AMICUS THERAPEUTICS INC
Form 10-K
March 13, 2013

Use these links to rapidly review the document
TABLE OF CONTENTS

Table of Contents

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, 2012
Commission File Number 001-33497

Amicus Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**71-0869350**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*

1 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 o No ý

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 o No ý

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 ý No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No o

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. o

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

Large accelerated filer o Accelerated filer ý Non-accelerated filer o Smaller Reporting Company o

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

The aggregate market value of the 18,960,703 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 30, 2012) was approximately $104,283,867. Shares of voting and non-voting stock held by executive officers, directors and holders of more than 10% 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 March 1, 2013, there were 49,631,672 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant's 2013 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.

Table of Contents

Table of Contents

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," "potential," "intend," "may," "plan," "predict," "project," "will," "should," "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 annual report on Form 10-K include, among other things, statements about:

- the progress and results of our clinical trials of our drug candidates, including migalastat HCl;
- the continuation of our collaboration with GlaxoSmithKline PLC and GSK's achievement of milestone payments thereunder;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of diseases of neurodegeneration;
- 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.

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.

Table of Contents

PART I

Item 1. ***BUSINESS.***

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of small molecule drugs known as pharmacological chaperones. We are developing pharmacological chaperones as next-generation medicines for a range of rare and orphan diseases, with a focus on improved therapies for lysosomal storage disorders. Our development programs include novel small molecules as monotherapy treatments and in combination with the current standard of treatment for Fabry and other lysosomal storage diseases, enzyme replacement therapy (ERT). Our Chaperone-Advanced Replacement Therapy, or CHART, programs include chaperones co-administered with currently marketed ERTs, as well as proprietary therapeutic enzymes co-formulated with our pharmacological chaperones as next-generation ERTs. We believe that our pharmacological chaperone and CHART platform technologies, our advanced product pipeline, a strong balance sheet and our strategic collaboration with GlaxoSmithKline PLC (GSK) uniquely position us at the forefront of developing therapies for rare and orphan diseases.

In Fabry and other lysosomal storage diseases such as Pompe and Gaucher diseases, a mutation in the specific disease-causing gene can lead to the production in the body of a mutant form of the enzyme that is less stable than the normal form, and that may be prematurely degraded before reaching the location in the cell where it is needed. For patients with lysosomal storage diseases who are receiving ERT, the infused (exogenous) protein may unfold and lose activity at any stage in the process from the infusion bag to the bloodstream, to the eventual uptake into cells and tissue. In both instances, the result is a loss of enzyme activity and disruption of proper trafficking of the enzyme to lysosomes. Our novel approach to the treatment of human genetic diseases consists of using pharmacological chaperones that are designed to selectively bind and stabilize either the endogenous or exogenous target proteins and facilitate trafficking to the location in cells where these proteins are needed.

We are developing our lead product candidiate, migalastat HCl for Fabry disease, in collaboration with GSK as a monotherapy and in combination with ERT. Current development within our Fabry program includes two monotherapy Phase 3 global registration studies for patients with genetic mutations identified as amenable to this pharmacological chaperone in a cell-based assay (Study 011 and Study 012), a recently completed Phase 2 study investigating migalastat HCl co-administered with currently marketed ERTs (Study 013), and the preclinical development of migalastat HCl co-formulated with a proprietary investigational ERT.

In Study 011, we are comparing migalastat HCl to placebo to potentially support the submission of a New Drug Application, or NDA, to the U.S. Food and Drug Administration (FDA) for marketing approval in the United States as well as to other regulatory agencies. In December 2012, Amicus and GSK announced top-line six-month (Stage 1) results from Study 011. While encouraging, these results did not achieve statistical significance (p=0.3) according to the pre-specified primary endpoint analysis. This responder analysis compared the number of patients in the migalastat HCl group to the number of patients in the placebo group who showed a 50% or greater reduction in interstitial capillary GL-3 in the kidney biopsies from baseline to month 6. In the 6-month open-label follow up period in Study 011 (Stage 2), all patients received migalastat HCl. Data from Stage 2 are anticipated in the third quarter of 2013. A meeting with the FDA is anticipated in mid-2013 to discuss a U.S. conditional approval pathway for migalastat HCl under subpart H.

In Study 012, we are comparing open-label migalastat HCl to current standard of care ERTs (Fabrazyme® and Replagal®) to support global registration. In December 2012, this study achieved full enrollment of 60 patients, who were randomized 1.5:1 to switch from ERT to migalastat HCl or remain

Table of Contents

on ERT. Data are anticipated in the second half of 2014 on the primary outcome measure, which is renal function assessed by measured Glomerular Filtration Rate (GFR) at 18 months.

Study 013 is an open-label Phase 2 drug-drug interaction study that evaluated the effects of a single oral dose of migalastat HCl co-administered with the currently marketed ERTs for Fabry disease (Fabrazyme® or Replagal®) in males with Fabry disease. Results from this study demonstrated consistent increase in levels of active α-Gal A activity, the enzyme deficient in Fabry patients, in plasma and increased uptake of α-Gal enzyme in skin compared to ERT alone.

We also continue to advance our pharmacological chaperone AT2220 (duvoglustat HCl) co-administered with the only approved ERTs (Myozyme®/Lumizyme®) for Pompe disease. Similar to Study 013, the results from a completed Phase 2 safety and PK study of AT2220 co-administered with Myozyme®/Lumizyme® showed an increase in GAA enzyme activity in plasma and muscle compared to ERT alone. GAA is the enzyme deficient in Pompe patients. Based on these results, we expect to initiate a repeat-dose clinical study of a novel intravenous formulation of AT2220 (AT2220-IV) co-administered with Myozyme®/Lumizyme® in the third quarter of 2013.

These clinical and preclinical co-administration studies have laid the foundation for developing our pharmacological chaperones co-formulated with our own proprietary enzymes as next-generation ERTs. We believe that these chaperone stabilizers have the potential to enhance ERT activity and tissue uptake while also significantly reducing the immunogenicity of the ERTs. With GSK, in collaboration with JCR Pharmaceutical Co Ltd, we are currently conducting preclinical formulation and IND-enabling studies of migalastat HCl co-formulated with JCR's proprietary investigational recombinant human α-Gal A enzyme (JR-051). We plan an IND submission for this chaperone-ERT co-formulated product by year-end 2013 for entry into clinic in early 2014. In addition, working with our contract manufacturer Laureate Pharmaceuticals, we have initiated development of AT2220 (duvoglustat HCl) co-formulated with our own proprietary recombinant human (rh) GAA enzyme as a next-generation ERT for Pompe disease. We believe this approach has the potential to improve the properties of the rhGAA enzyme itself while incorporating AT2220 as a small molecule stabilizer to increase circulating exposure and tissue uptake, and reduce immunogenicity relative to currently marketed ERTs. Successful development of a more stable ERT may also enable novel routes of delivery such as subcutaneous administration.

We also plan to continue our commitment to the broader application of the CHART technology as a potential next-generation treatment approach for other lysosomal storage diseases in 2013. Our preclinical studies include the pharmacological chaperones AT3375 and afegostat tartrate (AT2101) co-administered with ERT for Gaucher disease, and new undisclosed pharmacological chaperones in combination with other ERTs. In addition, we continue our preclinical work to investigate AT3375, which targets the glucocerobrosidase (GCase) enzyme in the brain, as a potential treatment for Parkinson's disease

Although Fabry, Gaucher and Pompe are relatively rare diseases, they represent substantial commercial markets due to the severity of the symptoms and the chronic nature of the diseases. The publicly-reported worldwide net product sales for the eight currently approved therapeutics to treat Fabry, Gaucher and Pompe disease were approximately $2.7 billion in 2012.

Our Pharmacological Chaperone Technology

Amicus is leveraging its pharmacological chaperone technology to develop next-generation treatments for human genetic diseases by targeting mutated proteins that are unstable, unfolded or misfolded. 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

Table of Contents

amino acid sequence of a protein, and these changes often reduce protein stability and may prevent them from folding properly.

Pharmacological chaperones are small molecules designed to selectively bind to a target protein, increase its stability and help keep it folded in the correct three-dimensional shape. For lysosomal storage diseases, pharmacological chaperones are designed to bind to, and facilitate trafficking of, both endogenous and exogenous enzymes to the location in cells where they are needed. This important feature has allowed Amicus to develop pharmacological chaperones as monotherapy agents (to be used without ERT) and our CHART platform of pharmacological chaperones in combination with ERT.

Pharmacological Chaperone Monotherapy

Many natural (endogenous) proteins are made in the endoplasmic reticulum (ER) and sent to other parts of the cell. Unstable, unfolded or misfolded proteins are generally eliminated or retained in the ER rather than being transported to the intended destination in the cell. The accumulation of unfolded or misfolded proteins in the ER and the interruption of trafficking of important proteins to their proper cellular locations can cause several types of problems including:

- complete or partial loss of appropriate protein function,
- accumulation of lipids and other substances that should be degraded, and
- disruption of cellular function and eventual cell death.

These defects may lead to various types of human genetic diseases, including lysosomal storage disorders. As monotherapy agents for lysosomal storage diseases, pharmacological chaperones are designed to bind to and stabilize endogenous protein (lysosomal enzyme) for proper trafficking to the lysosome, which also alleviates the toxic build-up of mutant proteins in the ER. Once in the lysosome, the pharmacological chaperone disassociates and the enzyme is free to break down substrate. Based on this mechanism, individuals with genetic mutations that result in some residual biological activity are potentially eligible for pharmacological chaperone monotherapy.

CHART Technology Platform

ERT is the standard of care for several lysosomal storage diseases, based on the intravenous infusion of recombinant or gene-activated human enzyme. The enzyme is delivered into the blood in order to be taken up by cells and then transported to the lysosome. Upon entering the lysosome, this enzyme is intended to perform the function of the absent or deficient endogenous enzyme. However, the pH in the infusion bag and in blood is higher than the enzyme's natural acidic environment in the lysosome. As a result, the infused enzyme may rapidly unfold and lose activity and may be misdirected to non-target tissues or rapidly cleared from the body. Exposure to high concentrations of infused enzymes can impact efficacy or cause adverse effects.

Possible problems related to the unfolding of infused enzyme include:

- rapid clearance or modified biodistribution,
- immunogenicity,
- poor delivery and uptake of active enzyme into key tissues of disease, and
- reduced activity.

In our Chaperone Advanced Replacement Therapy, or CHART, programs, each chaperone is designed to bind to and stabilize a specific therapeutic enzyme. We believe this technology may be able to improve the stability, uptake and activity of the enzyme, and may lower immunogenicity compared to

Table of Contents

currently marketed ERTs alone. This combination approach may benefit patients with lysosomal storage diseases, including patients with inactive endogenous proteins who are not amenable to chaperone monotherapy.

Migalastat HCl for Fabry Disease

Overview

Our most advanced product candidate, migalastat HCl, is an investigational, small molecule pharmacological chaperone for the treatment of Fabry disease. Migalastat HCl is being developed in collaboration with an affiliate of GSK pursuant to an Amended and Restated License and Expanded Collaboration Agreement (the "Expanded Collaboration Agreement") entered into in July 2012. As an orally administered monotherapy, migalastat HCl is designed to bind to and stabilize, or "chaperone" a patient's own alpha-galactosidase A (alpha-Gal A) enzyme in those patients with genetic mutations identified as amenable to this chaperone in a cell-based assay. For all other Fabry patients, migalastat HCl in combination with ERT may improve ERT outcomes by keeping infused α-Gal A enzyme in its properly folded and active form.

Under the terms of the Expanded Collaboration Agreement, the Company and GSK are co-developing all formulations of migalastat HCl for Fabry disease. The Company will commercialize all migalastat HCl products for Fabry disease in the United States while GSK will commercialize all such products in the rest of the world. For additional information regarding our collaboration with GSK, please see "Strategic Alliances and Arrangements" below.

Clinical Studies of Migalastat HCl Monotherapy for Fabry Disease

Study 011 is a global Phase 3 study of migalastat HCl for Fabry disease to support marketing applications for the FDA and other regulatory agencies. Study 011 randomized 67 patients (24 males and 43 females) diagnosed with Fabry disease who had genetic mutations amenable to chaperone monotherapy in a cell-based assay. For the 6-month, double-blind primary treatment period, Stage 1 patients were randomized to migalastat HCl 150 mg or placebo on an every-other-day (QOD) oral dosing schedule. During the period from month 6 to month 12 of Study 011 Stage 2, patients continued treatment with migalastat HCl or switched from placebo to migalastat HCl.

The primary analysis compared the number of responders in the migalastat HCl versus placebo groups, based on a 50% or greater reduction in interstitial capillary globotriaosylceramide (GL-3) during the 6-month, double-blind treatment period. GL-3 is the lipid substrate that accumulates in tissues of patients with Fabry disease, and is measured in kidney biopsies. Secondary endpoints for Study 011 include safety and tolerability, urine GL-3 and kidney function.

In the primary responder analysis, 13/32 (41%) in the migalastat HCl group versus 9/32 (28%) in the placebo group demonstrated a 50% or greater reduction in kidney interstitial capillary GL-3 from baseline to month 6 which was not statistically significant (p=0.3). Taken alone a pre-specified secondary analysis of the absolute percent change in kidney interstitial capillary GL-3 from baseline to month 6 showed a median reduction of 41% in the migalastat HCl group versus a median reduction of 6% in the placebo group (p=0.093). Certain 6-month secondary endpoints were presented in February 2013 and included urine GL-3 and renal function as measured by estimated glomerular filtration rate (eGFR).

During Stage 1, no drug-related serious adverse events were observed. No subjects discontinued migalastat HCl therapy due to a treatment emergent adverse event and the majority of adverse events in both treatment groups were mild in nature.

Table of Contents

In December 2012, the Stage 2 treatment periods in Study 011 were completed in a total of 59 patients, who received an additional kidney biopsy at month 12. The results from Stage 2 are expected in the third quarter of 2013 and will include 12-month data in the migalastat HCl group and 6-month data in the placebo crossover group. The FDA has indicated that it will consider the 12-month efficacy and safety data from Study 011 to support a potential U.S. conditional approval of migalastat HCl monotherapy.

Study 012 is our second Phase 3 study intended to support the worldwide registration of migalastat HCl for Fabry disease. Study 012 is a randomized, open-label 18-month Phase 3 study investigating the safety and efficacy of oral migalastat HCl (150 mg, every-other-day) compared to standard-of-care infused ERTs (Fabrazyme® and Replagal®). The study enrolled a total of 60 patients (males and females) with Fabry disease and genetic mutations identified as amenable to migalastat HCl monotherapy in a cell-based assay. Subjects were randomized 1.5:1 to switch to migalastat HCl or remain on ERT. All subjects had been receiving ERT infusions for a minimum of 12 months (at least 3 months at the labeled dose) prior to entering the study. The primary outcome measure is renal function assessed by Glomerular Filtration Rate (GFR) at 18 months, evaluated in the migalastat HCl and ERT groups using descriptive statistics. This study achieved full enrollment in December 2012 and top-line results are expected in the second half of 2014.

In February 2004, the FDA granted orphan drug designation to migalastat HCl for the treatment of Fabry disease and in May 2006, the EMA granted orphan medicinal product designation for migalastat HCl. In the United States, we intend to seek Accelerated Approval for migalastat HCl according to Subpart H regulations.

Migalastat HCl-ERT Combination Programs for Fabry Disease

We have investigated the use of migalastat HCl co-administered with currently marketed ERTs (Fabrazyme® and Replagal®) and are currently developing migalastat HCl co-formulated with a proprietary human recombinant α-Gal A enzyme (JCR Pharmaceutical Co Ltd's JR-051).

Phase 2 Chaperone-ERT Co-Administration Study of Migalastat HCl for Fabry Disease

We and GSK recently completed an open-label Phase 2 drug-drug interaction study in 23 males with Fabry disease to evaluate the safety and pharmacokinetic (PK) effects of two doses of migalastat HCl (150 mg and 450 mg) co-administered with currently marketed ERTs infused α-Gal A enzymes, Fabrazyme® (agalsidase beta) and Replagal® (agalsidase alfa). Unlike Study 011 and Study 012, patients in Study 013 were not required to have α-Gal A mutations amenable to chaperone therapy because, when co-administered with ERT, migalastat HCl is designed to bind to and stabilize the recombinant enzyme in the circulation in any patient receiving ERT. Each patient received their current dose and regimen of ERT at one infusion. A single oral dose of migalastat HCl (150 mg or 450 mg) was co-administered two hours prior to the next infusion of the same ERT at the same dose and regimen. Preliminary results from Study 013 showed increased levels of active α-Gal A enzyme levels in plasma and increased α-Gal A enzyme in skin following co-administration compared to ERT alone. Based on the results from this study, the next chaperone-ERT combination study for Fabry disease is being designed to investigate intravenous treatment of migalastat HCl co-formulated with JCR's proprietary recombinant human α-Gal A enzyme (JR-051).

Preclinical Studies of Migalastat HCl Co-formulated with ERT

We and GSK, in collaboration with JCR, are currently evaluating migalastat HCl co-formulated with JCR's proprietary investigational ERT (JR-051, recombinant human α-Gal A enzyme) in preclinical formulation and IND-enabling studies. This chaperone-ERT co-formulated product has the potential to enter the clinic in late-2013 or early 2014. Preclinical studies completed to date suggest

Table of Contents

that this co-formulated chaperone-ERT product may provide greater α-Gal A enzyme uptake into tissue and markedly reduced levels of GL-3 in Fabry disease-relevant tissues compared to JR-051 alone.

Causes of Fabry Disease and Rationale for Use of Migalastat HCl

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

Migalastat HCl monotherapy is designed to act as a pharmacological chaperone for α-Gal A by selectively binding to the enzyme, which increases its stability and helps the enzyme fold into its correct three-dimensional shape. This stabilization of α-Gal A 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.

Because migalastat HCl increases levels of a patient's naturally produced α-GAL, Fabry disease patients most likely to respond to treatment with migalastat HCl monotherapy are those with a missense mutation or other genetic mutations that result in production of α-Gal A that is less stable but with some residual enzyme activity. We estimate that approximately thirty to fifty percent of patients with Fabry disease may have α-Gal A mutations that are amenable to migalastat HCl as a monotherapy. Patients with genetic mutations leading to a partially made α-Gal A enzyme or α-Gal A enzyme with an irreversible loss of activity are less likely to respond to treatment with migalastat HCl as a monotherapy. However, we believe that all Fabry patients are potentially treatable with migalastat HCl in combination with ERT.

The combination of migalastat HCl and ERT is designed to bind to and stabilize infused enzyme in circulation as patients receive ERT. We believe migalastat HCl in combination with ERT may be able to improve the stability, uptake and activity of the therapeutic enzyme, and may lower immunogenicity compared to ERT alone. This combination approach may benefit patients with inactive endogenous proteins who are not amenable to chaperone monotherapy.

Fabry Disease Background

The clinical manifestations of Fabry disease span a broad spectrum of severity and roughly correlate with a patient's residual α-Gal A 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 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 α-Gal A levels than classic Fabry disease patients. Although the symptoms of Fabry

Table of Contents

disease span a spectrum of severity, it is useful to classify patients as having classic or later-onset Fabry disease when discussing the disease and the associated treatable population.

Classic Fabry Disease

Individuals with classic Fabry disease are in most instances males. They have little or no detectable α-Gal A 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 the Journal of the American Medical Association (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 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 α-Gal A 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.

Newborn screening studies in Italy, Taiwan and Austria, published in the American Journal of Human Genetics (2006), Human Mutation (2009) and the Lancet (2011) respectively, report that the incidence of Fabry mutations in newborns is over ten times higher than previous estimates for classic patients, Combined these studies screened over two-hundred and sixty-three thousand newborns, and found the incidence of Fabry mutations to be between 1:2,400 to 1: 3859. This high incidence was attributed to a large number of newborn males with α-Gal A mutations often associated with later-

Table of Contents

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

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 from recent newborn screening studies published in the American Journal of Human Genetics (2006), Human Mutation (2009) and the Lancet (2011) 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 α-Gal A with some residual enzyme activity, we believe patients with these mutations may benefit from treatment with monotherapy migalastat HCl. We also believe that other types of genetic mutations may result in misfolded α-Gal A and therefore may also respond to treatment with monotherapy migalastat HCl. Based on this, we believe that approximately thirty to fifty percent of the Fabry disease patient population may benefit from treatment with migalastat HCl as a monotherapy. However, the entire Fabry disease patient population has the potential to benefit from migalastat HCl in combination with ERT.

Existing Products for the Treatment of Fabry Disease and Potential Advantages of Migalastat HCl

Currently, two ERT products are approved for the treatment of Fabry disease: Fabrazyme® (agalsidase beta) and Replagal® (agalsidase alfa). Fabrazyme® is approved globally (conditionally in the U.S.) and commercialized by sanofi aventis through Genzyme Corporation, while Replagal® is commercialized by Shire and approved in the EU and other countries but not in the U.S. Orphan drug exclusivity for both Fabrazyme® and Replagal® has expired in the EU and for Fabrazyme® , in the U.S. as well. The net product sales of Fabrazyme® and Replagal® for 2012 were approximately $375 million as publicly reported by sanofi aventis and $498 million as publicly reported by Shire, respectively.

Prior to the availability of ERT, 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 migalastat HCl, we believe that the use of migalastat HCl 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

Table of Contents

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, migalastat HCl 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 migalastat HCl may be much more convenient for patients and may not have the safety risks associated with intravenous infusions.

In addition, as discussed above, we believe that migalastat HCl in combination with ERT may improve key characteristics of the infused enzymes used in ERT by allowing for increased transport of enzymes to the lysosomes and degradation of substrate, thereby potentially increasing ERT's safety and efficacy. Importantly, patients who may not have α-Gal A mutations amendable to migalastat HCl monotherapy treatment may benefit from migalastat HCl in combination with ERT, making migalastat HCl potentially available to all Fabry patients.

CHART Programs for Pompe Disease

Phase 2 Chaperone-ERT Co-Administration Study of AT2220 for Pompe Disease

We are also conducting clinical and preclinical studies examining our exclusively owned pharmacological chaperone AT2220 (duvoglustat HCl) co-administered with currently marketed ERTs and AT2220 co-formulated with our own proprietary GAA enzyme for Pompe disease. In January 2013, we announced positive preliminary results from all 4 dose cohorts in a Phase 2 open-label, multi-center study (Study 010) that evaluated the safety and pharmacokinetic (PK) effects of the pharmacological chaperone AT2220 (duvoglustat HCl) co-administered with Myozyme® or Lumizyme® (alglocosidase alfa. or recombinant human GAA enzyme. rhGAA), the only approved treatments for Pompe disease. Male and female Pompe patients enrolled in Study 010 were given a regularly scheduled ERT infusion. One hour prior to the initiation of the next ERT infusion, patients received a single oral dose of AT2220 (50 mg, 100 mg, 250 mg, or 600 mg). Plasma rhGAA activity and protein levels were evaluated during each infusion. Each patient underwent muscle biopsies three or seven days after each infusion to measure tissue GAA enzyme activity with and without the chaperone, as well as to measure the level of AT2220 in the muscle. The results from all 4 dose cohorts established human proof-of-concept that co-administration of AT2220 just prior to infusing ERT increases GAA enzyme activity in muscle tissue compared to ERT alone. Based on these results, we plan to initiate a repeat-dose clinical study to evaluate a novel intravenous formulation of AT2220 (AT2220-IV) co-administered with Myozyme®/Lumizyme® in the third quarter of 2013. AT2220-IV when co-administered with ERT will be designed to have an improved pharmacokinetic (PK) profile compared to oral AT2220 for all Pompe patients, many of whom are unable to swallow an oral small molecule.

Preclinical Studies of AT2220 Co-formulated with a Proprietary Amicus ERT

In February 2013, we presented data from preclinical studies of AT2220 co-formulated with rhGAA enzyme (Myozymc®/Lumizyme®) for the first time. These data showed that this chaperone-ERT co-formulation resulted in up to 2.5-fold greater enzyme uptake and glycogen reduction in multiple disease-relevant tissues compared to rhGAA alone in GAA knock-out mice. Collectively these data suggest that AT2220 directly binds to and stabilizes rhGAA, potentially leading to a larger fraction of properly folded, active enzyme that is more accessible for tissue uptake. AT2220 co-formulated with ERT may also mitigate Pompe ERT-related immunogenicity since properly-folded proteins are less prone to aggregation and less immunogenic.

Table of Contents

Following the completion of these preclinical studies, Amicus entered into a contract with Laureate Pharmaceuticals for the contract manufacture of AT2220 co-formulated with a proprietary rhGAA enzyme as a next-generation ERT product for Pompe disease. Through this approach Amicus believes it has the potential to improve the properties of the rhGAA enzyme itself while incorporating AT2220 as a small molecule stabilizer to increase exposure and tissue uptake, and reduce immunogenicity relative to currently marketed ERTs.

Pompe Disease Background

Like Fabry disease, Pompe disease is a lysosomal storage disease resulting from a deficiency in an enzyme, α-glucosidase (GAA). Signs and symptoms of Pompe can be severe and debilitating and include progressive muscle weakness throughout the body, particularly the heart and skeletal muscles. The enzyme deficiencies in Pompe patients are caused by inherited genetic mutations. Certain of these mutations cause changes in the amino acid sequence of the enzyme that may result in the production of an enzyme with reduced stability that does not fold into its correct three-dimensional shape. Although the enzymes produced in patient cells often retain the potential for some level of biological activity, the cell's quality control mechanisms recognize and retain the misfolded enzyme in the ER until it is ultimately moved to another part of the cell for degradation and elimination. Consequently, little or no GAA in Pompe patients moves to the lysosome, where it normally breaks down its substrate, a complex lipid called glycogen. This leads to accumulation of glycogen in cells, which is believed to result in the clinical manifestations of Pompe disease. 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. 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.

Strategic Alliances and Arrangements

On July 17, 2012, the Company entered into the Expanded Collaboration Agreement with an affiliate of GSK pursuant to which the Company and GSK will continue to develop and commercialize migalastat HCI, currently in Phase 3 development for the treatment of Fabry disease. The Expanded Collaboration Agreement amends and replaces in its entirety the License and Collaboration Agreement entered into between the Company and GSK on October 28, 2010 (the "Original Collaboration Agreement") for the development and commercialization of migalastat HCl. Under the terms of the Expanded Collaboration Agreement, the Company and GSK will co-develop all formulations of migalastat HCl for Fabry disease, including the development of migalastat HCl co-formulated with JR-051(the "Co-formulated Product"). The Company will commercialize all migalastat HCl products for Fabry disease in the United States while GSK will commercialize all such products in the rest of the world.

GSK is eligible to receive U.S. regulatory approval milestones totaling $20 million for migalastat HCl monotherapy and migalastat HCl for co-administration with ERT, and additional regulatory approval and product launch milestone payments totaling up to $35 million within seven years following the launch of the Co-formulated Product. The Company will also be responsible for certain pass-through milestone payments and single-digit royalties on the net U.S. sales of the Co-formulated Product that GSK must pay to a third party. In addition, the Company is no longer eligible to receive any milestones or royalties it would have been eligible to receive under the Original Collaboration

Table of Contents

Agreement other than a $3.5 million clinical development milestone achieved in the second quarter of 2012 and received in the third quarter of 2012.

The Company and GSK will continue to jointly fund development costs for all formulations of migalastat HCl in accordance with agreed upon development plans pursuant to which the Company and GSK funded 25% and 75% of such costs, respectively, for the monotherapy and co-administration development of migalastat HCl during 2012 and will fund 40% and 60%, respectively, in 2013 and beyond. Effective upon entry into the Expanded Collaboration Agreement, costs for the development of the Co-formulated Product are also split 40% and 60% between Amicus and GSK, respectively.

Additionally, simultaneous with entry into the Expanded Collaboration Agreement, the Company and GSK entered into a Stock Purchase Agreement pursuant to which GSK purchased approximately 2.9 million shares of Amicus common stock at a price of $6.30 per share. The total value of this equity investment to the Company is approximately $18.6 million. GSK purchased approximately 6.9 million shares for an aggregate investment of approximately $31 million in connection with entry into the Original Collaboration Agreement in 2010. As of December 31, 2012, GSK's ownership position in the Company is 19.8%.

We will continue to evaluate other business development opportunities as appropriate that build shareholder value and provide us with access to the financial, technical, clinical and commercial resources necessary to develop and market pharmacological chaperone therapeutics and other technologies or products. We are exploring potential collaborations, alliances and other business development opportunities on a regular basis. These opportunities may include the acquisition of preclinical-stage, clinical-stage or marketed products so long as such transactions are consistent with our strategic plan to develop and provide therapies to patients living with rare and orphan diseases and support our continued transformation from a development stage company into a commercial biotechnology company.

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.

Table of Contents

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 migalastat HCl, pharmacological chaperone and ERT combination therapy, diseases of neurodegeneration, afegostat tartrate and its derivates including AT3375 for Gaucher disease and AT2220 (duvoglustat HCl) for Pompe disease are described below and include both patents and patent applications we own or exclusively license:

We have an exclusive license to six issued U.S. patents that cover use of migalastat HCl to treat Fabry disease, as well as corresponding European, Japanese and Canadian patents. These exclusively licensed U.S. patents relating to migalastat HCl expire in 2018 (not including the Hatch-Waxman statutory extension, which is described below), while the European, Japanese and Canadian patents will expire in 2019 (not including the Supplemental Protection Certificates or SPC extensions, which are described below). The patents include claims covering methods of increasing the activity of and preventing the degradation of α-GAL, and methods for the treatment of Fabry disease using migalastat HCl. In addition, we own pending U.S. applications directed to dosing regimens with migalastat HCl, which, if granted, may result in patents that expire in 2027. Further, we own an issued U.S. patent directed to synthetic steps related to the commercial process for preparing migalastat HCl, which may result in a patent that expires in 2026. We jointly own one issued U.S. patent covering a method of determining whether male Fabry patients are likely to respond to treatment with migalastat HCl which expires in 2027. Lastly, we have one pending U.S. application covering a method of determining which *a*-Gal A mutations are likely to be amendable to therapy with migalastat HCl which, if granted, will expire in 2029. We have filed, or plan to file, U.S. and foreign counterparts of these applications, where appropriate, by the applicable deadlines.

We have an exclusive license to pending patent applications covering the co-administration of migalastat HCl with ERT (recombinant α-galactosidase A), afegostat tartrate with ERT (recombinant glucocerebrosidase) and AT2220 (duvoglustat HCl) with ERT(recombinant acid α-glucosidase). These applications are pending in the U.S., Europe, Canada, Brazil, China, Israel, Japan and Mexico while the application in India has issued. If patents issue from these applications, expiration will be in 2024. We also own a U.S. provisional patent application covering specific doses and dosing regimens of migalastat hydrochloride to treat Fabry disease in combination with ERT (recombinant α-galactosidase A). Similarly, we own a U.S. provisional patent application that covers specific doses and dosing regimens of duvoglustat HCl to treat Pompe disease in combination with ERT (recombinant acid α-glucosidase). If a patents issue from these applications, expiration will be in 2032.

As part of our License and Collaboration Agreement with GSK, we have licensed or sub-licensed to GSK all of our ex-US rights in our patents and applications to the extent that said patents and applications claim the use of migalastat HCl as a monotherapy or co-administered with ERT.

We own several US and foreign pending patent applications which cover the use of pharmacological chaperones to treat diseases of neurodegeneration. In particular we own two issued patents and two U.S. patent applications that cover the use of afegostat tartrate and/or its derivatives to treat Parkinson's disease as well as one patent application covering novel compounds, including AT3375, for the treatment of Parkinson's disease. We own another patent application covering the use of the same novel compounds, including AT3375, for the treatment of Gaucher disease as a monotherapy as well as in combination with ERT. If patents issue from these applications expiration dates range from 2026 to 2030.

Table of Contents

We have an exclusive license to several U.S. patents covering the use of afegostat tartrate to treat Gaucher disease. These patents expire in 2018 (not including the Hatch-Waxman statutory extension, which is described below). There are no ex-U.S. counterparts to the exclusively licensed U.S. patents, which expire in 2018 in the U.S., covering afegostat tartrate to treat Gaucher disease. We also have an exclusive license to two U.S. patents claiming afegostat tartrate, the active chemical moiety in afegostat tartrate, which expire in 2015 and 2016 (not including the Hatch-Waxman statutory extension, which is described below); and corresponding patents in the UK, France, Sweden, Germany, Switzerland and Japan all of which expire in 2015 (not including the SPC extensions, which are described below). We own a U.S. patent and its corresponding foreign patents covering afegostat tartrate, which is the specific salt form or the active pharmaceutical ingredient in afegostat tartrate, which expires in 2027. We own several other pending U.S. applications directed to the synthesis of afegostat tartrate, as well as specific treatment and monitoring regimens with afegostat tartrate 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 several U.S. patents that cover the use of AT2220 to treat Pompe disease. These U.S. patents will expire in 2018 (not including the Hatch-Waxman statutory extension, which is described below). There are no ex-U.S. counterparts to the exclusively licensed U.S. patents, which expire in 2018 in the U.S., covering AT2220 to treat Pompe disease.

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

Table of Contents

and our commercial consultants to ensure that any inventions resulting from the relationship are disclosed promptly, maintained in confidence until a patent application is filed and preferably until publication of the patent application, and assigned to us or subject to a right to obtain a license. We do not know whether any of our own patent applications or those patent applications that are licensed to us will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, narrowed, invalidated or circumvented or be found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products and reduce the term of patent protection that we may have for our products. Neither we nor our licensors can be certain that we were the first to invent the inventions claimed in our owned or licensed patents or patent applications. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us and the rights granted under any issued patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to or shortly after commencing commercialization, thereby reducing the advantage of the patent to our business and products.

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. For information regarding our migalastat HCl collaboration with GSK, please see "Strategic Alliances and Arrangements" above. For our other license agreements, 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 migalastat HCl, afegostat tartrate 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 (MSSM) of New York University. In connection with this agreement, we issued 232,266 shares of our common stock to MSSM in April 2002. In October 2006, we issued MSSM 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. 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. However, on October 31, 2008, we amended and restated this license agreement to, among other items, provide us with the sole right to control the prosecution of patent rights under such agreement and to clarify the portion of royalties and milestone payments we received from Shire that were payable to MSSM. In connection therewith, we agreed to pay MSSM $2.6 million in connection with the $50 million

Table of Contents

upfront payment that we received in November 2007 from Shire, our former collaborator, which was already accrued for at year-end 2007, and an additional $2.6 million for the sole right to and control over the prosecution of patent rights. In addition, we paid MSSM $3 million of the $30 million upfront payment received from GSK in the fourth quarter of 2010. This agreement expires upon expiration of the last of the licensed patent rights, which will be in 2019, subject to any patent term extension that may be granted, or 2024 if we develop a product for combination therapy (pharmacological chaperone plus ERT) and a patent issues from the pending application covering the combination therapy, 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 afegostat tartrate 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 $45 thousand. We are required to make a milestone payment upon the demonstration of safety and efficacy of afegostat tartrate for the treatment of Gaucher disease in a Phase 2 study, and another payment upon receiving FDA approval for afegostat tartrate 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 afegostat tartrate 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 afegostat tartrate, with a payment due after initiation of a Phase 3 clinical trial for afegostat tartrate for the treatment of Gaucher disease and a payment due upon each filing for regulatory approval of afegostat tartrate for the treatment of Gaucher disease in any of the U.S., Europe or Japan. An additional payment is due upon approval of afegostat tartrate for the treatment of Gaucher disease in the U.S. and a payment is also due upon each approval of afegostat tartrate for the treatment of Gaucher disease in either of Europe or Japan. Assuming successful development of afegostat tartrate 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 migalastat HCl and AT2220, we will owe royalties only to MSSM and will owe no milestone payments. We would expect to pay royalties to all three licensors with respect to afegostat tartrate.

Our rights with respect to these agreements to develop and commercialize migalastat HCl, afegostat tartrate 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 own certain trademarks in the U.S. and/or abroad, including A AMICUS THERAPEUTICS® & design and AMICUS THERAPEUTICS®. At present, all of the U.S. trademark applications for these marks have been either registered or approved by the U.S. Patent and Trademark Office. Although we previously obtained approval of the tradename "Amigal", we will re-apply for registration of a new tradename for migalastat HCl based on feedback from FDA

Table of Contents

prohibiting the use of Amigal for migalastat HCl. As part of our License and Collaboration Agreement with GSK, GSK will select and own the tradename for migalastat HCl.

Manufacturing

We continue to rely on contract manufacturers to supply the active pharmaceutical ingredients and clinical supplies for migalastat HCl and our other product candidates. The active pharmaceutical ingredients for these 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. In addition, several large pharmaceutical companies are increasingly focused on developing therapies for the treatment of rare diseases, both through organic growth and acquisitions and partnerships. While we believe that our technologies, knowledge, experience and scientific resources, along with our collaboration with GSK, provide us with competitive advantages, we face potential competition from many different sources, including commercial 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.

Table of Contents

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):

Competitor	Indication	Product	Class of Product	Status	2012 Sales (in millions)
sanofi aventis	Fabry disease	Fabrazyme®	Enzyme Replacement Therapy	Marketed	$ 375
	Gaucher disease	Cerezyme®	Enzyme Replacement Therapy	Marketed	$ 814
	Pompe disease	Myozyme®/ Lumizyme®	Enzyme Replacement Therapy	Marketed	$ 594
	Gaucher disease	Eliglustat tartrate	Substrate Reduction Therapy	Phase 3	N/A
Shire	Fabry disease	Replagal®	Enzyme Replacement Therapy	Marketed	$ 498
	Gaucher disease	VPRIV®	Enzyme Replacement Therapy	Marketed	$ 307
Actelion, Ltd.	Gaucher disease	Zavesca®	Substrate Reduction Therapy	Marketed	$ 90
Protalix Biotherapeutics	Gaucher disease	Elelyso®	Enzyme Replacement Therapy	FDA Approval May 2012	N/A

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 new drug applications (NDAs), warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, litigation, government investigation and criminal prosecution.

Pharmaceutical product development in the U.S. typically involves nonclinical laboratory and animal tests, the submission to the FDA of 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 an IND is required prior to the commencement of clinical testing in humans. The IND becomes effective 30 days after its receipt by the FDA, and trials may begin at that point unless the FDA notifies the sponsor that the investigations are subject to a clinical hold.

Table of Contents

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 applicable government regulations, good clinical practices (GCP), as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board (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 a new drug application (NDA) 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 3 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 holder of an approved NDA is 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. However, the FDA attempts to review a drug candidate that is eligible for priority review within six months, as discussed below. The review process may be extended by FDA for three additional months to evaluate major amendments to information already provided in the initial 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 and to be marketed.

Table of Contents

After FDA evaluates the NDA and the manufacturing facilities, it issues an approval letter or a complete response letter. Complete response letters 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 an amendment submitted to 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 route of administration, active ingredients strength 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 preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

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

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

The ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired (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

Table of Contents

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, communications regarding unindicated uses, 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 evaluation and mitigation strategies 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 certainsubcontractors are required to register their establishments with FDA and certain state agencies, and are subject to routine inspections by the FDA during which the agency inspects manufacturing facilities to access compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first NDA applicant with FDA orphan drug designation for a particular active ingredient to receive FDA approval of the designated drug for the disease 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 or if the license holder cannot supply sufficient quantities of the product. 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

Table of Contents

the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee for the orphan indication.

Pediatric Information

Under the Pediatric Research Equity Act of 2007 (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 an IND may request FDA to designate the drug candidate as a fast track drug if it is intended to treat a serious condition and fulfill an unmet medical need. 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 by providing more frequent communication with and guidance to the sponsor.

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 six-months from filing for a New Molecular Entity (NME) or six months from submission for a non-NMEif 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. The FDA makes its determination of priority or standard review during the 60-day filing period after an initial NDA submission.

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.

Table of Contents

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

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

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

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

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

Table of Contents

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. Most countries outside the U.S. require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, 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 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 EEA for migalastat HCl for the treatment of Fabry disease and for afegostat tartrate for the treatment of Gaucher disease. We anticipate filing for orphan medicinal product designation from the EMA for AT2220 for the treatment of Pompe disease. The EMA 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.

Table of Contents

Orphan drug designation provides opportunities for fee reductions for protocol assistance and 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 EMA marketing approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the EMA 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.

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.

Employees

As of December 31, 2012, we had 112 full-time employees, 81 of whom were primarily engaged in research and development activities and 31 of whom provide administrative services. A total of 30 employees have an M.D. or Ph.D. degree. None of our employees are represented by a labor union. We have not experienced any work stoppages and consider our employee relations to be good.

Table of Contents

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 1 Cedar Brook Drive, Cranbury, NJ 08512 and our telephone number is (609) 662-2000. Our website address is *www.amicusrx.com*. We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the 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.amicusrx.com* under the "Investors Corporate Governance" caption and in print to any stockholder upon request. Any waivers or material amendments to the Code will be posted promptly on our website.

We have filed applications to register certain trademarks in the U.S. and abroad, including A AMICUS THERAPEUTICS® and design and AMICUS THERAPETUICS®. Fabrazyme®, Cerezyme®, Myozyme®, Lumizyme®, Replagal® , VPRIV® and Zavesca® are the property of their respective owners.

ITEM 1A. RISK FACTORS

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. You should understand that it is not possible to predict or identify all such risks. Consequently, you should not consider the following to be a complete discussion of all potential risks or uncertainties.

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 cumulative net loss attributable to common stockholders since inception was $339.1 million and we had an accumulated deficit of $318.9 million as of December 31, 2012. To date, we have financed our operations primarily through private placements of our redeemable convertible preferred stock, proceeds from our initial public offering, the March 2010 registered direct offering, the March 2012 stock offering and from our collaboration agreement with GSK and prior collaboration agreement with Shire. 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 as we:

- continue our ongoing Phase 3 clinical trials of migalastat HCl for the treatment of Fabry disease to support regulatory approval in the United States (Study 011) and worldwide (Study 012);

- continue our ongoing Phase 2 clinical trial of migalastat HCl co-administered with ERT for Fabry disease and our Phase 2 clinical trial of AT2220 co-administered with ERT for Pompe disease;

Table of Contents

continue our preclinical studies on the use of pharmacological chaperones co-formulated and co-administered with ERT for Fabry, Pompe and other lysosomal storage diseases;

continue the research and development of additional product candidates;

seek regulatory approvals for our product candidates that successfully complete clinical trials; and

establish a sales and marketing infrastructure to commercialize products for which we may obtain regulatory approval.

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 to continue to incur substantial research and development expenses in connection with our ongoing activities, particularly as we continue our Phase 3 development of migalastat HCl. Further, subject to obtaining regulatory approval of any of our product candidates including migalastat HCl, we expect to incur significant commercialization expenses for product sales and marketing, securing commercial quantities of product from our manufacturers and product distribution. While research and development costs associated with our migalastat HCl program will be shared with GSK so long as our collaboration continues, we remain responsible for all costs related to our other programs.

Should GSK terminate our collaboration agreement, we would likely need to seek additional funding in order to complete any clinical trials related to migalastat HCl, seek regulatory approvals of migalastat HCl, and launch the product candidate outside of the United States and continue our other clinical and preclinical programs. Capital may not be available when needed on terms that are acceptable to us, or at all, especially in light of the current challenging economic environment. If adequate funds are not available to us on a timely basis, we may be required to reduce or eliminate research development programs or commercial efforts.

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

the progress and results of our clinical trials of migalastat HCl;

the continuation of our collaboration agreement with GSK and GSK's achievement of milestone payments thereunder;

the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates including those testing the use of pharmacological chaperones co-formulated and co-administered with ERT and for the treatment of diseases of neurodegeneration;

the costs, timing and outcome of regulatory review of our product candidates;

the number and development requirements of other product candidates that we pursue;

Table of Contents

- 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 or technologies; and
- our ability to establish additional 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 are able to raise capital by issuing equity securities, our stockholders will experience dilution. In addition, stockholders may experience dilution if the holders of the warrants issued in connection with our March 2010 offering continue to exercise their warrants. 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. Each of our current loan and security agreements with Silicon Valley Bank includes a covenant whereby we must maintain a minimum amount of liquidity measured at the end of each month where unrestricted cash, cash equivalents and marketable securities is greater than $20 million plus outstanding debt due to Silicon Valley Bank. 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 additional 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.

We may acquire other assets or businesses, or form collaborations or make investments in other companies or technologies, that could harm our operating results, dilute our stockholders' ownership, increase our debt or cause us to incur significant expense.

As part of our business strategy, we may pursue acquisitions of assets or businesses, or strategic alliances and collaborations, to expand our existing technologies and operations. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any such transaction, any of which could have a detrimental effect on our financial condition, results of operations and cash flows. We have no experience with acquiring other companies and limited experience with forming collaborations. We may not be able to find suitable acquisition candidates, and if we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business and we may incur additional debt or assume unknown or contingent liabilities in connection therewith. Integration of an acquired company or assets may also disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, especially the acquisition of commercial assets, and require management resources that would otherwise focus on developing our existing business. We may not be able to find suitable collaboration partners or identify other investment opportunities, and we may experience losses related to any such investments.

To finance any acquisitions or collaborations, we may choose to issue debt or shares of our common stock as consideration. Any such issuance of shares would dilute the ownership of our

Table of Contents

stockholders. If the price of our common stock is low or volatile, we may not be able to acquire other assets or companies or fund a transaction using our stock as consideration. Alternatively, it may be necessary for us to raise additional funds for acquisitions through public or private financings. Additional funds may not be available on terms that are favorable to us, or at all.

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 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 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, if we are successful in obtaining marketing approval for any of our lead product candidates or if we acquire commercial assets, 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. 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 our most advanced product candidates, including migalastat HCl, 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, including migalastat HCl. Our ability to generate product revenue, which may never occur, will depend heavily on the successful development and commercialization of these product candidates, and upon the continuation and success of any collaborations we may enter into, in particular our collaboration with GSK. The successful commercialization of our product candidates will depend on several factors, including the following:

- successful enrollment of patients in our clinical trials on a timely basis;
- obtaining supplies of our product candidates and, where required, third party marketed products including ERTs, for completion of our clinical trials on a timely basis;
- successful completion of preclinical studies and clinical trials;
- obtaining regulatory agreement in the structure and design of our clinical programs;
- 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;

Table of Contents

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 most advanced product candidates are being developed to address is 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 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 migalastat HCl 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 migalastat HCl is significantly higher than some previously reported estimates of Fabry disease generally. If our estimates of the prevalence of Fabry 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.

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. In addition, 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.

In addition, while the clinical trials of our drug candidates are designed based on the available relevant information, in view of the uncertainties inherent in drug development, such clinical trials may

Table of Contents

not be designed with focus on indications, patient populations, dosing regimens, safety or efficacy parameters or other variables that will provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting drugs. In addition, individual patient responses to the dose administered of a drug may vary in a manner that is difficult to predict. Also, the methods we select to assess particular safety or efficacy parameters may not yield statistical precision in estimating our drug candidates' effects on study participants. Even if we believe the data collected from clinical trials of our drug candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us or our partners, which could delay, limit or prevent regulatory approval. For example, in December 2012, we announced top-line six-month (Stage 1) results from Study 011. While we believe these data are encouraging, the results did not achieve statistical significance (p=0.3) according to the pre-specified primary endpoint analysis. Although the FDA has indicated that it will consider the 12-month efficacy and safety data from Study 011 to support a potential U.S. conditional approval of migalastat HCl monotherapy, there can be no assurance that such data will support such approval or that the FDA will interpret these data in the same way that we may, which could delay, limit or prevent regulatory approval.

Even if our early stage clinical trials are successful, we will need to conduct additional clinical trials with larger numbers of patients receiving the drug for longer periods for all of our product candidates before we are able to seek approvals to market and sell these product candidates from the FDA and regulatory authorities outside the 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, while we have reached agreement with the FDA that a surrogate primary endpoint may be evaluated in our Phase 3 study for migalastat HCl, we cannot be sure what endpoints the FDA will require us to measure in later-stage clinical trials of our other product candidates. If the FDA requires different endpoints than the endpoints we anticipate using or a different analysis of those endpoints, 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. We have not obtained regulatory approval nor commercialized any of our product candidates. Although we announced top-line six-month Stage 1 results for our Phase 3 study of migalastat HCl (Study 011) in December 2012, the results did not achieve statistical significance according to the primary endpoint analysis, and we have not yet completed 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.

This difference did not achieve statistical significance (p=0.3) according to the pre-specified primary endpoint analysis.

Table of Contents

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 rare and we expect only a subset of the patients with these diseases to be eligible for our clinical trials. 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. For example, the entry criteria for our ongoing Phase 3 study in migalastat HCl for Fabry disease to support approval in the United States (Study 011) requires that patients must have a genetic mutation that we believe is responsive to migalastat HCl, and may not have received ERT in the past or must have stopped treatment for at least six months prior to enrolling in the study. As a result, enrollment of the study lasted for over two years.

In addition, 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. 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;
- we may decide to amend existing protocols for on-going clinical trials;
- regulators or institutional review boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- conditions imposed on us by the FDA or any non-U.S. regulatory authority regarding the scope or design of our clinical trials 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;

Table of Contents

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, such as existing treatments like ERT, 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 and milestone payments from our collaborators;

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. In addition, GSK has significant influence on the conduct of our migalastat HCl program, and could compel us to perform unanticipated clinical trials of migalastat HCl or delay the approval process for a variety of reasons.

Even if migalastat HCl or any other product candidate that we develop receives marketing approval, we will continue to face extensive regulatory requirements and the product may still face future development and regulatory difficulties.

Even if marketing approval is obtained, a regulatory authority may still impose significant restrictions on a product's indications, conditions for use, distribution or marketing or impose ongoing requirements for potentially costly post-market surveillance, post-approval studies or clinical trials. For example, any labeling ultimately approved by the FDA for migalastat HCl, if it is approved for marketing, may include restrictions on use, such as limitations on how Fabry disease is defined and diagnosed. In addition, the labeling may include restrictions based upon evidence of specific genetic mutations or symptoms found in patients. Migalastat HCl will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, distribution, promotion, recordkeeping and submission of safety and other post-market information, including adverse events, and any changes to the approved product, product labeling, or manufacturing process. The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information, and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug. For products approved under the Accelerated Approval regulations, the FDA has the authority to require clinical studies to confirm the clinical benefit associated with the surrogate endpoint. In addition, manufacturers of drug products and their facilities are subject to

Table of Contents

continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current Good Manufacturing Practice, or cGMP, and other regulations.

If we, our drug products or the manufacturing facilities for our drug products fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements;
- seize or detain products, refuse to permit the import or export of products or request that we initiate a product recall; or
- refuse to allow us to enter into supply contracts, including government contracts.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. In particular, any labeling approved by the FDA for migalastat HCl or any of our other product candidates may include restrictions on use. The FDA may impose further requirements or restrictions on the distribution or use of migalastat HCl or any of our other product candidates as part of a REMS plan. If we receive marketing approval for migalastat HCl or any other product candidates, physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

The commercial success of any product candidates that we may develop, including migalastat HCl, 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 migalastat HCl, 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:

- prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;

efficacy and potential advantages over alternative treatments;

pricing;

Table of Contents

relative convenience and ease of administration;

willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

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

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

Our prospects for generating revenue and achieving profitability will depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third party payors, both in the 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 payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payor determines that a product is eligible for reimbursement, the payor may impose coverage limitations 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

Table of Contents

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.

In addition, the Patient Protection and Affordable Care Act of 2010 and the Health Care and Education Reconciliation Act of 2010 (collectively referred to as the "Health Care Reform Law") are designed to overhaul the United States health care system and regulate many aspects of health care delivery and financing. The Health Care Reform Law is intended to broaden access to health insurance, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program, reduce or constrain the growth of health care spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Health Care Reform Law will require the promulgation of substantial regulations with significant effects on the health care industry.

A number of provisions contained in the Health Care Reform Law may affect us and will likely increase certain of our costs. For example, the new law revised the definition of "average manufacturer price" for reporting purposes and the volume of rebated drugs has been expanded to include beneficiaries in Medicaid managed care organizations, which could increase the amount of Medicaid drug rebates to states. Also, beginning in 2013, drug manufacturers will be required to report information on payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians and their immediate family members during the preceding calendar year. Under a final rule issued by the Centers for Medicare & Medicaid Services (CMS), drug manufacturers must begin to collect the required data on August 1, 2013 and report the data to CMS by March 31, 2014. Failure to submit required information may result in civil monetary penalties. Additionally, the Health Care Reform Law includes a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, or "donut hole." We do not know the full effect that the Health Care Reform Law will have on our commercialization efforts if migalastat HCl, or any other of our drugs, is approved. Although it is too early to determine the effect of the Health Care Reform Law, the law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

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.

Table of Contents

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, including migalastat HCl, 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 for other product candidates on acceptable terms or at all, and if we do enter into a distribution arrangement, our success will be dependent upon the performance of our partner.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or successfully market to adequate numbers of physicians to prescribe our products;
- the lack of additional products to be marketed 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.

Table of Contents

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 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;

damage to our reputation;

regulatory investigations, prosecutions or enforcement actions 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 such product candidates or products.

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.

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, acquire 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 lysosomal storage diseases, including Fabry disease. These products include sanofi aventis' Fabrazyme® and Shire plc's Replagal®. In addition, sanofi aventis, Shire and Actelion, Ltd. market and sell Cerezyme®, VPRIV and Zavesca®, respectively, for the treatment of Gaucher disease, and sanofi aventis markets and sells Myozyme® and Lumizyme® for the treatment of Pompe disease. In addition, ELELYSO® (taliglucerase alfa), a new enzyme replacement therapy for the treatment of Gaucher