entity should be accounted for under other accounting literature; however required disclosure under EITF 07-1 applies to the entire collaborative agreement. This Issue is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years, and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. We do not expect this will have a significant impact on our financial statements.

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* (SFAS No. 141(R)), which replaces SFAS No. 141, *Business Combinations*, requires an acquirer to recognize the assets acquired, the liabilities assumed, and any non-controlling interest in the acquiree at the acquisition date, measured at their fair values as of that date, with limited exceptions. This Statement also requires the acquirer in a business combination achieved in stages to recognize the identifiable assets and liabilities, as well as the non-controlling interest in the acquiree, at the full amounts of their fair values. SFAS No. 141(R) makes various other amendments to authoritative literature intended to provide additional guidance or to confirm the guidance in that literature to that provided in this Statement. This Statement applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. We do not expect this will have a significant impact on our financial statements.

In December 2007, FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements* (SFAS No. 160), which amends Accounting Research Bulletin No. 51, *Consolidated Financial Statements*, to improve the relevance, comparability, and transparency of the financial information that a reporting entity provides in its consolidated financial statements. SFAS No. 160 establishes accounting and reporting standards that require the ownership interests in subsidiaries not held by the parent to be clearly identified, labeled and presented in the consolidated statement of financial position within equity, but separate from the parent's equity. This statement also requires the amount of consolidated net income attributable to the parent and to the non-controlling interest to be clearly identified and presented on the face of the consolidated statement of income. Changes in a parent's ownership interest while the parent retains its controlling financial interest must be accounted for consistently, and when a subsidiary is deconsolidated, any retained non-controlling equity investment in the former subsidiary must be initially measured at fair value. The gain or loss on the deconsolidation of the subsidiary is measured using the fair value of any non-controlling equity investment. The Statement also requires entities to provide sufficient disclosures that clearly identify and distinguish between the interests of the parent and the interests of the non-controlling owners.

This Statement applies prospectively to all entities that prepare consolidated financial statements and applies prospectively for fiscal years, and interim periods within those fiscal years, beginning on or after December 15, 2008. We do not expect this will have a significant impact on our financial statements.

In June 2007, the EITF of the FASB reached a consensus on Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities* (EITF 07-3). EITF 07-3 requires that non-refundable advance payments for goods or services that will be used or rendered for future research and

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development activities should be deferred and capitalized. As the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided, the deferred amounts would be recognized as an expense. This Issue is effective for financial statements issued for fiscal years beginning after December 15, 2007 and earlier application is not permitted. This consensus is to be applied prospectively for new contracts entered into on or after the effective date. The pronouncement is not expected to have a material effect on our financial statements.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities Including an amendment of FASB Statement No. 115* (SFAS No. 159), which is effective for fiscal years beginning after November 15, 2007. SFAS No. 159 permits the Company to choose to measure many financial instruments and certain other items at fair value. The objective is to improve financial reporting by providing entities with the opportunity to mitigate volatility in reported earnings caused by measuring related assets and liabilities differently without having to apply complex hedge accounting provisions. SFAS No. 159 is expected to expand the use of fair value measurement, which is consistent with the FASB's long-term measurement objectives for accounting for financial instruments. SFAS No. 159 is effective for fiscal year 2008 but early adoption is permitted. We are currently evaluating the impact, if any, that the adoption of SFAS No. 159 will have on our financial statements.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measures* (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 the Company's 2008 fiscal year. We do not expect this will have a significant impact on our financial statements.

**Item 7A. 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, 2007, we had cash and cash equivalents and investments in marketable securities of \$161.5 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.

**Table of Contents****Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.****Amicus Therapeutics, Inc.  
(a development stage company)****Consolidated Balance Sheets  
(in thousands, except share and per share amounts)**

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
<b>Assets:</b>		
Current assets:		
Cash and cash equivalents	\$ 12,127	\$ 44,188
Investments in marketable securities	42,572	117,339
Prepaid expenses and other current assets	321	1,513
Total current assets	55,020	163,040
Property and equipment, less accumulated depreciation and amortization of \$1,557 and \$2,793 at December 31, 2006 and 2007, respectively	4,358	3,790
Other non-current assets	267	267
<b>Total Assets</b>	<b>\$ 59,645</b>	<b>\$ 167,097</b>
<b>Liabilities and Stockholders (Deficiency) Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,195	\$ 530
Accrued expenses	7,704	9,935
Current portion of capital lease obligations	1,307	1,527
Current portion of deferred revenue		3,801
Total current liabilities	10,206	15,793
Warrant liability	609	
Deferred revenue, less current portion		46,813
Capital lease obligations, less current portion	2,256	1,194
Commitments and contingencies		
Series A redeemable convertible preferred stock, \$.01 par value, 444,443 shares authorized, issued and outstanding at December 31, 2006 (aggregate liquidation preference \$2,500 at December 31, 2006), no shares authorized, issued, or outstanding at December 31, 2007		2,476
Series B redeemable convertible preferred stock, \$.01 par value, 4,936,730 shares authorized, 4,877,056 shares issued and outstanding at December 31, 2006 (aggregate liquidation preference \$31,000 at December 31, 2006), no shares authorized, issued, or outstanding at December 31, 2007	30,868	
Series C redeemable convertible preferred stock, \$.01 par value, 5,820,020 shares authorized, issued and outstanding at December 31, 2006 (aggregate liquidation preferences \$54,999 at December 31, 2006), no shares authorized, issued, or	54,869	

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outstanding at December 31, 2007

Series D redeemable convertible preferred stock, \$.01 par value, 4,930,405 shares authorized, 2,953,878 issued and outstanding at December 31, 2006 (aggregate liquidation preference \$36,000), no shares authorized, issued, or outstanding at December 31, 2007

35,876

Stockholders' (deficiency) equity:

Common stock, \$.01 par value, 21,333,333 shares authorized, 990,492 shares issued and outstanding at December 31, 2006, 50,000,000 shares authorized, 22,408,731 shares issued and outstanding at December 31, 2007

70

285

Additional paid-in capital

6,067

227,438

Accumulated other comprehensive income

15

408

Deficit accumulated during the development stage

(83,667)

(124,834)

Total stockholders' (deficiency) equity

(77,515)

103,297

**Total Liabilities and Stockholders' (Deficiency) Equity**

\$ 59,645

\$ 167,097

*See accompanying notes to consolidated financial statements*

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Consolidated Statements of Operations**  
**(in thousands, except share and per share amounts)**

	<b>Years Ended December 31,</b>			<b>Period from</b>
	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>February 4,</b>
				<b>2002</b>
				<b>(Inception)</b>
				<b>to</b>
				<b>December</b>
				<b>31,</b>
				<b>2007</b>
Revenue:				
Research revenue	\$	\$	\$ 1,375	\$ 1,375
Collaboration revenue			409	409
Total revenue			1,784	1,784
Operating Expenses:				
Research and development	13,652	33,630	31,074	89,878
General and administrative	6,877	12,277	15,278	38,070
Impairment of leasehold improvements				1,030
Depreciation and amortization	303	952	1,237	2,794
In-process research and development				418
Total operating expenses	20,832	46,859	47,589	132,190
Loss from operations	(20,832)	(46,859)	(45,805)	(130,406)
Other income (expenses):				
Interest income	610	1,990	5,135	7,941
Interest expense	(82)	(273)	(348)	(1,430)
Change in fair value of warrant liability	(280)	(23)	(149)	(454)
Other expense		(1,180)		(1,180)
Loss before income tax benefit	(20,584)	(46,345)	(41,167)	(125,529)
Income tax benefit	612			695
Net loss	(19,972)	(46,345)	(41,167)	(124,834)
Deemed dividend		(19,424)		(19,424)
Preferred stock accretion	(139)	(159)	(351)	(802)
Net loss attributable to common stockholders	\$ (20,111)	\$ (65,928)	\$ (41,518)	\$ (145,060)

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Net loss attributable to common stockholders per common share basic and diluted	\$ (49.02)	\$ (89.58)	\$ (3.14)
Weighted-average common shares outstanding basic and diluted	410,220	735,967	13,235,755

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Consolidated Statements of Changes in Stockholders (Deficiency) Equity**  
**Period from February 4, 2002 (inception) to December 31, 2002,**  
**and the five year period ended December 31, 2007**  
**(in thousands, except share amounts)**

	Common Stock		Additional Paid-In Capital	Other Comprehensive Gain/ (Loss)	Deferred Compensation	Deficit Accumulated During the Development Stage	Total Stockholders (Deficiency) Equity
	Shares	Amount					
Balance at February 4, 2002 (inception)		\$	\$	\$	\$	\$	\$
Issuance of common stock to a consultant	74,938	6	78				84
Stock issued for in-process research and development	232,266	17	401				418
Deferred compensation			209		(209)		
Amortization of deferred compensation					27		27
Issuance of warrants with financing arrangements			8				8
Accretion of redeemable convertible preferred stock			(11)				(11)
Net loss						(1,775)	(1,775)
Balance at December 31, 2002	307,204	23	685		(182)	(1,775)	(1,249)
Stock issued from exercise of stock options	333						
Deferred compensation			14		(14)		
Amortization of deferred compensation					70		70
			210				210

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Issuance of stock warrants with convertible notes							
Issuance of stock options to consultants			4				4
Accretion of redeemable convertible preferred stock			(17)				(17)
Beneficial conversion feature related to bridge financing			41				41
Net loss					(6,768)		(6,768)
Balance at December 31, 2003	307,537	23	937		(126)	(8,543)	(7,709)
Deferred compensation			68		(68)		
Amortization of deferred compensation					60		60
Issuance of stock options to consultants			16				16
Accretion of redeemable convertible preferred stock			(126)				(126)
Interest waived on converted convertible notes			193				193
Beneficial conversion feature related to bridge financing			95				95
Comprehensive Loss: Unrealized holding loss on available-for-sale securities					(9)		(9)
Net loss						(8,807)	(8,807)
Net total comprehensive loss							(8,816)
Balance at December 31, 2004	307,537	23	1,183	(9)	(134)	(17,350)	(16,287)
Stock issued from exercise of stock options	97,156	7	17				24
Stock issued from exercise of warrants	133,332	10	65				75
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Deferred compensation			2,778		(2,778)		
Amortization of deferred compensation					365		365
Non-cash charge for stock options to consultants			112				112
Accretion of redeemable convertible preferred stock			(139)				(139)
Comprehensive Loss: Unrealized holding loss on available-for-sale securities					(7)		(7)
Net loss						(19,972)	(19,972)
Net total comprehensive loss							(19,979)
Balance at December 31, 2005	538,025	40	4,016	(16)	(2,547)	(37,322)	(35,829)

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Consolidated Statements of Changes in Stockholders (Deficiency) Equity**  
**Period from February 4, 2002 (inception) to December 31, 2002,**  
**and the five year period ended December 31, 2007**  
**(in thousands, except share amounts)**

	<b>Common Stock</b>		<b>Additional</b>	<b>Other</b>	<b>Deferred</b>	<b>Deficit</b>	<b>Total</b>
	<b>Shares</b>	<b>Amount</b>	<b>Paid-In</b>	<b>Comprehensive</b>	<b>Compensation</b>	<b>Accumulated</b>	<b>Stockholders</b>
			<b>Capital</b>	<b>Gain/ (Loss)</b>		<b>During the</b>	<b>(Deficiency)</b>
						<b>Development</b>	<b>Equity</b>
						<b>Stage</b>	
Balance at December 31, 2005	538,025	40	4,016	(16)	(2,547)	(37,322)	(35,829)
Stock issued from exercise of options	265,801	20	138				158
Stock issued for license payment	133,333	10	1,210				1,220
Reversal of deferred compensation upon adoption of FAS 123(R)			(2,547)		2,547		
Stock-based compensation	53,333		2,816				2,816
Issuance of stock options to consultants			476				476
Accretion of redeemable convertible preferred stock			(159)				(159)
Reclassification of warrant liability upon exercise of Series B redeemable convertible preferred stock warrants			117				117
Beneficial conversion on issuance of Series C redeemable convertible preferred stock			19,424				19,424
Beneficial conversion charge (deemed dividend) on issuance of			(19,424)				(19,424)

Series C redeemable convertible preferred stock							
Comprehensive (Loss)/ Income:							
Unrealized holding gain on available-for-sale securities				31			31
Net loss						(46,345)	(46,345)
Net total comprehensive loss							(46,314)
Balance at December 31, 2006	990,492	70	6,067	15		(83,667)	(77,515)
Stock issued from initial public offering	5,000,000	50	68,095				68,145
Stock issued from conversion of preferred shares	16,112,721	162	148,429				148,591
Stock issued from exercise of stock options, net	305,518	3	455				458
Stock based compensation			3,823				3,823
Issuance of stock options to consultants			162				162
Accretion of redeemable convertible preferred stock			(351)				(351)
Charge for warrant liability			758				758
Comprehensive (Loss)/ Income:							
Unrealized holding gain on available-for-sale securities				393			393
Net loss						(41,167)	(41,167)
Net total comprehensive loss							(40,774)
Balance at December 31, 2007	22,408,731	\$ 285	\$ 227,438	\$ 408	\$	\$ (124,834)	\$ 103,297



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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Consolidated Statements of Cash Flows**  
**(in thousands)**

	<b>Years Ended December 31,</b>			<b>Period from</b>
	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>February 4,</b>
				<b>2002</b>
				<b>(Inception)</b>
				<b>to</b>
				<b>December</b>
				<b>31,</b>
				<b>2007</b>
<b>Operating activities</b>				
Net loss	\$ (19,972)	\$ (46,345)	\$ (41,167)	\$ (124,834)
Adjustments to reconcile net loss to net cash used in operating activities:				
Non-cash interest expense				525
Depreciation and amortization	303	952	1,237	2,792
Amortization of non-cash compensation	365			522
Stock-based compensation		2,816	3,823	6,638
Non-cash charge for stock based compensation issued to consultants	111	475	162	853
Change in fair value of warrant liability	281	22	149	454
Stock-based license payment		1,220		1,220
Impairment of leasehold improvements				1,030
Non-cash charge for in process research and development				418
Beneficial conversion feature related to bridge financing				135
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(286)	120	(1,192)	(1,513)
Other non-current assets	(491)	265		(288)
Account payable and accrued expenses	1,565	6,586	1,566	10,465
Deferred revenue			50,614	50,614
Net cash (used in)/provided by operating activities	(18,124)	(33,889)	15,192	(50,969)
<b>Investing activities</b>				
Sale and redemption of marketable securities	3,093	37,441	126,370	169,066
Purchases of marketable securities	(16,990)	(62,013)	(200,743)	(286,114)
Purchases of property and equipment	(3,041)	(2,031)	(669)	(7,611)
Net cash used in investing activities	(16,938)	(26,603)	(75,042)	(124,659)
<b>Financing activities</b>				
Proceeds from the issuance of preferred stock, net of issuance costs	40,316	63,371	24,053	143,022

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Proceeds from issuance of common stock, net of issuance costs			68,093	68,093
Proceeds from the issuance of convertible notes				5,000
Payments of capital lease obligations	(273)	(881)	(1,388)	(2,866)
Payments from exercise of stock options	24	158	510	692
Proceeds from exercise of warrants (common and preferred)	75	91	97	264
Proceeds from capital asset financing arrangement	1,112	3,431	546	5,611
Net cash provided by financing activities	41,254	66,170	91,911	219,816
Net increase in cash and cash equivalents	6,192	5,678	32,061	44,188
Cash and cash equivalents at beginning of year/period	257	6,449	12,127	
Cash and cash equivalents at end of year/period	\$ 6,449	\$ 12,127	\$ 44,188	\$ 44,188
<b>Supplemental disclosures of cash flow information</b>				
Cash paid during the period for interest	\$ 482	\$ 273	\$ 348	\$ 1,136
<b>Non-cash activities</b>				
Conversion of preferred stock to common stock	\$	\$	\$ 148,591	148,951
Conversion of notes payable to Series B redeemable convertible preferred stock	\$	\$	\$	\$ 5,000
Accretion of redeemable convertible preferred stock	\$ 139	\$ 159	\$ 351	\$ 802
Beneficial conversion feature related to issuance of the additional issuance of Series C redeemable convertible preferred stock	\$	\$ 19,424	\$	\$ 19,424
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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Notes To Consolidated Financial Statements**

**1. Description of Business**

***Corporate Information, Status of Operations, and Management Plans***

Amicus Therapeutics, Inc. (the Company) was incorporated on February 4, 2002 in Delaware for the purpose of creating a premier drug development company at the forefront of therapy for human genetic diseases initially based on intellectual property in-licensed from Mount Sinai School of Medicine. The Company's activities since inception have consisted principally of raising capital, establishing facilities, and performing research and development. Accordingly, the Company is considered to be in the development stage.

In November 2007, the Company entered into a License and Collaboration Agreement with Shire Pharmaceuticals Ireland Ltd. (Shire). Under the agreement, the Company and Shire will jointly develop the Company's three lead pharmacological chaperone compounds for lysosomal storage disorders: Amigal (migalastat hydrochloride), Plicera (isofagomine tartrate) and AT2220. For further information, see Note 12. Development and Commercialization Agreement with Shire.

The Company has an accumulated deficit of approximately \$124.8 million at December 31, 2007 and anticipates incurring losses through the year 2008 and beyond. The Company has not yet generated commercial sales revenue and has been able to fund its operating losses to date through the sale of its redeemable convertible preferred stock, issuance of convertible notes, net proceeds from our initial public offering (IPO), the upfront licensing payment from Shire and other financing arrangements. The Company believes that its existing cash and cash equivalents and short-term investments will be sufficient to covers its cash flow requirements for 2008.

**2. Summary of Significant Accounting Policies**

***Reverse Stock Split***

As a result of the 1:7.5 reverse stock split that became effective on May 24, 2007, every 7.5 shares of the Company's redeemable convertible preferred stock and common stock were combined into one share of the Company's redeemable convertible preferred stock and one share of common stock, respectively. All references to redeemable convertible preferred stock, redeemable convertible preferred stock outstanding, common stock, common shares outstanding, average number of common shares outstanding and per share amounts in these consolidated financial statements and notes to consolidated financial statements prior to the effective date of the reverse stock split have been restated to reflect the 1:7.5 reverse stock split on a retroactive basis.

***Basis of Presentation***

The accompanying consolidated financial statements have been prepared in accordance with United States (U.S.) generally accepted accounting principles (U.S. GAAP) and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

***Consolidation***

The financial statements include the accounts of Amicus Therapeutics, Inc. and its wholly owned subsidiary, Amicus Therapeutics UK Limited. All significant intercompany transactions and balances are eliminated in consolidation.

***Use of Estimates***

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Notes To Consolidated Financial Statements (Continued)**

***Cash and Cash Equivalents***

The Company considers all highly liquid investments purchased with a maturity of three months or less at the date of acquisition, to be cash equivalents.

***Investment in Marketable Securities***

Marketable securities consist of fixed income investments with a maturity of greater than three months and other highly liquid investments that can be readily purchased or sold using established markets. In accordance with Financial Accounting Standards Board (FASB) Statement of Financial Accounting Standards (SFAS) No. 115, *Accounting for Certain Investments in Debt and Equity Securities*, these investments are classified as available-for-sale and are reported at fair value on the Company's balance sheet. Unrealized holding gains and losses are reported within accumulated other comprehensive income/ (loss) as a separate component of stockholders (deficiency) equity. If a decline in the fair value of a marketable security below the Company's cost basis is determined to be other than temporary, such marketable security is written down to its estimated fair value as a new cost basis and the amount of the write-down is included in earnings as an impairment charge. No other than temporary impairment charges have been recorded in any of the years presented herein.

***Concentration of Credit Risk***

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and cash equivalents and marketable securities. The Company maintains its cash and cash equivalents in bank accounts, which, at times, exceed federally insured limits. The Company invests its marketable securities in high-quality commercial financial instruments. The Company has not recognized any losses from credit risks on such accounts during any of the periods presented. The Company believes it is not exposed to significant credit risk on cash and cash equivalents or its marketable securities.

***Fair Value of Financial Instruments***

SFAS No. 107, *Disclosures about Fair Value of Financial Instruments* (SFAS No. 107), requires disclosures of fair value information about financial instruments, whether or not recognized in the balance sheet, for which it is practicable to estimate that value. Due to the short-term nature, the carrying amounts reported in the financial statements approximate the fair value for cash and cash equivalents, accounts payable and accrued expenses. The estimated fair values of the Company's redeemable convertible preferred stock at December 31, 2006 was approximately \$171.3 million, based on the September 2006 Series D redeemable convertible preferred stock price of \$12.15 per share. The redeemable convertible preferred stock was converted into common stock of the Company upon completion of the Company's IPO. The warrants to purchase shares of Series B redeemable convertible preferred stock were recorded at fair value based on the Black-Scholes-Merton methodology and were valued at \$0.6 million at December 31, 2006.

***Property and Equipment***

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is calculated over the estimated useful lives of the respective assets, which range from three to five years, or the lesser of the related initial term of the lease or useful life for leasehold improvements. Assets under capital leases are amortized over the terms of the related leases or their estimated useful lives, whichever is shorter.

The initial cost of property and equipment consists of its purchase price and any directly attributable costs of bringing the asset to its working condition and location for its intended use. Expenditures incurred after the fixed assets have been put into operation, such as repairs and maintenance, are charged to income in the period in which the costs are incurred. Major replacements, improvements and additions are capitalized in accordance with Company policy.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

***Impairment of Long-Lived Assets***

The Company performs a review of long-lived assets for impairment when events or changes in circumstances indicate the carrying value of such assets may not be recoverable. If an indication of impairment is present, the Company compares the estimated undiscounted future cash flows to be generated by the asset to its carrying amount. If the undiscounted future cash flows are less than the carrying amount of the asset, the Company records an impairment loss equal to the excess of the asset's carrying amount over its fair value. The fair value is determined based on valuation techniques such as a comparison to fair values of similar assets or using a discounted cash flow analysis. The Company reported an impairment charge of \$1.0 million during 2003 related to impaired capitalized leasehold improvements. There were no other impairment charges recognized during the years ended December 31, 2005, 2006 and 2007.

***In-Process Research and Development***

During 2002, the Company acquired certain development rights to intellectual property in the form of patent rights owned by Mount Sinai School of Medicine of New York University in exchange for 232,266 shares of common stock. The patent rights cover compounds that improve protein folding and protein stability.

The patent rights were reviewed to determine the stage of their development, the achievement of technological feasibility, and the technical milestones needed before commercialization is possible. It was determined, as of the acquisition date that each patent had significant technical risk associated with achieving the technological feasibility needed for U. S. Food and Drug Administration (FDA) approval and each patent has significant milestones to reach before commercialization is reasonably certain. It was also determined that all of the patents had no alternative future uses if they were not successful. Accordingly, the license was classified as in-process research and development and expensed immediately as of the acquisition date and included in research and development expense. The Company valued the acquired patents using fair value techniques, as a quoted market price was not available. The estimated fair value of the transfer at the date of the transaction was approximately \$0.4 million.

***Revenue Recognition***

The Company recognizes revenue in accordance with the Securities and Exchange Commission (SEC) Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition in Financial Statements* (SAB 101), as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13* (SAB 104).

In determining the accounting for collaboration agreements, the Company follows the provisions of Emerging Issues Task Force (EITF) Issue 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). EITF 00-21 provides guidance on whether an arrangement involves multiple revenue-generating deliverables that should be accounted for as a single unit of accounting or divided into separate units of accounting for revenue recognition purposes and, if this division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement represents a single unit of accounting, the revenue recognition policy and the performance obligation period must be determined (if not already contractually defined) for the entire arrangement. If the arrangement represents separate units of accounting according to the EITF's separation criteria, a revenue recognition policy must be determined for each unit. Revenues for non-refundable upfront license fee payments will be recognized on a straight line basis as Collaboration Revenue over the period of the performance obligations.

Revenues for research and development costs that are reimbursable under collaboration agreements in accordance with EITF Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* (EITF 99-19) are recognized. The revenue associated with these reimbursable amounts is included in Research Revenue and the costs associated with these reimbursable amounts are included in research and development expenses. The Company records these reimbursements as revenue and not as a reduction of research and development expenses as the Company has the risks and rewards as the principal in the research and development activities.

***Research and Development Costs***

Research and development costs are expensed as incurred. Research and development expense consists primarily of costs related to personnel, including salaries and other personnel-related expenses, consulting fees and the cost of

facilities and support services used in drug development. Assets acquired that are used for research and development and have no future alternative use are expensed as in-process research and development.

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**Amicus Therapeutics, Inc.  
(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

***Interest Income and Interest Expense***

Interest income consists of interest earned on the Company's cash and cash equivalents and marketable securities. Interest expense consists of interest incurred on capital leases.

***Other Income and Expenses***

During the second and third quarter of 2006, the Company deferred and capitalized \$1.2 million of costs directly attributable to the planned offering of its securities as other non-current assets. These costs were recorded as other expenses when the planned offering was withdrawn during the third quarter of 2006.

***Income Taxes***

The Company accounts for income taxes under the liability method. Under this method deferred income tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax basis of assets and liabilities and for operating losses and tax credit carryforwards, using enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance is recorded if it is more likely than not that a portion or all of a deferred tax asset will not be realized.

In June 2006, the FASB issued FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes - an Interpretation of FASB Statement No. 109* (FIN 48). FIN 48 addresses the accounting and disclosure of uncertain tax positions. FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken. The Company adopted FIN 48 on January 1, 2007 as required and determined that the adoption of FIN 48 did not have a material impact on the Company's financial position and results of operations.

***Other Comprehensive Income/ (Loss)***

SFAS No. 130, *Reporting Comprehensive Income*, requires components of other comprehensive income/(loss), including unrealized gains and losses on available-for-sale securities, to be included as part of total comprehensive income/(loss). The components of comprehensive gain/loss are included in the statements of changes in stockholders (deficiency) equity.

***Leases***

In the ordinary course of business, the Company enters into lease agreements for office space as well as leases for certain property and equipment. The leases have varying terms and expirations and have provisions to extend or renew the lease agreement, among other terms and conditions, as negotiated. Once the agreement is executed, the lease is assessed to determine whether the lease qualifies as a capital or operating lease.

When a non-cancelable operating lease includes any fixed escalation clauses and lease incentives for rent holidays or build-out contributions, rent expense is recognized on a straight-line basis over the initial term of the lease. The excess between the average rental amount charged to expense and amounts payable under the lease is recorded in accrued expenses.

***Redeemable Convertible Preferred Stock***

The carrying value of redeemable convertible preferred stock is increased by periodic accretions so that the carrying amount will equal the redemption amount at the earliest redemption date. These increases are reflected through charges to additional paid-in capital since the Company does not have retained earnings. Redeemable convertible preferred stock was converted into common stock upon completion of the Company's IPO on a one-for-one basis.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

***Warrants to Purchase Redeemable Convertible Preferred Stock***

The Company accounted for its warrants to purchase shares of its Series B redeemable convertible preferred stock (Series B Warrants) in accordance with FASB Staff Position 150-5: *Issuer's Accounting under FASB Statement No. 150 for Freestanding Warrants and Other Similar Instruments on Shares That Are Redeemable (FSP 150-5)*. As the Series B Preferred shares underlying the warrants had redemption rights, the warrants to purchase Series B shares were classified as a liability. The Company measured the fair value of its warrant liability using the Black-Scholes option pricing model with changes in fair value recognized as non-operating income or expense. The value of the warrant liability at issuance was \$0.4 million. In connection with the Company's IPO, the Series B warrants were exercised for 40,797 shares of Series B redeemable convertible preferred stock and automatically converted into common stock on a one-for-one basis.

***Stock-Based Compensation***

At December 31, 2007, the Company had two stock-based employee compensation plans, which are described more fully in Note 7. Stock Option Plans. Until May 2007, the Company had one stock-based employee compensation plan. Prior to January 1, 2006, the Company accounted for this plan under the recognition and measurement provisions of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB No. 25) and related interpretations, as permitted by SFAS No. 123, *Accounting for Stock-Based Compensation*. 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 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 No. 123(R). Results for prior periods have not been restated. As a result of adopting SFAS No. 123(R) on January 1, 2006, net income for the year ended December 31, 2006 was less than it would have been had the Company continued to account for stock-based compensation under APB No. 25.

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS No. 123(R), *Share-Based Payment* (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 January 1, 2006, based upon the grant-date fair value estimated in accordance with the provisions of SFAS No. 123(R). For options granted prior to January 1, 2006, as a non-public company and accounted for using the intrinsic value method, the Company will continue to expense any intrinsic value recognized over the vesting period. The grant-date fair value of awards expected to vest 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 and pro forma disclosures for outstanding awards accounted for under the intrinsic value method of APB No. 25 are not presented since the Company used the minimum value method for pro forma disclosure purposes prior to January 1, 2006.

Prior to the adoption of SFAS No. 123(R), the Company presented its unamortized portion of deferred compensation cost for non-vested stock options in the statement of changes in stockholders' (deficiency) equity with a corresponding credit to additional paid in capital. Upon the adoption of SFAS No. 123(R), these amounts were offset against each other. Under SFAS No. 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, and the deferred compensation balance of \$2.5 million at January 1, 2006 was net against additional paid in capital during the first quarter of 2006.

During the years ended December 31, 2005, 2006 and 2007, the Company recorded total employee stock-based compensation expense of approximately \$0.5 million, \$3.3 million and \$4.0 million, respectively. During the year ended December 31, 2006, the Company recorded incremental stock-based compensation expense of approximately \$2.2 million (\$2.99 per basic and diluted share) related to expensing of stock options under SFAS No. 123(R). Stock-based compensation expense had no impact on the Company's cash flows from operations and financing

activities.

SFAS No. 123(R) does not change the accounting guidance for how the Company accounts for options issued to non-employees. The Company accounts for options issued to non-employees in accordance with SFAS No. 123 and EITF Issue No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* (EITF 96-18). As such, the value of such options is periodically re-measured and income or expense is recognized during the vesting terms.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

Upon adoption of SFAS No. 123(R), the Company 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 is then 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 the Company's stock and the weighted average of historical information of similar public entities for which historical information was available. The Company will continue to use a weighted average approach using its own historical volatility and other similar public entity volatility information until historical volatility of the Company 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 SAB No. 107, *Share-Based Payment* (SAB No. 107), 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:

	<b>Years Ended December</b>	
	<b>31,</b>	
	<b>2006</b>	<b>2007</b>
Expected stock price volatility	74.8%	78.3%
Risk free interest rate	4.7	4.5
Expected life of options (years)	6.25	6.25
Expected annual dividend per share	\$0.00	\$0.00

***Beneficial Conversion Charges***

When the Company issues 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 financing is committed, a beneficial conversion charge is measured as the difference between the closing price and the conversion price at the commitment date. The beneficial conversion charge is presented as a discount or reduction to the related security, with an offsetting amount increasing additional paid-in capital. The Company also recorded a beneficial conversion charge (also referred to as a deemed dividend) during April 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 equity instruments is recorded with offsetting charges and credits to additional paid in capital with no effect on total shareholder equity. The Series C investors committed to finance the additional issuance of the Series C redeemable convertible preferred stock on March 31, 2006. The estimated fair value of the common stock was approximately \$16.13 per share at the commitment date of the additional issuance and the beneficial conversion charge was recognized upon issuance of the Series C redeemable convertible preferred stock as such stock could be converted upon issuance. The Company did not record a beneficial conversion charge for any other redeemable convertible preferred stock issuances as the common stock fair value was less than the conversion price of each offering on the respective commitment dates of those offerings.

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

The Company calculates net loss per share in accordance with SFAS No. 128, *Earnings Per Share*. The Company has determined that its Series A, B, C, and D redeemable convertible preferred stock represent participating securities in accordance with EITF Issue No. 03-6, *Participating Securities and the Two Class Method under FASB Statement No. 128*. However, since the Company operates at a loss, and losses are not allocated to the redeemable convertible preferred stock, the two class method does not affect the Company's calculation of earnings per share. The Company has 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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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

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 (in thousands except share amounts):

	<b>Years Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
<b>Historical</b>			
Numerator:			
Net loss	\$ (19,972)	\$ (46,345)	\$ (41,167)
Deemed dividend		(19,424)	
Accretion of redeemable convertible preferred stock	(139)	(159)	(351)
Net loss attributable to common stockholders	\$ (20,111)	\$ (65,928)	\$ (41,518)
Denominator:			
Weighted average common shares outstanding basic and diluted	410,220	735,967	13,235,755

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 9.5 million, 17.5 million and 24.9 million for the years ended December 31, 2005, 2006 and 2007, respectively. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect.

**Dividends**

The Company has not paid cash dividends on its capital stock to date. The Company currently intends to retain its future earnings, if any, to fund the development and growth of the business and do not foresee payment of a dividend in any upcoming fiscal period.

**Recent Accounting Pronouncements**

In December 2007, the EITF of the FASB reached a consensus on issue No. 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). The EITF concluded on the definition of a collaborative arrangement and that revenues and costs incurred with third parties in connection with collaborative arrangements would be presented gross or net based on the criteria in EITF 99-19 and other accounting literature. Based on the nature of the arrangement, payments to or from collaborators would be evaluated and its terms, the nature of the entity's business, and whether those payments are within the scope of other accounting literature would be presented. Companies are also required to disclose the nature and purpose of collaborative arrangements along with the accounting policies and the classification and amounts of significant financial-statement balances related to the arrangements. Activities in the arrangement conducted in a separate legal entity should be accounted for under other accounting literature; however required disclosure under EITF 07-1 applies to the entire collaborative agreement. This Issue is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years, and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. The Company does not expect this will have a significant impact on the financial statements of the Company.

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* (SFAS No. 141(R)), which replaces SFAS No. 141, *Business Combinations*, requires an acquirer to recognize the assets acquired, the liabilities assumed, and any non-controlling interest in the acquiree at the acquisition date, measured at their fair values as of

that date, with limited exceptions. This Statement also requires the acquirer in a business combination achieved in stages to recognize the identifiable assets and liabilities, as well as the non-controlling interest in the acquiree, at the full amounts of their fair values. SFAS No. 141(R) makes various other amendments to authoritative literature intended to provide additional guidance or to confirm the guidance in that literature to that provided in this Statement. This Statement applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. The Company does not expect this will have a significant impact on the financial statements of the Company.

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**Amicus Therapeutics, Inc.**  
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**Notes To Consolidated Financial Statements (Continued)**

In December 2007, FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements* (SFAS No. 160), which amends Accounting Research Bulletin No. 51, *Consolidated Financial Statements*, to improve the relevance, comparability, and transparency of the financial information that a reporting entity provides in its consolidated financial statements. SFAS No. 160 establishes accounting and reporting standards that require the ownership interests in subsidiaries not held by the parent to be clearly identified, labeled and presented in the consolidated statement of financial position within equity, but separate from the parent's equity. This statement also requires the amount of consolidated net income attributable to the parent and to the non-controlling interest to be clearly identified and presented on the face of the consolidated statement of income. Changes in a parent's ownership interest while the parent retains its controlling financial interest must be accounted for consistently, and when a subsidiary is deconsolidated, any retained non-controlling equity investment in the former subsidiary must be initially measured at fair value. The gain or loss on the deconsolidation of the subsidiary is measured using the fair value of any non-controlling equity investment. The Statement also requires entities to provide sufficient disclosures that clearly identify and distinguish between the interests of the parent and the interests of the non-controlling owners. This Statement applies prospectively to all entities that prepare consolidated financial statements and applies prospectively for fiscal years, and interim periods within those fiscal years, beginning on or after December 15, 2008. The Company does not expect this will have a significant impact on the financial statements of the Company.

In June 2007, the EITF of the FASB reached a consensus on Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities* (EITF 07-3). EITF 07-3 requires that non-refundable advance payments for goods or services that will be used or rendered for future research and development activities should be deferred and capitalized. As the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided, the deferred amounts would be recognized as an expense. This Issue is effective for financial statements issued for fiscal years beginning after December 15, 2007 and earlier application is not permitted. This consensus is to be applied prospectively for new contracts entered into on or after the effective date. The pronouncement is not expected to have a material effect on the financial statements of the Company.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities Including an amendment of FASB Statement No. 115* (SFAS No. 159), which is effective for fiscal years beginning after November 15, 2007. SFAS No. 159 permits the Company to choose to measure many financial instruments and certain other items at fair value. The objective is to improve financial reporting by providing entities with the opportunity to mitigate volatility in reported earnings caused by measuring related assets and liabilities differently without having to apply complex hedge accounting provisions. SFAS No. 159 is expected to expand the use of fair value measurement, which is consistent with the FASB's long-term measurement objectives for accounting for financial instruments. SFAS No. 159 is effective for fiscal year 2008 but early adoption is permitted. The Company is currently evaluating the impact, if any, that the adoption of SFAS No. 159 will have on the Company's financial statements.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measures* (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 the Company's 2008 fiscal year. The Company does not expect this will have a significant impact on the financial statements of the Company.

**Segment Information**

The Company currently operates in one business segment focusing on the development and commercialization of small molecule, orally administered therapies to treat a range of human genetic diseases. The Company is not organized by market and is managed and operated as one business. A single management team reports to the chief operating decision maker who comprehensively manages the entire business. The Company does not operate any separate lines of business or separate business entities with respect to its products. Accordingly, the Company does not

accumulate discrete financial information with respect to separate service lines and does not have separately reportable segments as defined by SFAS No. 131, *Disclosure About Segments of an Enterprise and Related Information*.

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**Notes To Consolidated Financial Statements (Continued)**

**3. Investments in Marketable Securities**

The following is a summary of available for sale securities held by the Company (in thousands):

	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
<b>December 31, 2006</b>				
Corporate Debt Securities	\$ 42,557	\$ 16	\$ (1)	\$ 42,572
<b>December 31, 2007</b>				
Corporate Debt Securities	\$ 116,931	\$ 423	\$ (15)	\$ 117,339

All of the Company's available for sale investments as of December 31, 2006 and 2007 are due in one year or less.

Unrealized gains and losses are reported as a component of accumulated other comprehensive gain/loss in stockholders' (deficiency) equity. For the years ended December 31, 2006 and 2007, unrealized holding gains included in accumulated other comprehensive income/(loss) were \$0.03 million and \$0.4 million, respectively.

For the years ended December 31, 2006 and 2007, there were no realized gains or losses. The cost of securities sold is based on specific identification method.

Unrealized loss positions in the available for sale securities as of December 31, 2006 and 2007 reflect temporary impairments that have not been recognized and have been in a loss position for less than twelve months. The fair value of these available for sale securities in unrealized loss positions was \$4.8 million and \$14.7 million as of December 31, 2006 and 2007, respectively.

Unrealized gains and losses in the Company's portfolio relate to fixed income debt securities. For these securities, the unrealized losses are due to increases in interest rates. There are no changes in credit risk of the debt securities. The Company has concluded that the unrealized losses in its marketable securities are not other-than-temporary as the Company has the ability to hold the securities to maturity or a planned forecasted recovery.

**4. Property and Equipment**

Property and equipment consist of the following (in thousands):

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
Property and equipment consist of the following:		
Computer equipment	\$ 564	\$ 694
Computer software	105	167
Research equipment	2,685	3,089
Furniture and fixtures	525	579
Leasehold improvements	2,036	2,054
	5,915	6,583
Less accumulated depreciation and amortization	(1,557)	(2,793)
	\$ 4,358	\$ 3,790



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**Amicus Therapeutics, Inc.**  
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**Notes To Consolidated Financial Statements (Continued)**

Included in property and equipment are costs capitalized pursuant to capital lease obligations of \$4.8 million and \$5.5 million at December 31, 2006 and 2007. Depreciation and amortization expense relating to the capital lease obligations was \$0.1 million, \$0.8 million, \$1.1 million and \$2.0 million for the years ended December 31, 2005, 2006, and 2007, and for the Period February 4, 2002 (inception) to December 31, 2007, respectively.

**5. Accrued Expenses**

Accrued expenses consist of the following (in thousands):

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
Accrued professional fees	\$ 253	\$ 979
Accrued contract manufacturing & contract research costs	5,682	6,035
Accrued compensation and benefits	1,236	2,279
Accrued facility costs	482	364
Accrued other	51	278
	<b>\$ 7,704</b>	<b>\$ 9,935</b>

**6. Capital Structure****Common Stock**

As of December 31, 2007, the Company was authorized to issue 50,000,000 shares of common stock. Dividends on common stock will be paid when, and if declared by the board of directors. Each holder of common stock is entitled to vote on all matters and is entitled to one vote for each share held.

In June 2007, the Company closed its IPO of 5,000,000 shares of its common stock at a public offering price of \$15.00 per share. Net proceeds to the Company were approximately \$68.1 million, after deducting underwriting discounts, commissions and offering expenses totaling approximately \$6.9 million. In connection with the initial public offering, the outstanding shares of Series A redeemable convertible preferred stock were converted into 444,443 shares of common stock, the outstanding shares of Series B redeemable convertible preferred stock were converted into 4,877,056 shares of common stock, the outstanding shares of Series C redeemable convertible preferred stock were converted into 5,820,020 shares of common stock and the outstanding shares of Series D redeemable convertible preferred stock were converted into 4,930,405 shares of common stock. In connection with the IPO, the outstanding warrants to purchase Series B redeemable convertible preferred stock were automatically exercised and the shares of Series B redeemable convertible preferred stock automatically converted into 40,797 shares of the common stock. As a result, the Company no longer recognizes accretion expense for preferred stock or non-operating income or expense for changes in the fair value of the warrant liability.

In connection with an employment agreement and director compensation agreement, the Company issued 53,333 shares of common stock in return for services in 2005. The shares will vest over three and four year periods. The Company recorded \$0, \$0.04 million and \$0.1 million as compensation expense during 2005, 2006 and 2007, respectively, in connection with the issuance of these restricted shares.

In connection with the formation of the Company, the Company issued 232,266 shares of common stock to the Mount Sinai School of Medicine of New York University (MSSM) in exchange for exclusive license rights for certain intellectual property. The value of the shares was accounted for as in-process research and development; see Note 2. Summary of Significant Accounting Policies In-Process Research and Development. In October of 2006, the Company amended its license agreement MSSM to expand its exclusive worldwide patent rights to develop and commercialize pharmacological chaperones. In connection with the amendment, the Company paid \$1.0 million and



issued 133,333 shares of its common stock valued at \$1.2 million to MSSM.

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**Amicus Therapeutics, Inc.**  
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**Notes To Consolidated Financial Statements (Continued)**

**Redeemable Convertible Preferred Stock**

In June 2007 in connection with the IPO, all outstanding redeemable convertible preferred stock was converted to common stock. As of the IPO conversion date, Series A, Series B, Series C, and Series D were converted at their respected stated values (estimated fair value of \$5.63 per share, \$6.32 per share, \$9.45 per share, and \$12.17 per share, respectively, less issuance costs and accretion adjustments).

	Series A		Series B		Series C		Series D	
	Shares	Amount (in thousands)	Shares	Amount (in thousands)	Shares	Amount (in thousands)	Shares	Amount (in thousands)
Balance at February 4, 2002 (inception)		\$		\$		\$		\$
Issuance of Series A at \$5.63 per share	444,443	2,500						
Issuance costs		(95)						
Accretion		10						
Balance at December 31, 2002	444,443	2,415						
Accretion		17						
Balance at December 31, 2003	444,443	2,432						
Issuance of Series B at \$6.38 per share			2,823,523	18,000				
Issuance cost				(122)				
Issuance of warrants with Series B				(422)				
Accretion		17		109				
Balance at December 31, 2004	444,443	2,449	2,823,523	17,565				
Issuance of Series B at \$6.38 per share			2,039,211	13,000				
Issuance cost				(6)				

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Issuance of Series C at \$9.45 per share					2,910,010	27,500
Issuance cost						(178)
Accretion		17		110		12
Balance at December 31, 2005	444,443	2,466	4,862,734	30,669	2,910,010	27,334

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**Notes To Consolidated Financial Statements (Continued)**

	Series A		Series B		Series C		Series D	
	Shares	Amount (in thousands)	Shares	Amount (in thousands)	Shares	Amount (in thousands)	Shares	Amount (in thousands)
Balance at December 31, 2005	444,443	2,466	4,862,734	30,669	2,910,010	27,334		
Exercise of warrants with Series B at \$6.38			14,322	91				
Issuance of Series C at \$9.45 per share					2,910,010	27,500		
Issuance of Series D at \$12.15 per share							2,953,878	35,947
Issuance cost								(76)
Accretion to redemption value		10		108		35		5
Balance at December 31, 2006	444,443	2,476	4,877,056	30,868	5,820,020	54,869	2,953,878	35,876
Issuance of Series D at \$12.15 per share							1,976,527	24,053
Series B warrant exercise			40,797	98				
Accretion to redemption value		24		126		130		71
Conversion of preferred stock to common	(444,443)	(2,500)	(4,917,853)	(31,092)	(5,820,020)	(54,999)	(4,930,405)	(60,000)
Balance at December 31, 2007		\$		\$		\$		\$

***Warrants***

During 2002, the Company issued 5,333 common stock warrants to a vendor as part of a capital lease agreement. These warrants were outstanding at December 31, 2005 and 2006. The warrants have an exercise price of \$5.63 per share (adjusted for stock splits, stock dividends, etc.). The value of the warrants was calculated using the Black-Scholes option pricing model and was capitalized as debt issuance cost and amortized to interest expense over the term of the obligation. The value of the warrants and total charge to interest expense was not material for each of the years presented.

In 2003, the Company issued 133,332 common stock warrants to certain investors in connection with its Bridge Loans. The warrants had an exercise price of \$0.56 per share (adjusted for stock splits, stock dividends, etc.). The value of the warrants of \$0.2 million was calculated using the Black-Scholes option pricing model and was accounted for as debt discount and amortized to interest expense over the term of the loans. These same warrant shares were exercised in 2005. The total charge to interest expense was \$0.1 million for the year ended December 31, 2004.

In 2004, the Company issued warrants to purchase 73,996 Series B shares to certain investors as part of the Series B financing. The warrants had an exercise price of \$6.38 per share (adjusted for stock splits, stock dividends, etc.) and could have been exercised for cash or net shares at the option of the warrant holders. During 2006 there were 14,322 warrants exercised for Series B shares. In connection with the IPO, the remaining 40,797 warrants were automatically exercised and converted into 40,797 common shares. As the Series B Preferred shares underlying the warrants had redemption rights, the warrants to purchase Series B shares were classified as a liability in accordance with FSP 150-5.

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**Notes To Consolidated Financial Statements (Continued)**

The Company measures the fair value of its warrant liability using the Black-Scholes option pricing model with changes in fair value recognized in earnings. The value of the warrant liability at issuance was \$0.4 million. The Company recognized changes in the fair value of the warrant liability as non-operating income or (expense) of \$0, \$(0.3 million), and \$(0) in 2004, 2005, and 2006, respectively. In connection with the Company's IPO, the Series B warrants were exercised for 40,797 shares of Series B redeemable convertible preferred stock and automatically converted into common stock on a one-for-one basis.

**7. Stock Option Plans**

In April 2002, the Company's board of directors and shareholders approved the Company's 2002 Stock Option Plan (the 2002 Plan). In May 2007, the Company's Board of Directors and shareholders approved the Company's 2007 Stock Option Plan (the 2007 Plan). Both the 2002 Plan and 2007 Plan provide for the granting of restricted stock and options to purchase common stock in the Company to employees, advisors and consultants at a price to be determined by the Company's board of directors. The 2002 Plan and the 2007 Plan are intended to encourage ownership of stock by employees and consultants of the Company and to provide additional incentives for them to promote the success of the Company's business. The Options may be incentive stock options (ISOs) or non-statutory stock options (NSOs). Under the provisions of each plan, no option will have a term in excess of 10 years.

The Board of Directors, or its committee, is responsible for determining the individuals to be granted options, the number of options each individual will receive, the option price per share, and the exercise period of each option. Options granted pursuant to the both the 2002 Plan and the 2007 Plan generally vest 25% on the first year anniversary date of grant plus an additional 1/48th for each month thereafter and may be exercised in whole or in part for 100% of the shares vested at any time after the date of grant.

As of December 31, 2007, the Company reserved up to 3,168,000 shares for issuance under the 2002 Plan and 966,667 shares under the 2007 Plan.

The Company recognized stock-based compensation expense of \$0.5 million, \$3.3 million and \$4.0 million in 2005, 2006 and 2007, respectively. In 2006, research and development expense and general and administrative expense include \$1.7 million and \$1.6 million of stock compensation expense, respectively. In 2007, research and development expense and general and administrative expense include \$1.6 million and \$2.4 million of stock compensation expense, respectively.

Upon adoption of SFAS No. 123(R) on January 1, 2006, the Company 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. The Company 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 SAB No. 107, 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 grant-date fair value per share of options granted during 2006 and 2007 were \$10.20 and \$9.45, respectively. The weighted average assumptions used in the Black-Scholes option pricing model are as follows:

<b>Years Ended December</b>	
<b>31,</b>	
<b>2006</b>	<b>2007</b>

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Expected stock price volatility	74.8%	78.3%
Risk free interest rate	4.7%	4.5%
Expected life of options (years)	6.25	6.25
Expected annual dividend per share	\$0.00	\$0.00

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**Amicus Therapeutics, Inc.**  
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**Notes To Consolidated Financial Statements (Continued)**

The following table summarizes information about stock options outstanding:

	Number of Shares (in thousands)	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value  (in millions)
Options outstanding, December 31, 2004	426.6	\$ 0.45		
Granted	1,010.2	\$ 2.17		
Exercised	(97.2)	0.22		
Forfeited	(102.5)	\$ 0.45		
Options outstanding, December 31, 2005	1,237.1	\$ 2.10		
Granted	1,005.1	\$ 6.00		
Exercised	(265.8)	\$ 0.60		
Forfeited	(108.0)	\$ 2.20		
Options outstanding, December 31, 2006	1,868.4	\$ 4.27		
Granted	1,035.6	\$ 13.16		
Exercised	(308.6)	\$ 1.80		
Forfeited	(152.2)	\$ 8.94		
Options outstanding, December 31, 2007	2,443.2	\$ 8.08	8.3 years	\$ 9.0
Vested and unvested expected to vest, December 31, 2007	2,214.0	\$ 7.78	8.2 years	\$ 7.1
Exercisable at December 31, 2007	746.6	\$ 4.66	7.2 years	\$ 4.5

The aggregate intrinsic value of options exercised during the years ended December 31, 2005, 2006, and 2007, was \$0.1 million, \$2.5 million and \$2.7 million, respectively. As of December 31, 2007, the total unrecognized compensation cost related to non-vested stock options granted was \$11.8 million and is expected to be recognized over a weighted average period of 2.8 years. Cash proceeds from stock options exercised during the years ended December 31, 2005, 2006 and 2007 was \$0, \$0.2 million and \$0.5 million, respectively.

**Restricted Stock Awards** Restricted stock awards are granted subject to certain restrictions, including in some cases service conditions (restricted stock). The grant-date fair value of restricted stock awards, which has been determined based upon the market value of the Company's shares on the grant date, is expensed over the vesting period.

The following table summarizes the Company's restricted stock activity as of and for the year ended December 31, 2007:



	<b>Number of Shares (in thousands)</b>	<b>Restricted Stock Weighted Average Grant Date Fair Value</b>
Unvested at December 31, 2006	51.1	\$ 8.94
Granted		\$
Vested	(16.1)	\$ 8.88
Forfeited		\$
Unvested at December 31, 2007	35.0	\$ 8.96

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**Notes To Consolidated Financial Statements (Continued)**

Upon vesting, 3,085 shares were surrendered by the Company to fund the Company's minimum statutory tax withholding requirements. There were no restricted stock awards in 2007 or prior to 2006. As of December 31, 2007, the total unrecognized compensation cost related to unvested restricted stock awards was \$0.3 million. This cost is expected to be recognized over a weighted average period of 2.6 years. The total fair value of restricted stock awards which vested during 2007 was \$0.1 million.

**8. 401(k) Plan**

The Company has a 401(k) plan (the Plan) covering all eligible employees. The Plan allows for a discretionary employer match. Through December 31, 2007, the Company has not made any match of employee contributions. During 2007, the Board of Directors approved a company matching program that began on January 1, 2008. The matching program allows for a company match of up to 5% of salary and bonus paid during the year.

**9. Leases****Operating Leases**

On May 12, 2005, the Company entered into a Sublease Agreement for its Corporate Office in Cranbury, NJ. The sublease term will expire on February 28, 2012 or on such earlier date upon mutual agreement of both parties. On August 14, 2006, the Company entered into another sublease agreement to expand office space in an adjacent building. This sublease term will expire on August 31, 2009 or on such earlier date upon mutual agreement of both parties. At December 31, 2007, aggregate annual future minimum lease payments under these leases are as follows (in thousands):

Operating Leases Years ending December 31:

2008	\$ 1,655
2009	1,527
2010	1,295
2011	1,307
2012	219
	\$ 6,003

Rent expense for the years ended December 31, 2005, 2006 and 2007 were \$1.0 million, \$1.6 million and \$1.8 million, respectively.

**Capital Lease Facility**

In August 2002, the Company entered into financing agreements that provides for up to \$1 million of equipment financing through August 2004. The facility was increased to \$3 million in May of 2005 and to \$5 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 leasehold improvements.

At December 31, 2006, the total amount available to the Company under these agreements is \$1.4 million. The funding period of the facility expired by its own term in 2007.

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**Notes To Consolidated Financial Statements (Continued)**

The remaining future minimum payments due for all non-cancelable capital leases as of December 31, 2007 are as follows (in thousands):

Capital Leases Years ending December 31:	
2008	\$ 1,745
2009	957
2010	295
2011	42
	3,039
Less payments for interest	(318)
Total principal obligation	2,721
Less short-term portion	(1,527)
Long-term portion	\$ 1,194

The capital lease obligation is secured by the related assets financed by the leases.

**10. Income Taxes**

In June 2006, the FASB issued FIN 48 to create a single model to address accounting for uncertainty in tax positions. FIN 48 clarifies the accounting for income taxes, by prescribing a minimum recognition threshold a tax position is required to meet before being recognized in the financial statements. FIN 48 also provides guidance on de-recognition, measurement, and classification of amounts relating to uncertain tax positions, accounting for and disclosure of interest and penalties, accounting in interim periods, disclosures and transition relating to the adoption of the new accounting standard. FIN 48 is effective for fiscal years beginning after December 15, 2006. The Company adopted FIN 48 as of January 1, 2007, as required and determined that the adoption of FIN 48 did not have a material impact on the Company's financial position and results of operations. The Company did not recognize interest or penalties related to income tax during the period ended December 31, 2007 and did not accrue for interest or penalties as of December 31, 2007. The Company does not have an accrual for uncertain tax positions as of December 31, 2007. Tax returns for all years 2002 and thereafter are subject to future examination by tax authorities.

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**Notes To Consolidated Financial Statements (Continued)**

Deferred income taxes reflect the net effect of temporary difference between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The significant components of the deferred tax assets and liabilities are as follows (in thousands):

	<b>For Years Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Current deferred tax asset			
Non cash stock issue to consultants	\$ 64	\$ 246	\$ 283
Others	33	1,309	1,232
	97	1,555	1,515
Non current deferred tax assets			
Amortization/depreciation	132	1,289	1,129
Research tax credit	1,344	3,611	5,403
Net operating loss carry forwards	14,464	27,257	42,282
Others	29	121	478
Total deferred tax asset	16,066	33,833	50,807
Non current deferred tax liability			
Depreciation	(57)		
Total net deferred tax asset	16,009	33,833	50,807
Less valuation allowance	(16,009)	(33,833)	(50,807)
Net deferred tax asset	\$	\$	\$

The Company records a valuation allowance for temporary differences for which it is more likely than not that the Company will not receive future tax benefits. At December 31, 2005, 2006, and 2007, the Company recorded valuation allowances of \$16.0 million, \$33.8 million and \$50.8 million, respectively, representing a change in the valuation allowance of \$17.8 million and \$17.0 million for the two previous fiscal year-ends, due to the uncertainty regarding the realization of such deferred tax assets, to offset the benefits of net operating losses generated during those years.

As of December 31, 2007, the Company had federal and state net operating loss carry forwards of approximately \$106 million and \$103 million, respectively. The federal carry forward will begin to expire in 2024 and will end in 2028. The state carry forward will begin to expire in 2012 and will end in 2015. Utilization of the net operating loss carry forwards and credits may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. The Company is conducting an analysis to determine if there has been a change in ownership as defined by the Tax Reform Act of 1986. This analysis does not impact the 2007 financial statements.

The Company recognized a tax benefit of \$0.6 million in connection with the sale of net operating losses in the New Jersey Tax Transfer Program during the year ended December 31, 2005.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**  
**Notes To Consolidated Financial Statements (Continued)**

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2005, 2006 and 2007 are as follows:

	<b>Years Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Statutory rate	(34)%	(34)%	(34)%
State taxes, net of federal benefit	(6)	(6)	(5)
Permanent adjustments	1	1	3
Non deductible interest			
R&D credit	(3)	(4)	(4)
Other	(1)	2	(1)
Benefit from sale of net operating loss	(3)		
Valuation allowance	43	41	41
Net	(3)%	0%	0%

Income tax benefit consisted of the following components (in thousands):

	<b>Years Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Current benefit:			
Federal	\$	\$	\$
State	(612)		
Deferred:			
Federal			
State			
Income tax benefit	\$ (612)	\$	\$

**11. Licenses**

The Company acquired rights to develop and commercialize its product candidates through licenses granted by various parties. The following summarizes the Company's material rights and obligations under those licenses:

*Mt. Sinai School of Medicine of New York University (MSSM)* The Company acquired exclusive worldwide patent rights to develop and commercialize Amigal, Plicera and AT2220 and other pharmacological chaperones for the treatment of diseases which can be achieved by enhancing lysosomal enzyme activity pursuant to a license agreement with MSSM. In connection with this agreement, the Company issued 232,266 shares of common stock to MSSM in April 2002. In 2006, the Company amended its license agreement with MSSM to expand its exclusive worldwide patent rights to develop and commercialize pharmacological chaperones. In connection with the amendment, the Company paid \$1.0 million and issued 133,333 shares of its common stock with an estimated fair value of \$1.2 million to MSSM. In total, the Company recorded \$2.2 million of research and development expense in connection with the amendment in 2006. 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, subject to any patent term extension

that may be granted. Under this agreement, the Company has no milestone or future payments other than royalties on net sales. In conjunction with the \$50 million upfront payment from Shire in November 2007, the Company recorded an accrual for its best estimate of royalties due to MSSM on the upfront payment.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

*University of Maryland, Baltimore County* The Company 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, the Company paid upfront and annual license fees of \$29,500, which were expensed as research and development expense. The Company is required to make a milestone payment upon the demonstration of safety and efficacy of Plicera for the treatment of Gaucher disease in a Phase 2 study, and another payment upon receiving FDA approval for Plicera for the treatment of Gaucher disease. Upon satisfaction of both milestones, the Company could be required to make up to \$0.2 million in aggregate payments. The Company is 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* The Company acquired exclusive patent rights to develop and commercialize Plicera for all human indications. Under this agreement, to date the Company paid \$0.4 million in license fees which were expensed as research and development expense. The Company is also required to make milestone payments based on clinical progress of Plicera, with a payment due after initiation of a Phase 2 clinical trial for Plicera for the treatment of Gaucher disease, and a payment due upon each filing for regulatory approval of Plicera for the treatment of Gaucher disease in any of the US, Europe or Japan. An additional payment is due upon approval of Plicera for the treatment of Gaucher disease in the U.S. and a payment is also due upon each approval of Plicera for the treatment of Gaucher disease in either Europe or Japan. Assuming successful development of Plicera for the treatment of Gaucher disease in the U.S., Europe and Japan, total milestone payments would be \$7.8 million. The Company is also required to pay royalties on net sales. This license will terminate in 2016.

Under its license agreements, if the Company owes royalties on net sales for one of its products to more than one of the above licensors, then it has 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, the Company will owe royalties only to MSSM and will owe no milestone payments. The Company expects to pay royalties to all three licensors with respect to Plicera.

The Company's rights with respect to these agreements to develop and commercialize Amigal, Plicera and AT2220 may terminate, in whole or in part, if the Company fails to meet certain development or commercialization requirements or if the Company does not meet its obligations to make royalty payments.

**12. Development and Commercialization Agreement with Shire**

In November 2007, the Company entered into a License and Collaboration Agreement with Shire. Under the agreement, the Company and Shire will jointly develop the Company's three lead pharmacological chaperone compounds for lysosomal storage disorders: Amigal, Plicera and AT2220. The Company granted Shire the rights to commercialize these products outside the U.S. The Company retains all rights to its other programs and to develop and commercialize Amigal, Plicera and AT2220 in the U.S.

The Company received an initial, non-refundable license fee payment of \$50 million from Shire. Joint development costs toward global approval of the three compounds will be shared 50/50 going forward. In addition, The Company is eligible to receive, for all three drug product candidates, aggregate potential milestone payments of up to \$150 million if certain clinical and regulatory milestones are achieved for all three of the programs, and \$240 million in sales-based milestones. The Company will also be eligible to receive tiered double-digit royalties on net sales of the products which are marketed outside of the U.S.

In accordance with the guidance in EITF 00-21, the Company determined that its various deliverables due under the collaboration agreement represent as a single unit of accounting for revenue recognition purposes. The initial, non-refundable upfront license fee payment of \$50 million will be recognized on a straight line basis as Collaboration Revenue over the period of the performance obligations. The Company determined that the period of performance obligations is 18 years as contractually defined.

Under the collaboration agreement, the Company will also receive reimbursement of up to 50% of research and development costs incurred in the development of the products covered by the agreement. The Company will recognize revenue for reimbursed research and development costs in accordance with EITF Issue 99-19 as Research



Revenue when the underlying costs associated with these reimbursable amounts are recorded in research and development expenses since the Company is currently and for the foreseeable future, conducting all of the research activities.

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**Amicus Therapeutics, Inc.**  
**(a development stage company)**

**Notes To Consolidated Financial Statements (Continued)**

As of December 31, 2007, the Company recorded \$1.4 million in Research Revenue and deferred \$1.0 million of reimbursed research and development costs to the current portion of deferred revenue.

As of December 31, 2007, the Company also recorded \$0.4 million in Collaboration Revenue related to the \$50 million upfront license fee payment from Shire and deferred \$2.8 million to the current portion of deferred revenue and \$46.8 million to long-term deferred revenue.

**13. Selected Quarterly Financial Data** (Unaudited in thousands except per share data)

	Quarters Ended			
	March 31	June 30	September 30	December 31
<b>2006</b>				
Net loss	\$(8,287)	\$ (8,624)	\$(11,643)	\$(17,791)
Net loss attributable to common stockholders	(8,328)	(28,089)	(11,684)	(17,828)
Basic and diluted net loss per common share				
(1)	(15.43)	(39.04)	(15.01)	(19.77)
<b>2007</b>				
Net loss	(9,695)	(9,396)	(10,303)	(11,773)
Net loss attributable to common stockholders	(9,736)	(9,706)	(10,303)	(11,773)
Basic and diluted net loss per common share				
(1)	(10.21)	(1.37)	(0.46)	(0.53)

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amounts because of differences on the weighted-average common shares outstanding during each period principally due to the effect of the Company's issuing shares of its common stock during the year.

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders of  
Amicus Therapeutics, Inc.

We have audited the accompanying consolidated balance sheets of Amicus Therapeutics, Inc. and subsidiary (a development stage company) as of December 31, 2007 and 2006, and the related consolidated statements of operations, stockholders' (deficiency) equity and cash flows for each of the three years in the period ended December 31, 2007 and the period February 4, 2002 (inception) to December 31, 2007. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Amicus Therapeutics, Inc. and subsidiary at December 31, 2007 and 2006, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2007, and the period February 4, 2002 (inception) to December 31, 2007, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the consolidated financial statements, effective January 1, 2006, the Company adopted Statement of Financial Accounting Standards No. 123(R), Share Based Payments, applying the prospective method.  
/s/ Ernst & Young LLP

MetroPark, New Jersey  
February 5, 2008

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**Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.**

None.

**Item 9A. CONTROLS AND PROCEDURES.**

**Evaluation of Disclosure Controls and Procedures**

Rule 13a-15(e) under the Securities and Exchange Act of 1934, as amended (the Exchange Act ), defines the term disclosure controls and procedures as those controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission (SEC) rules and forms and that such information is accumulated and communicated to the company s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Based on their evaluation as of December 31, 2007, our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures (as defined by Rules 13a-15(e) and 15d-15(e) under the Exchange Act) were effective as of December 31, 2007.

There have been no changes in our internal controls over financial reporting during the fourth quarter of the year ended December 31, 2007 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

**Exemption from Management s Report on Internal Control Over Financial Reporting for 2007**

This annual report does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

**Item 9B. OTHER INFORMATION.**

None.

**Table of Contents****PART III**

Certain information required by Part III is omitted from this Annual Report on Form 10-K as we intend to file our definitive proxy statement for our 2008 annual meeting of stockholders, pursuant to Regulation 14A of the Securities Exchange Act, not later than 120 days after the end of the fiscal year covered by this Annual Report of Form 10-K, and certain information to be included in the proxy statement is incorporated herein by reference.

**Item 10. DIRECTORS, EXECUTIVE OFFICERS OF THE REGISTRANT AND CORPORATE GOVERNANCE.****Executive Officers**

The following table sets forth certain information regarding our current executive officers as of February 1, 2008.

*John F. Crowley* has served as President and Chief Executive Officer since January 2005, and has also served as a Director of Amicus since August 2004, with the exception of the period from September 2006 to March 2007 when he was not an officer or director of Amicus while he was in active duty service in the United States Navy (Reserve). He was President and Chief Executive Officer of Orexigen Therapeutics, Inc. from September 2003 to December 2004. Mr. Crowley was President and Chief Executive Officer of Novazyme Pharmaceuticals, Inc., from March 2000 until that company was acquired by Genzyme Corporation in September 2001; thereafter he served as Senior Vice President of Genzyme Therapeutics until December 2002. Mr. Crowley received a B.S. degree in Foreign Service from Georgetown University's School of Foreign Service, a J.D. from the University of Notre Dame Law School, and an M.B.A. from Harvard Business School.

*Matthew R. Patterson* has served as Chief Operating Officer since September 2006. From December 2004 to September 2006 he served as Chief Business Officer. From 1998-2004, Mr. Patterson worked at BioMarin Pharmaceuticals Inc. where he was Vice President, Regulatory and Government Affairs from 2001 to 2003 and later Vice President, Commercial Planning from 2003-2004. From 1993-1998, Mr. Patterson worked at Genzyme Corporation in Regulatory Affairs and Manufacturing. Mr. Patterson received a B.A. in Biochemistry from Bowdoin College.

*James E. Dentzer* has served as Chief Financial Officer since October 2006. From November 2003 to October 2006, Mr. Dentzer was Corporate Controller at Biogen Idec Inc. From 2001 until the 2003 merger of Biogen, Inc. and IDEC Pharmaceuticals Corporation, Mr. Dentzer served as Corporate Controller of Biogen, Inc. Prior to that, he served in a variety of financial positions at E. I. du Pont de Nemours and Company, most recently as Chief Financial Officer of DuPont Flooring Systems. Mr. Dentzer received his B.A. from Boston College and his M.B.A. from the University of Chicago.

*David J. Lockhart*, Ph.D., has served as Chief Scientific Officer since January 2006. Prior to joining Amicus, Dr. Lockhart served as President, Chief Scientific Officer and co-founder of Ambit Biosciences, a biotechnology company specializing in small molecule kinase inhibitors, from March 2001 to July 2005. Dr. Lockhart served as a consultant to Ambit Biosciences from August 2000 to March 2001, and as a visiting scholar at the Salk Institute for Biological Studies from October 2000 to March 2001. Prior to that, Dr. Lockhart served in various positions, including Vice President of Genomics Research at Affymetrix, and was the Director of Genomics at the Genomics Institute of the Novartis Research Foundation from February 1999 to July 2000. He received his Ph.D. from Stanford University and was a post-doctoral fellow at the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology.

*David Palling*, Ph.D., has served as Senior Vice President, Drug Development, since August, 2002. From September 1998 until August, 2002, Dr. Palling was with Johnson & Johnson, most recently serving as Vice President of Worldwide Assay Research and Development at Ortho Clinical Diagnostics, a subsidiary of Johnson & Johnson. Dr. Palling received B.Sc. and Ph.D. degrees in Chemistry from the University of London, King's College, and conducted post-doctoral research in Biochemistry at Brandeis University.

*Gregory P. Licholai*, M.D., has served as Vice President, Medical Affairs since December 2004. From November 2002 to December 2004, Dr. Licholai was with Domain Associates, a venture capital firm. From September 2000 to November 2002, he was director of Ventures and Business Associates for Medtronic Neurological, a division of Medtronic, Inc. Dr. Licholai received his B.A. from Boston College and completed Pre-Medical studies at Columbia University, his M.D. from Yale Medical School and his M.B.A. from Harvard Business School.

*S. Nicole Schaeffer* has served as Vice President, Human Resources and Leadership Development since March 2005. From 2001 to 2004, she served as Senior Director, Human Resources, for three portfolio companies of Flagship Ventures, a venture capital firm, and in that capacity she managed human resources for three life sciences companies. Ms. Schaeffer received her B.A. from the University of Rochester and her M.B.A. from Boston University.

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*Bradley L. Campbell* has served as Vice President, Business Planning since May 2007. From April 2006 until May 2007, he served as Senior Director, Business Development. From 2002 until 2006, Mr. Campbell served as Senior Product Manager and later Business Director of CV Gene Therapy at Genzyme Corporation. Mr. Campbell received his B.A. from Duke University and his M.B.A. from Harvard Business School.

*John R. Kirk* has served as Vice President, Regulatory Affairs since January 1, 2008. Prior to joining Amicus, Mr. Kirk served as Executive Director, Regulatory Affairs at Aegerion Pharmaceuticals. From 2003 to 2007, Mr. Kirk held positions of increasing responsibility with Esperion Therapeutics which was acquired during this time by Pfizer. From 2000 to 2002, Mr. Kirk was Director, Worldwide Regulatory Affairs for Pfizer Global Research and Development. From 1988 to 2000, Mr. Kirk held various Regulatory positions with Parke-Davis Pharmaceutical Research. Mr. Kirk holds both his M.S. and B.S. from Wright State University in Ohio.

*Andrew Shenker M.D., Ph.D.* has served as Vice President, Clinical Research since December 2007. From 2002 to 2007, Dr. Shenker was with Bristol-Myers Squibb where he served most recently as Medical Director in the Clinical Discovery Group. From 1995 to 2002, Dr. Shenker was Assistant Professor of Pediatrics, Molecular Pharmacology and Biological Chemistry at Northwestern University Medical School. Dr. Shenker obtained his Ph.D. in pharmacology and M.D. from the Mount Sinai School of Medicine in NYC, completed his internship and residency in Pediatrics at the Johns Hopkins Hospital and was a post-doctoral fellow at the National Institutes of Health.

The other information required by this item is incorporated by reference from the definitive proxy statement which Amicus will file with the Securities and Exchange Commission no later than 120 days after March 30, 2008 (the Proxy Statement ), under the captions Election of Directors and Section 16(a) Beneficial Ownership Reporting Compliance.

In 2007, we adopted a Code of Business Ethics and Conduct for Employees, Executive Officers and Directors that applies to our employees, officers and directors and incorporates guidelines designed to deter wrongdoing and to promote the honest and ethical conduct and compliance with applicable laws and regulations. In addition, the code of ethics incorporates our guidelines pertaining to topics such as conflicts of interest and workplace behavior. We have posted the text of our code on our website at [www.amicustherapeutics.com](http://www.amicustherapeutics.com) in connection with Investors/Corporate Governance materials. In addition, we intend to promptly disclose (1) the nature of any amendment to our code of ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date the waiver on our website in the future.

**Item 11. EXECUTIVE COMPENSATION.**

The information required by this item is incorporated by reference from the Proxy Statement under the caption Executive Compensation Compensation Discussion and Analysis.

**Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.**

The information required by this item is incorporated by reference from the Proxy Statement under the captions Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters and Equity Compensation Plan Information.

**Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE.**

The information required by this item is incorporated by reference from the Proxy Statement under the captions Certain Relationships and Related Transactions, Director Independence, Committee Compensation and Meetings of the Board of Directors, and Compensation Committee Interlock and Insider Participation.

**Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.**

The information required by this item is incorporated by reference from the Proxy Statement under the caption Ratification of Independent Registered Public Accounting Firm.

**Table of Contents****PART IV****Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULE**(a) 1. *Consolidated Financial Statements*

The Consolidated Financial Statements are filed as part of this report.

2. *Consolidated Financial Statement Schedules*

All schedules are omitted because they are not required or because the required information is included in the Consolidated Financial Statements or notes thereto.

3. *Exhibits*

Exhibit No.	Filed Exhibit Description	Incorporated by Reference to SEC Filing		Exhibit No.	Filed with this Form 10-K
		Form	Date		
3.1	Restated Certificate of Incorporation of the Registrant.	S-1 (333-141700)	5/17/07	3.2	
3.2	Restated By-laws of the Registrant.	S-1/A (333-141700)	4/27/07	3.4	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1 (333-141700)	3/30/07	4.1	
4.2	Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended	S-1 (333-141700)	3/30/07	4.3	
4.3	Warrant to purchase shares of common stock, dated August 28, 2002	S-1 (333-141700)	3/30/07	4.6	
10.1	2002 Equity Incentive Plan, as amended, and forms of option agreements thereunder	S-1/A (333-141700)	4/27/07	10.1	
10.2	2007 Equity Incentive Plan and forms of option agreements	S-1/A (333-141700)	5/17/07	10.2	
+ 10.3	License Agreement, dated as of April 15, 2002, by and between the Registrant and Mount Sinai School of Medicine of New York University, as amended	S-1 (333-141700)	3/30/07	10.3	
+10.4	License Agreement, dated as of June 26, 2003, by and between the Registrant and University of Maryland, Baltimore County, as amended	S-1 (333-141700)	3/30/07	10.4	
+10.5	Exclusive License Agreement, dated as of June 8, 2005, by and between the Registrant and Novo Nordisk, A/S	S-1 (333-141700)	3/30/07	10.5	
10.6	Sublease Agreement, dated as of May 12, 2005, by and between the Registrant and Purdue Pharma, L.P.	S-1 (333-141700)	3/30/07	10.6	
10.7	Amended and Restated Employment Agreement, dated as of April 28, 2006, by and between the Registrant and John F. Crowley	S-1 (333-141700)	3/30/07	10.7	
10.8	Letter Agreement, dated as of November 9, 2004, by and between the Registrant and Matthew R. Patterson	S-1 (333-141700)	3/30/07	10.8	



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10.9	Letter Agreement, dated as of July 27, 2006, by and between the Registrant and James E. Dentzer	S-1 (333-141700)	3/30/07	10.9
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<b>Exhibit No.</b>	<b>Filed Exhibit Description</b>	<b>Incorporated by Reference to SEC Filing</b>		<b>Exhibit No.</b>	<b>Filed with this Form 10-K</b>
		<b>Form</b>	<b>Date</b>		
10.10	Letter Agreement, dated as of December 19, 2005, by and between the Registrant and David Lockhart, Ph.D.	S-1 (333-141700)	3/30/07	10.10	
10.11	Consulting Agreement, dated as of February 28, 2006, by and between the Registrant and Donald J. Hayden, Jr.	S-1 (333-141700)	3/30/07	10.15	
10.12	Form of Director and Officer Indemnification Agreement	S-1 (333-141700)	3/30/07	10.17	
10.13	Employment Agreement, dated as of September 11, 2006, by and between the Registrant and Donald J. Hayden, Jr.	S-1/A (333-141700)	4/27/07	10.19	
10.14	Restricted Stock Agreement, dated as of March 8, 2007, by and between the Registrant and James E. Dentzer	S-1/A (333-141700)	4/27/07	10.20	
10.15	Restricted Stock Agreement, dated as of March 8, 2007, by and between the Registrant and Glenn P. Sblendorio	S-1/A (333-141700)	4/27/07	10.21	
10.16	Lease Agreement, dated as of July 31, 2006, by and between the Registrant and Cedar Brook II Corporate Center, L.P.	S-1/A (333-141700)	4/27/07	10.22	
10.17	2007 Director Option Plan and form of option agreement	S-1/A (333-141700)	5/17/07	10.23	
10.18	2007 Employee Stock Purchase Plan	S-1/A (333-141700)	5/17/07	10.24	
10.19	Severance and Change in Control Agreement, dated as of May 10, 2007, by and between the Registrant and Bradley L. Campbell	S-1/A (333-141700)	5/17/07	10.25	
++10.20	License and Collaboration Agreement, dated as of November 7, 2007, by and between Registrant and Shire Pharmaceuticals Ireland, Ltd.				
10.21	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and David Lockhart, Ph.D.	Form 8-K Current Report	11/13/07	10.1	
10.22	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and James E. Dentzer	Form 8-K Current Report	11/13/07	10.2	
10.23	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Matthew R. Patterson	Form 8-K Current Report	11/13/07	10.3	

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10.24	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and David Palling, Ph.D.	Form 8-K Current Report	11/13/07	10.4
10.25	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Bradley L. Campbell	Form 8-K Current Report	11/13/07	10.6

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<b>Exhibit No.</b>	<b>Filed Exhibit Description</b>	<b>Incorporated by Reference to SEC Filing</b>		<b>Exhibit No.</b>	<b>Filed with this Form 10-K</b>
		<b>Form</b>	<b>Date</b>		
10.26	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Gregory P. Licholai, M.D.	Form 8-K Current Report	11/13/07	10.7	
10.27	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Mark Simon	Form 8-K Current Report	11/13/07	10.9	
10.28	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and S. Nicole Schaeffer	Form 8-K Current Report	11/13/07	10.9	
21.1	Subsidiaries of the Registrant	S-1 (333-141700)	3/30/07	21.1	
23.1	Consent of Independent Registered Public Accounting Firm.				
31.1	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
31.2	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
32.1	Certificate of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2	Certificate of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				
+	Confidential treatment has been granted as to certain portions of the document, which portions have been omitted and filed separately with the Securities and Exchange Commission.				

++ Confidential treatment has been requested as to certain portions of the document, which portions have been omitted and filed separately with the Securities and Exchange Commission.

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**Table of Contents****SIGNATURES**

Pursuant to the requirements of Section 13 or 15 (d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on February 8, 2008.

AMICUS THERAPEUTICS, INC.  
(Registrant)

By: /s/ John F. Crowley  
John F. Crowley  
*Chief Executive Officer*

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ John F. Crowley (John F. Crowley)	Chief Executive Officer (Principal Executive Officer)	February 6, 2008
/s/ James E. Dentzer (James E. Dentzer)	Chief Financial Officer (Principal Financial and Accounting Officer)	February 6, 2008
/s/ Donald J. Hayden (Donald J. Hayden)	Chairman of the Board	February 6, 2008
/s/ Alexander E. Barkas, Ph.D. (Alexander E. Barkas, Ph.D.)	Director	February 6, 2008
/s/ Stephen Bloch, M.D. (Stephen Bloch, M.D.)	Director	February 6, 2008
/s/ P. Sherrill Neff (P. Sherrill Neff)	Director	February 6, 2008
/s/ Michael G. Raab (Michael G. Raab)	Director	February 6, 2008
/s/ Glenn Sblendorio (Glenn Sblendorio)	Director	February 6, 2008
/s/ James N. Topper, M.D., Ph.D.	Director	

(James N. Topper, M.D., Ph.D.)

February 6,  
2008

/s/ Gregory M. Weinhoff, M.D.

Director

February 6,  
2008

(Gregory M. Weinhoff, M.D.)

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<b>Exhibit No.</b>	<b>Filed Exhibit Description</b>	<b>Incorporated by Reference to SEC Filing</b>			<b>Filed with this Form 10-K</b>
		<b>Form</b>	<b>Date</b>	<b>Exhibit No.</b>	
3.1	Restated Certificate of Incorporation of the Registrant.	S-1 (333-141700)	5/17/07	3.2	
3.2	Restated By-laws of the Registrant.	S-1/A (333-141700)	4/27/07	3.4	
4.1	Specimen Stock Certificate evidencing shares of common stock	S-1 (333-141700)	3/30/07	4.1	
4.2	Third Amended and Restated Investor Rights Agreement, dated as of September 13, 2006, as amended	S-1 (333-141700)	3/30/07	4.3	
4.3	Warrant to purchase shares of common stock, dated August 28, 2002	S-1 (333-141700)	3/30/07	4.6	
10.1	2002 Equity Incentive Plan, as amended, and forms of option agreements thereunder	S-1/A (333-141700)	4/27/07	10.1	
10.2	2007 Equity Incentive Plan and forms of option agreements	S-1/A (333-141700)	5/17/07	10.2	
+10.3	License Agreement, dated as of April 15, 2002, by and between the Registrant and Mount Sinai School of Medicine of New York University, as amended	S-1 (333-141700)	3/30/07	10.3	
+10.4	License Agreement, dated as of June 26, 2003, by and between the Registrant and University of Maryland, Baltimore County, as amended	S-1 (333-141700)	3/30/07	10.4	
+10.5	Exclusive License Agreement, dated as of June 8, 2005, by and between the Registrant and Novo Nordisk, A/S	S-1 (333-141700)	3/30/07	10.5	
10.6	Sublease Agreement, dated as of May 12, 2005, by and between the Registrant and Purdue Pharma, L.P.	S-1 (333-141700)	3/30/07	10.6	
10.7	Amended and Restated Employment Agreement, dated as of April 28, 2006, by and between the Registrant and John F. Crowley	S-1 (333-141700)	3/30/07	10.7	
10.8	Letter Agreement, dated as of November 9, 2004, by and between the Registrant and Matthew R. Patterson	S-1 (333-141700)	3/30/07	10.8	
10.9	Letter Agreement, dated as of July 27, 2006, by and between the Registrant and James E. Dentzer	S-1 (333-141700)	3/30/07	10.9	
10.10	Letter Agreement, dated as of December 19, 2005, by and between the Registrant and David Lockhart, Ph.D.	S-1 (333-141700)	3/30/07	10.10	
10.11	Consulting Agreement, dated as of February 28, 2006, by and between the Registrant and Donald J. Hayden, Jr.	S-1 (333-141700)	3/30/07	10.15	



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10.12	Form of Director and Officer Indemnification Agreement	S-1 (333-141700)	3/30/07	10.17
10.13	Employment Agreement, dated as of September 11, 2006, by and between the Registrant and Donald J. Hayden, Jr.	S-1/A (333-141700)	4/27/07	10.19
10.14	Restricted Stock Agreement, dated as of March 8, 2007, by and between the Registrant and James E. Dentzer	S-1/A (333-141700)	4/27/07	10.20
10.15	Restricted Stock Agreement, dated as of March 8, 2007, by and between the Registrant and Glenn P. Sblendorio	S-1/A (333-141700)	4/27/07	10.21
10.16	Lease Agreement, dated as of July 31, 2006, by and between the Registrant and Cedar Brook II Corporate Center, L.P.	S-1/A (333-141700)	4/27/07	10.22
10.17	2007 Director Option Plan and form of option agreement	S-1/A (333-141700)	5/17/07	10.23

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		<b>Form</b>	<b>Date</b>	<b>Exhibit No.</b>	
10.18	2007 Employee Stock Purchase Plan	S-1/A (333-141700)	5/17/07	10.24	
10.19	Severance and Change in Control Agreement, dated as of May 10, 2007, by and between the Registrant and Bradley L. Campbell	S-1/A (333-141700)	5/17/07	10.25	
++10.20	License and Collaboration Agreement, dated as of November 7, 2007, by and between the Registrant and Shire Pharmaceuticals Ireland, Ltd.				
10.21	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and David Lockhart, Ph.D.	Form 8-K Current Report	11/13/07	10.1	
10.22	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and James E. Dentzer	Form 8-K Current Report	11/13/07	10.2	
10.23	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Matthew R. Patterson	Form 8-K Current Report	11/13/07	10.3	
10.24	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and David Palling, Ph.D.	Form 8-K Current Report	11/13/07	10.4	
10.25	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Bradley L. Campbell	Form 8-K Current Report	11/13/07	10.6	
10.26	Severance and Change in Control Agreement, dated as of November 12, 2007, by and between the Registrant and Gregory P. Licholai, M.D.	Form 8-K Current Report	11/13/07	10.7	
10.27	Severance and Change in Control Agreement, dated as of November 9, 2007, by and between the Registrant and S. Nicole Schaeffer	Form 8-K Current Report	11/13/07	10.9	
10.28	Severance and Change of Control Agreement, dated November 12, 2007, by and between the Registrant and Mark Simon	Form 8-K Current Report	11/13/07	10.8	
21.1	Subsidiaries of the Registrant	S-1 (333-141700)	3/30/07	21.1	

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<b>Exhibit</b>	<b>Incorporated by Reference to SEC Filing</b>	<b>Filed with this</b>	<b>Exhibit</b>		
			<b>Form</b>	<b>Date</b>	<b>No.</b>
<b>No.</b>	<b>Filed Exhibit Description</b>				<b>Form 10-K</b>
23.1	Consent of Independent Registered Public Accounting Firm.				
31.1	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
31.2	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934.				
32.1	Certificate of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2	Certificate of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 and Section 906 of the Sarbanes-Oxley Act of 2002.				
+	Confidential treatment has been granted as to certain portions of the document, which portions have been omitted and filed separately with the Securities and Exchange Commission.				
++	Confidential treatment has been requested as to certain portions of the document, which portions have been omitted and filed separately with the Securities and Exchange Commission.				

Commission.

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