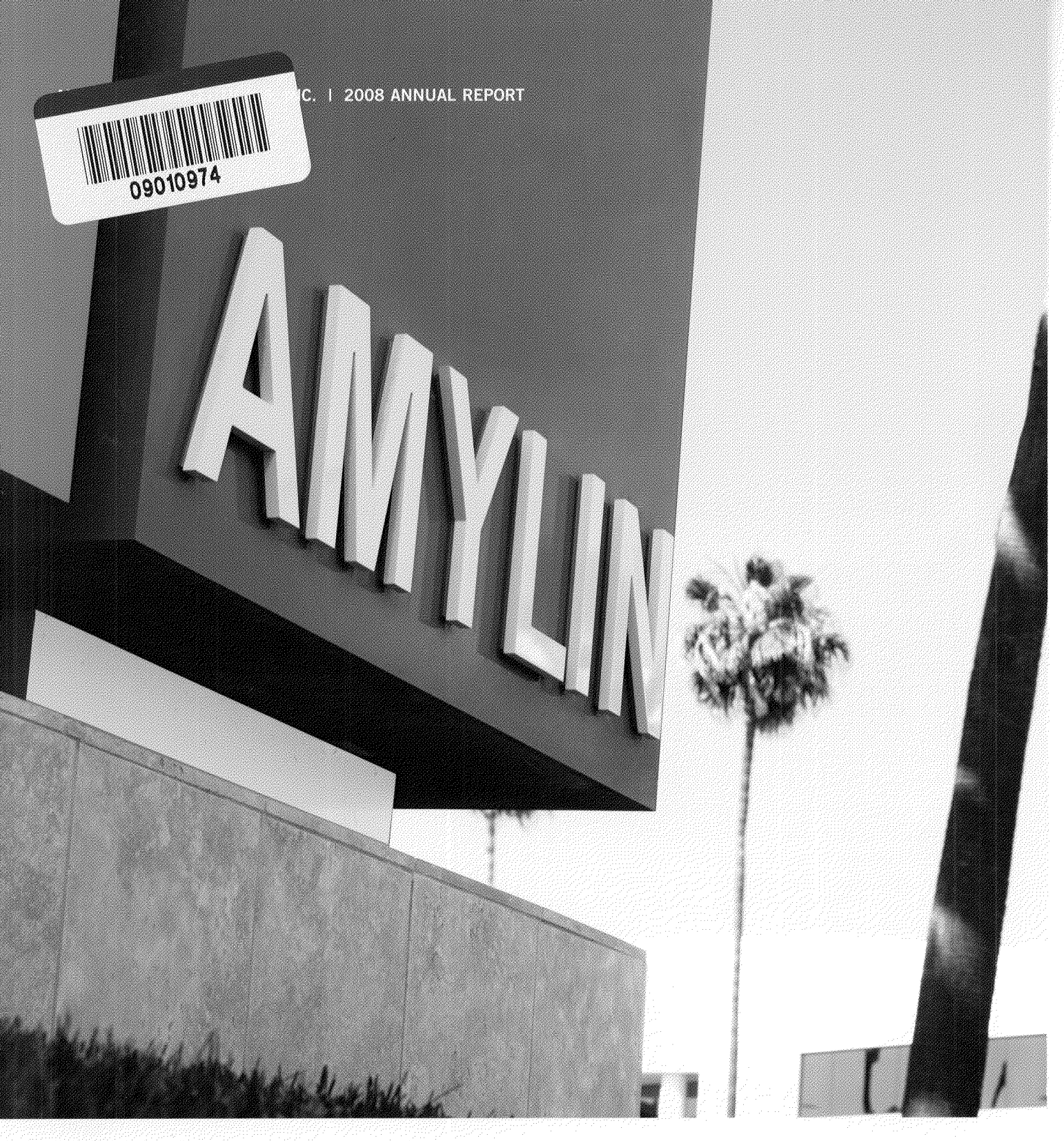
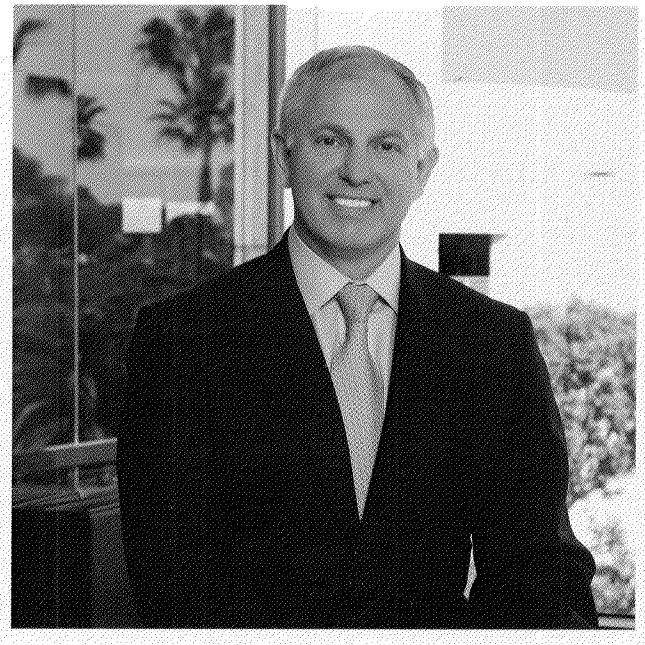
C. | 2008 ANNUAL REPORT



AMYLIN®

Challenging Science. Changing Lives.



In 2009, we are focused on five major opportunities: growing revenue from BYETTA, our first-in-class marketed product for type 2 diabetes; bringing exenatide once weekly to patients as quickly as possible; growing revenue from our second marketed diabetes product, SYMLIN; continuing development of potentially breakthrough therapies for obesity; and lowering our cost structure to improve operating results and shorten our path to profitability.

Daniel M. Bradbury
President and Chief Executive Officer

MESSAGE TO OUR SHAREHOLDERS

Amylin had a challenging year in 2008, yet we achieved significant revenue gains. Net product sales rose to $765.3 million, a 9 percent year-over-year increase, despite a turbulent economic environment, limited market growth, and unanticipated regulatory actions. We restructured and streamlined our organization, improving our operating efficiencies and lowering our cost structure to support our stated goal to be cash flow positive by the end of 2010.

Our strategic initiatives, clinical studies and marketing programs have created a solid platform for value creation. We believe the progress we made during the past year has positioned our company for sustainable long-term growth, continually fueled by the innovative science that is emblematic of Amylin.

In moving forward, our roadmap is a five-point strategy focused on:

- Growing revenue from our first-in-class marketed product, BYETTA® (exenatide) injection for type 2 diabetes;
- Bringing our new drug candidate exenatide once weekly to patients as quickly as possible;
- Growing revenue from our second marketed diabetes product, SYMLIN® (pramlintide acetate) injection;
- Continuing development of potentially breakthrough therapies for obesity; and
- Lowering our cost structure with a focus on rigorous financial discipline to improve operating results.

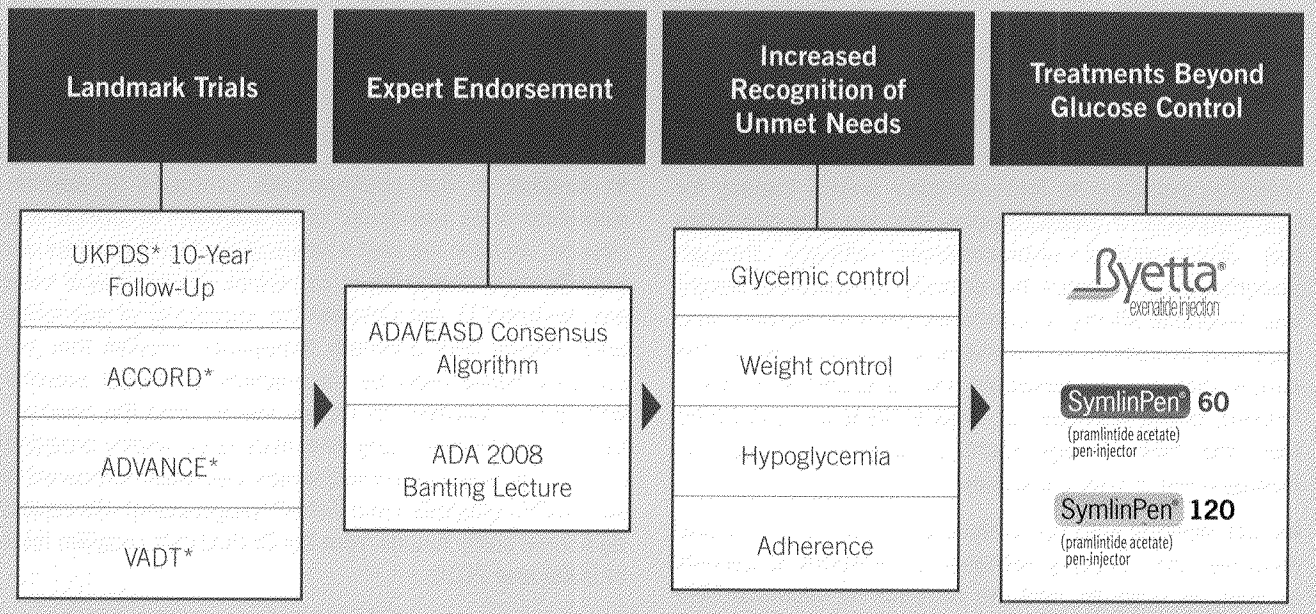
BYETTA: Positioned for Growth

BYETTA is the first and only approved glucagon-like peptide-1 (GLP-1) receptor agonist, and is currently indicated for use with common oral therapies to improve glycemic control in adults with type 2 diabetes. This represents a market of approximately nine million patients in the United States alone.

Since its launch in 2005, net product sales of BYETTA have increased annually, reaching $678.5 million in 2008, a year-over-year gain of 7 percent. Sales were driven by prescribers and patients as they increasingly recognized the strong therapeutic benefits of BYETTA—powerful, sustained glycemic control with potential weight loss, a lowered risk of hypoglycemia and a favorable cardiovascular risk profile. This steady growth was interrupted, however, by an August 2008 decision of the U.S. Food and Drug Administration (FDA) to update a prior alert referencing reports of severe pancreatitis in patients treated with BYETTA injection. In response, we committed our field organization to an educational effort in the medical community, disseminating the facts about pancreatitis and BYETTA, and underscoring the product's robust safety database, based on the experience of more than one million patients over nearly four years. In the fourth quarter of 2008, we resumed our focus on the product's therapeutic advantages, and believe that demand has stabilized.

Together with Eli Lilly and Company, our partner in the development and commercialization of exenatide, we are working to better understand the relationship between BYETTA and pancreatitis described in some spontaneously reported cases. In keeping with our focus on patient safety,

THE MARKET IS SHIFTING – TREATMENTS BEYOND GLUCOSE CONTROL ARE INCREASINGLY VALUED



Our diabetes therapies are unique because they offer the dual benefits of powerful, sustained glucose control with potential weight loss.

we continue to implement a drug safety program that includes thorough investigation of case reports, along with clinical and epidemiologic studies. Within the detection limits of an initial epidemiology study, we have not observed an increased incidence of pancreatitis associated with BYETTA compared to other treatments for diabetes and, consequently, believe that a definite causal relationship between BYETTA and pancreatitis has not been proved.

Marketplace Opportunities

Early in 2008, we filed a regulatory submission for a monotherapy indication that would enable BYETTA to be used as a stand-alone therapy for people diagnosed with type 2 diabetes. In clinical studies, patients who had been unable to control their blood glucose through diet and exercise alone showed significant improvement in glycemic control and weight loss when treated with BYETTA.

This new indication would give physicians another treatment option for patients with type 2 diabetes, and one that could be used relatively early in the continuum of care. Based on recent discussions with the FDA, we expect to receive approval for BYETTA as a stand-alone therapy—along with updated safety labeling language—in the near term.

Also of great significance is a shift in the medical community's criteria for diabetes therapy. Based on recently reported results from long-term, landmark studies demonstrating that weight gain is associated with increased cardiovascular risk—especially among people with type 2 diabetes—weight effects have become a critical consideration in choosing diabetes therapies. And in clinical studies, BYETTA has consistently shown weight reduction.

This new concern with weight effects is reflected in the latest treatment guidelines of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), which endorse the approach of treating diabetes with glucose control therapies that promote weight loss without increasing hypoglycemia. Importantly, BYETTA is the only new medicine added to these guidelines in the 2008 update, placing it in a much more prominent position and suggesting it as the treatment of choice for type 2 diabetes patients when either weight management or hypoglycemia is a concern. This represents 80 to 90 percent of the more than 23 million Americans living with this disease.

* UKPDS = United Kingdom Prospective Diabetes Study; ACCORD = Action to Control Cardiovascular Risk in Diabetes; ADVANCE = Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation; VADT = Veterans Affairs Diabetes Trial

Based on these new market opportunities, anticipated regulatory actions, and strong commercial programs, we expect to return BYETTA to growth in 2009, bringing its unique benefits to an increasing number of patients with type 2 diabetes.

Exenatide Once Weekly: Positioning for Rapid Adoption at Launch and Beyond

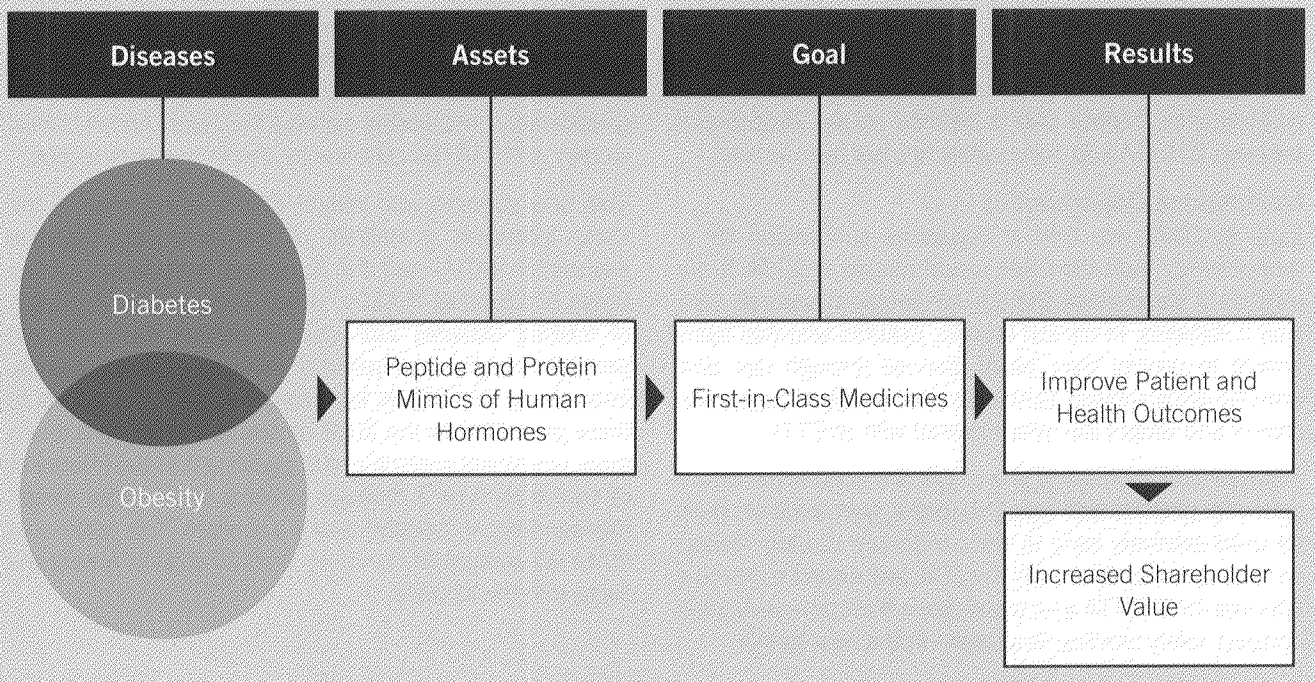
Exenatide once weekly is generating palpable excitement in the U.S. and international medical communities, and is poised to become the first-ever once weekly therapy for type 2 diabetes. In clinical studies, this new drug candidate has demonstrated unprecedented efficacy through powerful glucose control, the potential for sustained weight loss, favorable effects on cardiovascular risk markers, and improved tolerability. In commenting on these data in *The Lancet*, diabetes and metabolic disease expert Dr. Andre J. Scheen, of the University of Liege in Belgium, concluded that "this new strategy might substantially change the management of type 2 diabetes."

We are working with our collaboration partners, Lilly and Alkermes, Inc., to bring exenatide once weekly to patients as soon as possible, and are on track to submit a New Drug Application (NDA) in the second quarter of 2009. Based on feedback from the FDA, we believe we have the necessary safety and efficacy data, and have completed the manufacturing comparability analyses necessary for the regulatory submission. These analyses include data from the ongoing extension of the DURATION-1 study, and will be used as the basis for demonstrating comparability between intermediate-scale clinical trial material made in Alkermes' manufacturing facility and commercial-scale drug product made at Amylin's manufacturing facility.

In support of our post-approval strategies to position exenatide once weekly for rapid adoption at launch and beyond, we have initiated a series of studies that reflect our confidence in this product candidate. These clinical trials are designed to demonstrate the superiority of exenatide once weekly over alternate therapeutic choices that are currently being used by the majority of treated patients with type 2 diabetes. In topline results from the head-to-head DURATION-2 study, exenatide once weekly provided superior glucose control and weight loss when compared to Januvia™ (sitagliptin) and Actos® (pioglitazone). We expect additional study results from the DURATION program later in 2009 and 2010.

Our biologic approach to drug development leverages naturally occurring peptides and proteins that mimic human hormones.

RISK-ADVANTAGED VALUE CREATION STRATEGY



Also, given the encouraging clinical cardiovascular data we have already seen and the regulatory interest in cardiovascular outcomes, we engaged a steering committee of outside experts for assistance in designing a robust cardiovascular (CV) outcomes trial. This large CV superiority study will evaluate the effects of exenatide once weekly on major CV events, compared to traditional anti-diabetic regimens. The global study will be sponsored by Amylin and Lilly, already in active discussions with two academic research centers that will lead the study: The Diabetes Trial Unit at the Oxford Centre for Diabetes, Oxford, England; and Duke Clinical Research Institute, Duke University, Raleigh, NC. This study will give us the opportunity to determine the extent to which exenatide once weekly may reduce CV risk, in addition to lowering glucose.

Because of its demonstrated profile and impressive clinical results, we are confident exenatide once weekly has the potential to transform the treatment of diabetes.

We believe we have taken all necessary steps to position exenatide once weekly for commercial success:

- Strengthened our sales and marketing organization by adding senior management with proven leadership and expertise in the diabetes market and relevant experience in launching new diabetes therapies.
- Designed our clinical studies not only to demonstrate the safety and efficacy of exenatide once weekly in treating type 2 diabetes, but also to demonstrate its superiority over diabetes treatments now in common use.
- Partnered with Lilly for development and commercialization. Lilly continues to be a formidable presence in the diabetes marketplace, and we believe together we have the appropriate resources to maximize the commercial potential of this exciting drug candidate.

Because of its demonstrated profile and impressive clinical results, we are confident exenatide once weekly has the potential to transform the treatment of diabetes.

SYMLIN:
Focused on Education and Patient Support

SYMLIN is indicated as an adjunct treatment for patients with type 2 or type 1 diabetes who use mealtime insulin and have not achieved desired glucose control despite optimal insulin therapy. This therapy addresses their unmet needs by improving blood glucose control while increasing satiety, which can lead to weight loss. SYMLIN has already been used by more than 100,000 people.

Market acceptance has increased steadily since the product's introduction as the first and only approved amylin agonist nearly four years ago. In 2008, net product sales rose to $86.8 million, a 33 percent year-over-year gain, and our innovative new SymlinPen™ was a strong contributor. From the launch of these convenient pre-filled pen-injectors in early 2008 to year-end, total SYMLIN prescriptions increased 10 percent and approximately 20 percent more patients are now using SYMLIN.

Amylin owns 100 percent of the global rights to this first-in-class product, which is truly unique and fulfills an important role in diabetes therapy. Our growth initiatives include a sharpened focus on physician targeting and patient selection, leveraging our educational programs for healthcare professionals, and providing high-touch support programs for patients, offering them not only a "pen," but also a "partner."

Obesity Therapies:
Our Next Frontier in Metabolic Disease

Obesity is our next frontier in developing safe and effective treatments for metabolic disease that meet the needs of doctors, patients, regulators and payors. Our risk-advantaged development strategy leverages the diabetes and peptide expertise we have gained over the past 20 years, and focuses on peptide and protein mimics of human hormones.

One of our most promising drug candidates is a combination of pramlintide, an analog of human amylin (the same molecule in SYMLIN), and metreleptin, an analog of human leptin. In a proof of concept study completed in 2007, patients using this pramlintide/metreleptin combination achieved a 12.7 percent reduction in body weight over 24 weeks. Another exciting pipeline opportunity is davalintide (AC2307), a second-generation amylin analog optimized for obesity that offers the potential for enhanced efficacy and less frequent dosing, including once weekly. Phase 2 trials for both compounds are now underway and results are expected in the second half of 2009.

Our science is extraordinary, our first-in-class medicines have excellent growth opportunities, our product development pipeline is flourishing, and our financial position is sound.

Positioned for Value Creation

Amylin is already improving the health of millions of people worldwide and has the potential to make a life-changing difference for millions more struggling with diabetes and obesity. Our science is extraordinary, our first-in-class medicines have excellent growth opportunities, our product development pipeline is flourishing, and our financial position is sound. We finished 2008 with a strong balance sheet with $816.8 million in cash, cash equivalents and short-term investments.

VALUE CREATION ROADMAP FOR 2009

	1Q	2Q	3Q	4Q
BYETTA Monotherapy & Label Revision		Pending		
DURATION-1 Extension Comparability Results	✓			
DURATION-2 Results		✓		
DURATION-3 Results				
Submit Exenatide Once Weekly NDA				
Initiate Exenatide Once Weekly CV Outcomes Study				
Pramlintide/Metreleptin Phase 2B Results				
Davalintide (AC2307) Phase 2 Results				
Finalize Obesity Development and Funding Strategy				

Every quarter in 2009 should provide us with new opportunities for sustainable growth and value creation.

In October, we entered into a product supply agreement with Lilly for exenatide once weekly. Under its terms, Lilly made an initial cash payment to Amylin of $125 million, and, as the product is sold in future years, will reimburse us for its share of the cost of our exenatide once weekly manufacturing facility in Ohio, which was completed in 2008. Additionally, Lilly will make available a $165 million line of credit that Amylin can draw upon beginning in the fourth quarter of 2009 through the second quarter of 2011, with a due date three years from the final draw.

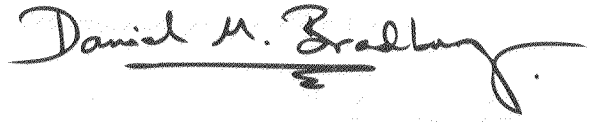
In the fourth quarter of 2008, we implemented a difficult but necessary strategic restructuring that included the reduction of our San Diego workforce by approximately 25 percent, and we expect to lower our anticipated 2009 cash expenditures by more than $80 million. The benefits of these actions are twofold. By optimizing our operating model, we will improve our flexibility and enhance our ability to adapt fluidly to changing business conditions. Secondly, by more closely aligning our cost structure with our projected revenues, we are on target with our business plan to generate positive operating cash flow by the end of 2010.

In keeping with our continuing emphasis on value creation and disciplined cost control, we are also pursuing options to offset research and development expense associated with our obesity pipeline and early-stage programs. We are exploring partnership opportunities and other financing options, and expect to finalize our obesity funding and development strategy by the end of the year.

I am grateful for the dedication and resolve of the people of Amylin, and for the ongoing commitment of our board of directors. I extend my thanks to each of them, and particularly to Ginger Graham and former director Howard (Ted) Greene, Jr., who are not standing for re-election at our 2009 annual stockholders' meeting. A former Amylin president and CEO, Ginger has been a director for more than 13 years. Ted is the company's co-founder, a former CEO, and was a director for 22 years. Their dedicated service and countless contributions are greatly appreciated.

Our vision at Amylin is shaped by two overriding goals that are inseparable: unleashing the potential of peptide and protein science to transform lives; and building a sustainable, profitable company that delivers superior shareholder value.

Thank you for supporting that vision.



10-K

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, 2008

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from **to** .

Commission File No. 0-19700

AMYLIN PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**33-0266089**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
9360 Towne Centre Drive San Diego, California	**92121**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(858) 552-2200**

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

Title of Each Class	**Name of each Exchange on Which Registered**
Common Stock, $.001 par value	The NASDAQ Stock Market, LLC

Securities registered pursuant to Section 12(g) of the Act:
NONE
(Title of Class)

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a 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. (Check one):

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ (Do not check if a smaller reporting company) Smaller reporting company ☐

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

The aggregate market value of the common stock of the registrant as of June 30, 2008 held by non-affiliates was $782,726,805.

The number of shares outstanding of the registrant's common stock was 138,072,689 as of February 10, 2009.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be filed with the Securities and Exchange Commission (the "Commission") pursuant to Regulation 14A in connection with the 2009 Annual Meeting of Stockholders to be held on May 27, 2009 are incorporated herein by reference into Part III of this Annual Report. Such Definitive Proxy Statement will be filed with the Commission not later than 120 days after December 31, 2008.

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You should read the following together with the more detailed information regarding our company, our common stock and our financial statements and notes to those statements appearing elsewhere in this document or incorporated by reference. The Securities and Exchange Commission, or SEC, allows us to "incorporate by reference" information that we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this annual report on Form 10-K.

Except for the historical information contained herein, this annual report on Form 10-K and the information incorporated by reference contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results may differ materially from those discussed here. Factors that could cause or contribute to such differences are described in Part I, Item 1A, entitled "Risk Factors," as well as those discussed in Part II, Item 7, entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations," and elsewhere throughout this annual report on Form 10-K and in any other documents incorporated by reference into this annual report on Form 10-K. We disclaim any obligation to update any forward-looking statement.

PART I

Item 1. *Business*

Business Overview

We are a biopharmaceutical company committed to improving the lives of people with diabetes, obesity and other diseases through the discovery, development and commercialization of innovative medicines. We are marketing two first-in-class medicines to treat diabetes, BYETTA® (exenatide) injection and SYMLIN® (pramlintide acetate) injection. Our near-term business strategy is to create value for patients and our stockholders by capitalizing on market drivers, such as the recent inclusion of BYETTA as the only new addition to the treatment guidelines of the American Diabetes Association, or ADA. Our focus remains on increasing BYETTA and SYMLIN revenue, submitting a New Drug Application, or NDA, for exenatide once weekly, significantly improving operating results and progressing toward positive operating cash flow by the end of 2010. Our long term strategy is focused on making prudent investment decisions based on strong clinical data to advance our obesity program. By the end of 2009, we intend to finalize our obesity funding and development strategy.

BYETTA is the first and only approved medicine in a new class of compounds called glucagon-like peptide-1 (GLP-1) receptor agonists. It is approved as an adjunctive therapy to improve glycemic control in patients with type 2 diabetes who have not achieved adequate glycemic control using metformin, a sulfonylurea and/or a thiazolidinediene (TZD), three common oral therapies for type 2 diabetes. In October 2008, the ADA and the European Association for the Study of Diabetes updated their type 2 diabetes treatment guidelines, placing the GLP-1 receptor agonist class, of which BYETTA is the only approved product, as a secondary treatment option for type 2 diabetes patients. In August 2008, the FDA updated a prior alert for BYETTA referencing pancreatitis. Prescriptions declined in the second half of 2008. During that time period we committed our field resources to educating the medical community on the facts about BYETTA, pancreatitis, and the product's safety profile. We believe the decline in BYETTA prescriptions and demand for the products stabilized at the end of the fourth quarter of 2008. Net product sales of BYETTA were $678.5 million in 2008, $636.0 million in 2007 and $430.2 million in 2006.

We have an agreement with Eli Lilly and Company, or Lilly, for the global development and commercialization of exenatide. This agreement includes BYETTA and other formulations of exenatide such as exenatide once weekly. Under the terms of the agreement, operating profits from products sold in the United States are shared equally between Lilly and us, and Lilly will pay us royalties for product

sales outside of the United States. Lilly has primary responsibility for developing and commercializing BYETTA outside of the United States, including any sustained release formulations of exenatide such as exenatide once weekly. In late 2006, BYETTA was approved in the European Union, or EU, and, by the end of 2008, BYETTA was commercially launched in 49 countries worldwide.

SYMLIN is the first and only approved medicine in a new class of compounds called amylinomimetics. It is approved as an adjunctive therapy to improve glycemic control in patients with either type 2 or type 1 diabetes who are treated with mealtime insulin but who have not achieved adequate glycemic control. In early 2008, we introduced the SYMLIN pen-injector device which we believe enables patients to more easily deliver proper dosing than using a vial and syringe and improves the convenience of administering SYMLIN. We own 100% of the global rights to SYMLIN. Net product sales of SYMLIN were $86.8 million in 2008, $65.5 million in 2007 and $43.8 million in 2006.

We have a field force of approximately 650 people dedicated to marketing BYETTA and SYMLIN in the United States. Our field force includes our specialty and primary care sales forces, a managed care and government affairs organization, a medical science organization and diabetes care specialists. Lilly co-promotes BYETTA in the United States. In May 2008, we amended our United States co-promotion agreement with Lilly, resulting in a 40% increase in the total number of sales representatives promoting BYETTA beginning July 1, 2008. To achieve this increase, Lilly's existing third party sales force for Cialis® (tidafil) co-promotes BYETTA in the United States and we increased the number of sales representatives in our primary care sales force by approximately 15%. In exchange for Lilly sharing in 50% of the costs related to our additional sales representatives and paying 100% of the third party sales force discussed above, our primary care sales force co-promotes Cialis in the United States. We are currently evaluating this element of the co-promotion arrangement with Lilly.

In addition to our marketed products, we are working with Lilly and Alkermes, Inc., or Alkermes, to develop exenatide once weekly. We are also working with Parsons, Inc., or Parsons, on the construction of a manufacturing facility in Ohio for exenatide once weekly. Construction of this facility was substantially completed in 2008. We are now manufacturing exenatide once weekly at commercial scale in this facility and we began supplying clinical trials with this material in the third quarter of 2008. In October 2008, we received a $125 million cash payment from Lilly representing an amount to compensate us for the cost of carrying Lilly's share of the capital investment made in the manufacturing facility. In addition to the $125 million cash payment, we will recover Lilly's share of the over $500 million capital investment in the facility through an allocation of depreciation to cost of goods sold in accordance with our collaboration agreement with Lilly. The total amount that will ultimately be recovered from Lilly will be dependent upon the proportion of product supplied for sale in the United States, the cost of which is shared equally by the parties, and the proportion of product supplied for sale outside the United States, the cost of which is paid for 100% by Lilly.

During the second quarter of 2008, we held our pre-NDA meeting with the FDA to discuss open items for our exenatide once weekly regulatory submission. Based on the pre-NDA meeting and our ongoing dialog with the FDA, we continue to believe that the pacing item for an NDA submission is to collect sufficient data to demonstrate the comparability between material manufactured by Alkermes in its facility and used in previous clinical studies and the commercial scale material produced in our Ohio facility. In December 2008, we announced that the FDA has indicated that data from an ongoing extension of our DURATION-1 study could be used to demonstrate comparability. Acceptance by the FDA of the comparability data is dependent upon the DURATION-1 study extension results that we expect to have in early 2009. Although we believe that our exenatide once weekly NDA submission is on track to be completed in the first half of 2009, if we are required to initiate a new clinical study to demonstrate comparability, the timing of the NDA submission would depend on the parameters of the new study, and our submission could be delayed.

In 2009 we will continue to focus on building a superior profile for exenatide once weekly by conducting three clinical trials that will compare exenatide once weekly against competing products. The objective of these studies is to support the launch of exenatide once weekly and demonstrate superiority and the transformational nature of our exenatide once weekly therapy.

In November 2008, we announced a strategic restructuring and workforce reduction that reduced the size of our San Diego workforce by approximately 25%, or 330 employees. The goal of the restructuring was to better align our cost structure with anticipated revenues and is part of our business plan to achieve positive operating cash flow by the end of 2010. We believe we have the appropriate resources to market BYETTA and SYMLIN, bring exenatide once weekly to market as soon as possible and continue to advance our obesity programs.

Our long-term growth strategy is focused on making prudent investment decisions based on strong clinical data to advance our obesity program and includes our Integrated Neurohormonal Treatment of Obesity, or INTO, strategy. In November 2007, we announced that overweight or obese subjects in a 24-week proof-of-concept study treated with a combination of pramlintide, an analog of human amylin and the same active ingredient in SYMLIN, and metreleptin, an analog of human leptin, lost an average of 25 pounds from baseline, resulting in reduced body weight on average of 12.7%. In 2009 we plan to continue the development of a potential obesity medicine that is a combination of pramlintide and metreleptin and the development of a second generation amylinomimetic (AC2307), now known as davalintide, which we have now moved into Phase 2 clinical trials. Data from both of these programs is expected in the second half of 2009. By the end of 2009, we intend to finalize our obesity funding and development strategy.

Although our efforts will remain focused on our near-term opportunities including BYETTA, SYMLIN and exenatide once weekly, we maintain an active discovery research program focused on novel peptide and protein therapeutics. We have also entered into a number of strategic alliances and business initiatives that support our expansion into new therapeutic areas.

Our principal executive offices are located at 9360 Towne Centre Drive, San Diego, CA 92121, and our telephone number is (858) 552-2200. We were incorporated in Delaware in September 1987. We maintain a website at *www.amylin.com*. The reference to our worldwide web address does not constitute incorporation by reference into this report of any of the information contained on our website.

Our periodic and current reports that we file with the SEC are available free of charge on our website at *www.amylin.com* as soon as reasonably practicable after we have electronically filed them with, or furnished them to, the SEC.

Diabetes

Diabetes is a major worldwide health problem and is the fifth leading cause of death by disease in the United States. Diabetes is a complex, metabolic disorder of carbohydrate, fat and protein metabolism, primarily resulting from the failure of pancreatic beta cells to produce sufficient insulin to match the demands for insulin in the body. Insulin is a hormone that plays a central role in helping the body process, convert and store energy from glucose. Another important hormone in glucose regulation is glucagon which is released from the alpha-cells of the pancreas. Its action opposes insulin by increasing glucose appearance in the bloodstream. With the discovery of incretin hormones, GLP-1, gastric inhibitory peptide and the pancreatic hormone amylin, it is now understood that several organs and hormones play a role in maintaining glucose balance in the body. In individuals with diabetes, the relative shortage of insulin impairs the ability of glucose to enter and fuel the body's cells and as a result, glucose builds up in the bloodstream causing hyperglycemia (high blood sugar). Prolonged elevation of blood glucose may result in damage to the kidney, retina and nerves—and may lead to kidney failure, permanent nerve damage, blindness and amputation. High glucose also increases the risk of cardiovascular disease. Conversely, too much insulin in the bloodstream can cause hypoglycemia (low

blood sugar). Individuals who manage their diabetes with insulin or other oral antidiabetic medication are especially vulnerable to swings of high to low blood sugar level and the risk of very low blood sugar which, if left untreated, can be fatal.

It is estimated that over 240 million people worldwide have diabetes. Of that population, it is estimated that approximately 90-95% have type 2 diabetes, previously known as adult-onset diabetes, and the remainder have type 1 diabetes, previously known as juvenile-onset diabetes. In the United States alone, there are approximately 23.6 million people, or 7.8% of the population, with diabetes. Only 17.9 million of these people have been diagnosed, while 5.7 million people with diabetes have not been diagnosed. From 1980 through 2005, newly diagnosed cases of diabetes among Americans aged 18-79 nearly tripled. In addition, there are currently approximately 57 million people in the United States with pre-diabetes, a condition that raises the risk of developing type 2 diabetes, heart disease and stroke. People with pre-diabetes have blood glucose levels higher than normal but not high enough to establish a diagnosis of diabetes.

Long term control of blood glucose is known to limit the risk of developing diabetes-related retinal, renal and neurologic complications. Glycated hemoglobin (A1C) is the most widely used measure of long-term blood glucose control. A1C level is a recognized indicator of an individual's average blood glucose concentrations over the preceding three- to four-month period. Lower A1C levels indicate better average blood glucose control, with values in people without diabetes usually being less than 6%. The ADA suggests that people with diabetes should aim for an A1C value that is lower than 7%. It is estimated that less than half of Americans being treated for diabetes are failing to achieve recommended blood glucose levels and, according to research studies conducted in the United States and abroad, these patients would significantly benefit from improved glycemic control. Additionally, aggressive use of insulin and some oral medications to reduce glucose levels can be associated with an increased risk of hypoglycemia and weight gain. Consequently, there has long been a need to develop new treatment strategies that safely improve glucose control, improve the overall health profile of patients with diabetes and reduce the risk of complications.

In 2008, findings from various long-term clinical trials, including the 10-year follow up of the UK Prospective Diabetes Study and the "Action to Control Cardiovascular Risk in Diabetes, or ACCORD, trial suggested that it is important to treat patients with less advanced diabetes earlier. These studies also suggest that it is important to lower blood glucose without weight gain, associated cardiovascular risk and hypoglycemia which are often associated with older diabetes therapies. The cardiovascular outcomes of these studies suggest that blood glucose control strategies employing weight conscious therapies will be increasingly valued.

For people suffering from diabetes, poor control of blood glucose levels has been shown to result in severe long-term complications. For instance, the United States Centers for Disease Control, or CDC, has stated that complications due to diabetes include:

- heart disease and stroke;
- high blood pressure;
- blindness due to retinopathy, a condition manifested by damage to the retina;
- nephropathy, or kidney disease;
- neuropathy, a condition where there is damage to the nervous system;
- amputations due to peripheral vascular disease; and
- periodontal disease.

Obesity is common in patients with type 2 diabetes and weight control is a major problem for many patients with both type 1 and type 2 diabetes. In fact, more than 80% of people with type 2

diabetes are overweight. Weight gain is particularly common in those using insulin and certain oral medications as part of their treatment regimen. In addition, patients with diabetes frequently have wide fluctuations in blood sugar following meals. These fluctuations in blood sugar can significantly affect a patient's quality of life. Blood glucose fluctuations, weight gain and diabetes complications may each contribute to substantial disability, reduced quality of life, reduced productivity in the workplace, increased pain and suffering and premature death. Obesity increases the risk of cardiovascular disease 44% in people with type 2 diabetes and cardiovascular death accounts for three quarters of all deaths among people with diabetes. In fact, the risk of coronary heart disease, cardiovascular disease and death are significantly increased in the overweight population and to an even greater extent in obese patients with type 2 diabetes.

In 2005, we introduced two new treatment options for the management of diabetes, BYETTA and SYMLIN. BYETTA offers patients with inadequate glycemic control using oral medications the opportunity to better control their blood glucose levels and lose weight. SYMLIN offers patients with inadequate glycemic control using mealtime insulin a treatment option that can both improve glucose control and result in weight loss. These novel first-in-class medicines provide new options in disease management and glucose control to millions of people suffering with diabetes.

Marketed Products

BYETTA® (exenatide) injection

BYETTA is the first and only approved medicine in a new class of compounds called incretin mimetics, or GLP-1 receptor agonists. We began selling BYETTA in the United States in June 2005 as an add-on therapy to improve glycemic control in patients with type 2 diabetes who have not achieved adequate glycemic control and who are taking metformin and/or a sulfonylurea, two common oral therapies for type 2 diabetes. Lilly also co-promotes BYETTA in the United States. In December 2006, the FDA approved an additional use for BYETTA as an add-on therapy to improve glycemic control in people with type 2 diabetes who have not achieved adequate glycemic control by using a TZD. We estimate the number of people in the United States currently using metformin, sulfonylurea and/or a TZD to be approximately 8.4 million. Less than half of all diabetes patients using oral medications are believed to have an A1C higher than the ADA's recommendation of less than 7% and the vast majority of these patients could be candidates for BYETTA.

BYETTA provides glucose control by augmenting the body's natural physiologic processes, allowing the body to respond to blood glucose changes as they occur. BYETTA directly affects the beta cells' responses to elevated glucose by enhancing insulin secretion; this effect dissipates as glucose levels approach the normal range. BYETTA also restores first-phase insulin response, an effect which is evident following the initial dose. BYETTA is administered twice a day by using a fixed dose injection, and requires no dose adjustments due to changes in meal size or composition, exercise or other variables. No additional glucose monitoring is required with BYETTA therapy.

The most common adverse effect of BYETTA is mild to moderate nausea, which tends to dissipate with time. Mild to moderate hypoglycemia has also been observed, primarily when used in conjunction with a sulfonylurea, agents that are known to cause hypoglycemia.

In August 2008, the FDA updated a prior alert for BYETTA referencing pancreatitis. Prescriptions for BYETTA declined in the second half of 2008. During that time period we committed our field resources to educating the medical community on the facts about BYETTA, pancreatitis, and the product's safety profile. We believe the decline in BYETTA prescriptions and demand for the products stabilized at the end of the fourth quarter of 2008. We are working to better understand the relationship between BYETTA and pancreatitis described in some spontaneously reported cases. In keeping with our focus on patient safety, we continue to pursue our drug safety program that includes thorough investigation of individual spontaneous case reports along with clinical and epidemiologic

studies. Within the detection limits of an initial epidemiology study which we provided to the FDA, we have not observed an increased incidence of pancreatitis associated with BYETTA compared to other treatments for diabetes and thus believe a definite causal relationship between BYETTA and pancreatitis has not been proved.

By the end of 2008, our field force expanded to approximately 650 individuals and, together with the Lilly field organization, our goal is to provide education, through both one-on-one interactions and educational programs, to ensure that physicians understand BYETTA, including its mechanisms of action, potential benefits and important use considerations. Primary care physicians write approximately 70% of diabetes prescriptions in the United States. We have refined our marketing efforts to remind primary care physicians of BYETTA's unique benefits of glucose control with weight loss. Additionally, we have access to health care plan reimbursement for BYETTA at over 80% coverage nationally on tier 2, which requires a relatively low co-payment from patients who are covered under such plans.

Lilly has primary responsibility for developing and commercializing BYETTA outside the United States, including any sustained-release formulations such as exenatide once weekly. In late 2006, we announced that the European Commission granted marketing authorization for BYETTA for the treatment of type 2 diabetes. Lilly commercially launched BYETTA in various EU member states and other countries in 2007 and by the end of 2008 BYETTA was launched in 49 countries worldwide.

We continue to support initiatives to facilitate the successful initiation of therapy by primary care physicians. This effort includes: increased patient educational material for health care providers to distribute in their offices; a network of approximately 475 diabetes educators to work with physicians and their patients within their local communities; direct support to patients through the BYETTA easy start line, which provides a toll-free number that allows patients to contact trained medical professionals to better understand the benefits of BYETTA therapy and to get assistance starting and using the BYETTA pen; a pharmacy support component partnering with managed care plans designed specifically to assist patient refills; and an enhanced BYETTA website. We believe this support is helpful to patients who may be on their first injectable therapy and to primary care providers who may be less accustomed to treating patients with an injectable product earlier in the disease cycle and who have fewer resources in their offices.

BYETTA Development Activities

In April 2005, concurrently with BYETTA's initial approval, the FDA issued an approvable letter for BYETTA when used as a monotherapy (stand-alone therapy) for people with type 2 diabetes. In December 2007, we announced the results of a 24-week BYETTA monotherapy study in drug-naïve patients. In this study participants taking 5 micrograms, or mcg, or 10 mcg of monotherapy BYETTA twice daily showed reductions in A1C by 0.7% and 0.9%, respectively, from an average baseline A1C ranging from 7.8% to 7.9%. In addition, approximately 60% of study participants on either 5 mcg or 10 mcg of monotherapy BYETTA at the conclusion of the study had an A1C of 7% or less. There was a low incidence of nausea reported in both treatment arms of the study of approximately 3% and 13% in the 5 mcg and 10 mcg arms, respectively. There were no instances of severe hypoglycemia in this study. Overall hypoglycemia was similar to that seen in studies where BYETTA was used in conjunction with metformin only.

In June 2008, we announced additional results from the monotherapy study. Treatment with exenatide resulted in a statistically significant lowering of fasting glucose concentrations in study participants taking 5 or 10 mcg of −17.5 mg/dL and −18.7 mg/dL at endpoint, respectively, compared with placebo reductions of −5.2 mg/dL. Participants taking 5 or 10 mcg also experienced statistically significant weight loss of 6.1 pounds and 6.8 pounds, respectively, compared with weight loss of 3.2 pounds for those taking placebo. In addition, fasting serum lipid profiles, including total cholesterol and high- and low-density lipoprotein, remained unchanged and systolic and diastolic blood pressure levels

improved for participants taking monotherapy BYETTA. We completed a regulatory submission to the FDA for BYETTA use as monotherapy in the first quarter of 2008. In December 2008, we issued an update on the timing of the FDA's review of our submission which we expect to be completed in the first quarter of 2009.

In September 2008, we announced results from a randomized, double-blind, cross-over, four-week head-to-head study demonstrating that BYETTA provided significantly lower glucose levels in the post-meal setting compared to Januvia™ (sitagliptin), a DPP-4 inhibitor. Additionally, patients treated with BYETTA reduced post-meal glucagon, showed more efficient use of their body's own insulin and decreased their food intake when compared to Januvia. In response to a standard meal, patients treated with BYETTA had significantly improved post-meal glucose levels two hours after the standard meal compared to Januvia. As patients switched from Januvia to BYETTA after two weeks, the post-meal glucose was further improved, while patients who switched from BYETTA to Januvia partially lost the post-meal glucose control achieved with BYETTA. The most common adverse events for both BYETTA and Januvia were mild to moderate nausea and vomiting. There were no major hypoglycemic events; a single event of minor hypoglycemia was reported in a patient treated with BYETTA.

SYMLIN® (pramlintide acetate) injection

SYMLIN is the first and only approved medicine in a new class of compounds called amylinomimetics. We began selling SYMLIN in the United States in April 2005 as adjunctive therapy to mealtime insulin to treat diabetes. Other than insulin and insulin analogues, SYMLIN is the first FDA-approved medication addressing glucose control for patients with type 1 diabetes since the discovery of insulin over 80 years ago. SYMLIN is indicated for use in people treated with insulin alone or, in the case of patients with type 2 diabetes, treated with insulin with or without one or more oral medications to help improve blood glucose control.

SYMLIN works with insulin to smooth out the peaks in blood glucose levels to give patients more stable blood glucose levels after meals and throughout the day. SYMLIN also lowers the A1C levels of most patients beyond what insulin alone can achieve. SYMLIN induces satiety, which leads to eating less and weight loss in most patients. In addition, because SYMLIN works with insulin to control blood sugar, patients often need less insulin to achieve desired blood sugar levels after meals.

SYMLIN is used with insulin and has been associated with an increased risk of insulin-induced severe hypoglycemia. The risk can be reduced by appropriate patient selection, careful patient instruction and insulin dose adjustments. Other adverse effects commonly observed are primarily gastrointestinal, including nausea, which decrease over time in most patients.

Our SYMLIN marketing is focused on a target physician population of approximately 20,000, with a goal of educating these physicians on SYMLIN, including its mechanisms of action, potential benefits, use considerations and appropriate patient selection for initiating SYMLIN therapy. These physicians write approximately 31% of all insulin prescriptions in the United States. In January 2008, we announced the availability of the SymlinPen® 120 and the SymlinPen® 60 pen-injector devices for administering SYMLIN. These pre-filled pen-injector devices feature fixed dosing to improve mealtime glucose control and can be stored at room temperature not to exceed 86 degrees F (30 degrees C) after first use. We continue to educate physicians about the SymlinPen and believe the SymlinPen will enable patients to more easily deliver proper dosing than using a vial and syringe and will also improve the convenience of administering SYMLIN. Our near-term goals for SYMLIN are to continue growing SYMLIN prescriptions by highlighting how the product addresses the key unmet needs of patients using mealtime insulin.

SYMLIN Development Activities

In June 2008, we published data showing that the use of mealtime SYMLIN with basal insulin therapy for 24 weeks resulted in more type 2 diabetes patients achieving diabetes treatment goals of improved glucose control without weight gain or hypoglycemia compared to the use of rapid-acting insulin with basal insulin. Among those patients treated with mealtime SYMLIN, 1 in 3 achieved this composite set of diabetes treatment goals while only 1 in 10 patients treated with rapid-acting insulin achieved the same result. In October 2007 we received a not approvable letter from the FDA for SYMLIN use with basal insulin and we are in continuing discussions with the FDA.

Research and Development

Product Pipeline Programs

We have late-stage and early-stage development programs in the therapeutic areas of diabetes and obesity. Our years of research in diabetes and deep understanding of peptide hormones—their physiology, functionality and impact on the disease—are being leveraged to develop potential treatments for obesity. The metabolic components of these diseases are linked in numerous ways, which are reflected in the impact each has on the other.

Diabetes

Exenatide Once Weekly

Exenatide once weekly is our late stage development program in diabetes. Exenatide is the active ingredient in BYETTA and is combined with proprietary technology developed by us and our partner, Alkermes, to provide a sustained release delivery of exenatide. The combination of potency and the glucose-dependent mechanism of action inherent in exenatide makes it well suited to development of a once weekly formulation. We have an agreement with Alkermes to assist us in the development, manufacture and commercialization of exenatide once weekly and this program is included in our collaboration agreement with Lilly. We are aggressively working with Lilly and Alkermes to develop exenatide once weekly and to bring it to market as soon as possible.

In October 2007, we announced positive results of our DURATION-1 pivotal comparator study comparing treatment with exenatide once weekly to treatment with BYETTA over a 30-week period. The study enrolled 295 patients not achieving adequate glucose control either with use of diet and exercise or with use of oral glucose-lowering agents. Exenatide once weekly showed a statistically significant improvement in A1C of approximately 1.9% from baseline, compared to an improvement of approximately 1.5% for BYETTA. Approximately three out of four subjects treated with exenatide once weekly achieved an A1C of 7% or less.

After 30 weeks of treatment, both exenatide once weekly and BYETTA treatment resulted in an average weight loss of approximately eight pounds. Nearly 90% of subjects in both groups completed the study. There was no major or severe hypoglycemia regardless of background therapy. As expected, based on prior BYETTA studies, minor hypoglycemia with exenatide once weekly use was limited to subjects using background sulfonylurea therapy. Exenatide once weekly was associated with approximately 30% less nausea than twice-daily BYETTA. Approximately one out of five subjects receiving exenatide once weekly reported treatment-related nausea during the 30-week study. In both groups nausea was predominately mild and transient.

In June 2008, we announced additional results of our 30-week DURATION-1 study. In addition to showing improvements in A1C, type 2 diabetes patients treated with exenatide once weekly experienced the following effects on several cardiovascular risk factors, including: a reduction of total cholesterol 11.9 mg/dL from a baseline of 173 mg/dL; a reduction of LDL of 4.9 mg/dL from a baseline 91.6 mg/dL; and a reduction of HDL of 0.9 mg/dL from a baseline of 43.9 mg/dL.

In June 2008, we announced results from a 52-week open-label clinical study that showed the durable efficacy of exenatide once weekly. In this extension of our 30-week DURATION-1 study, patients either remained on exenatide once weekly or switched from BYETTA to exenatide once weekly for an additional 22 weeks. Patients taking exenatide once weekly over the course of one year sustained a similar improvement in glucose control of 2.0% lower A1C and lower fasting plasma glucose from baseline compared to those receiving treatment for 30 weeks who achieved 1.9% lower A1C from baseline.

This 52-week study also showed that patients who switched from BYETTA after 30 weeks to exenatide once weekly experienced additional improvements in A1C and fasting plasma glucose. Following the 30-week comparison period, patients who continued on exenatide once weekly showed sustained improvements in A1C and fasting plasma glucose while patients who switched from BYETTA to exenatide once weekly had further improvements in glycemic control that were consistent with those patients receiving exenatide once weekly for 52 weeks. Seventy-two percent of patients treated with exenatide once weekly achieved an endpoint A1C of 7% or less and 54% achieved an A1C of 6.5% or less. In patients who switched from BYETTA to exenatide once weekly, 75% of patients achieved an endpoint A1C of 7% or less and 53% achieved an A1C of 6.5% or less. Exenatide once weekly was associated with an average weight loss of 9.5 pounds over 52 weeks. Exenatide once weekly was well tolerated during the first 30 weeks and the following 22-week, open-ended treatment period with overall tolerability improving over the course of the study. No major hypoglycemia events regardless of background therapy were observed with exenatide once weekly. Cases of minor hypoglycemia with exenatide once weekly and BYETTA use were limited to patients using background sulfonylurea therapy. In both groups, nausea was predominately mild and transient and occurred less frequently in exenatide once weekly patients.

Based on the favorable data from the DURATION-1 study, we have initiated three superiority clinical trials that compare exenatide once weekly against competing products. The purpose of this clinical trial program is to support the launch of exenatide once weekly, if it is approved by the FDA. In the third quarter of 2008, we completed enrollment of our DURATION-2 study, which compares exenatide once weekly against a TZD and a DPP-4 inhibitor on a background of metformin therapy. We expect results from the DURATION-2 study in the second quarter of 2009. We have completed enrollment for our superiority DURATION-3 study, which compares exenatide once weekly against insulin glargine on a background of oral agent therapy. We expect to report results from DURATION-3 in the third quarter of 2009. Finally, in the fourth quarter of 2008, we initiated our DURATION-4 superiority trial comparing exenatide once weekly as a stand-alone therapy to metformin, a TZD or a DPP-4 inhibitor and expect to complete this study in 2010. We believe our DURATION clinical program will provide powerful data that demonstrates the value of this potential medicine to physicians, payors and patients.

During the second quarter of 2008, we held our pre-NDA meeting with the FDA to discuss open items for our exenatide once weekly regulatory submission. Based on the pre-NDA meeting and our ongoing dialog with the FDA, we continue to believe that the pacing item for an NDA submission is to collect sufficient data to demonstrate the comparability between material manufactured by Alkermes in its facility and used in previous clinical studies and the commercial scale material produced in our Ohio facility. In December 2008, we announced that the FDA has indicated that the data from an ongoing extension of our DURATION-1 study could be used to demonstrate comparability. Acceptance by the FDA of comparability data is dependent upon the DURATION-1 study extension results we expect to have in early 2009. In response to the FDA's recently published guidance on requirements that all investigational new drug (IND) application holders of antidiabetic therapies show that their compounds do not increase the risk of cardiovascular events, we requested feedback from the agency which indicated we can proceed with a meta-analysis of the entire exenatide safety database to evaluate cardiovascular risk. A preliminary analysis of that database indicated there is no increased risk of

cardiovascular events associated with exenatide treatment. An alternative path toward a regulatory submission is to demonstrate comparability by initiating a new bridging study which would likely include both pharmacokinetic and clinical endpoints. Although we believe that our exenatide once weekly NDA submission is on track to be completed in the first half of 2009, if we are required to initiate a new clinical study to demonstrate comparability, the timing of the NDA submission would depend on the parameters of the new study, and our submission could be delayed.

Given the positive effects on cardiovascular surrogate outcomes observed with exenatide, the encouraging data from the ACCORD trial, which indicates decreased cardiovascular events with BYETTA, and the current regulatory interest in cardiovascular outcomes, we have engaged a steering committee composed of outside experts to assist us in designing a cardiovascular outcomes trial for exenatide once weekly. This study will give us the opportunity to demonstrate the effect of exenatide once weekly on cardiovascular outcomes and other end points of interest to our stakeholders. We do not believe this study will be a requirement for exenatide once weekly approval. We expect interim data from this study to be available in 2012 with final data available in 2016.

Nasal Exenatide

In June 2006, we entered into an agreement with Nastech Pharmaceutical Company, or Nastech, to develop a nasal spray formulation of exenatide. In 2008, we reported the results of a nasal exenatide Phase 1 clinical trial which showed that intranasal administration of exenatide was well tolerated and resulted in enhanced glucose-dependent insulin secretion and improved postprandial glucose control. In June 2008, Nastech announced that it had changed its name to MDRNA, Inc., or MDRNA, and that it had initiated a new corporate direction which included seeking to monetize its legacy nasal drug delivery business. We recently amended our agreement with MDRNA to reduce our royalty payment structure and eliminate future milestone payments to MDRNA.

Obesity

Obesity is a chronic condition that affects millions of people and is linked to increased health risk of several medical conditions including type 2 diabetes, high blood pressure, heart disease, stroke, osteoarthritis, sleep disorders and several types of cancers. Obesity is also rapidly becoming a major health problem in all industrialized nations and many developing countries. According to NAASO (The Obesity Society), obesity is the second leading cause of preventable death in the United States. It is estimated that 64% of the adult population in the United States are overweight and nearly 60 million adult Americans are considered obese. It is also estimated that the total direct and indirect costs attributed to overweight and obesity health issues exceed $100 billion in the United States each year.

Genetic, metabolic, psychological and environmental factors can all contribute to obesity. Obesity is measured by Body Mass Index, or BMI, a mathematical formula using a person's height and weight. BMI is calculated by dividing a person's weight in kilograms by the person's height in meters squared. A person with a BMI between 25 and 29.9 is considered overweight. A person with a BMI of 30 or more is considered obese, and a person with a BMI of 40 or more is considered severely obese. Current treatments for obesity include diet, exercise, drug therapy and surgery.

The National Heart, Lung and Blood Institute and the World Health Organization have issued evidence-based guidelines for the identification, evaluation and treatment of obesity. Non-pharmacological treatment modalities (dietary modifications, behavioral interventions and increased physical activity) are considered the cornerstone of clinical obesity management. If lifestyle changes do not promote weight loss after six months, pharmacotherapy is considered helpful for eligible high-risk patients. Only two pharmacological agents are currently approved for the long-term treatment of obesity in the United States. Bariatric surgery is considered an option only for patients with severe obesity and serious co-morbid conditions.

The National Institutes of Health, Surgeon General and FDA recognize a large unmet medical need for safe and efficacious therapies to prevent the debilitating metabolic diseases and mortality associated with obesity.

Integrated Neurohormonal Therapy for Obesity (INTO)

Since 2006, we have been executing an obesity strategy to assess the safety and efficacy of multiple neurohormones used in combination to treat obesity. We refer to this strategy as Integrated Neurohormonal Therapy for Obesity, or INTO. Integrated neurohormonal therapy is designed to restore the body's metabolism to a reduced obese or non-obese state by using neurohormones that work together to address the physiologic imbalances that cause complex chronic diseases such as obesity. Our INTO strategy is based on combination therapies and as part of this program we are studying combinations of peptide and protein hormones.

Three molecular franchises are the primary focus of our INTO strategy: amylin and, in particular, pramlintide, its synthetic version (a first generation amylinomimetic); leptin, and in particular, metreleptin, its recombinant version, a protein hormone produced from the fat cell that plays a fundamental role in metabolism via its communication to the brain; and PYY 3-36, and in particular, a more potent Y-family analog molecule, that is secreted by the gut and provides a satiety signal in the post-meal period. We are also studying a second-generation amylinomimetic, which is a compound that has been optimized in preclinical models to reduce body weight. Our near-term goals for our obesity program are to complete two clinical trials with amylin and leptin analogs and to finalize our obesity funding and development strategy in 2009.

Pramlintide

Pramlintide plays an important role in our current INTO strategy. Pramlintide has been studied extensively in people with and without diabetes and is the active ingredient in SYMLIN. In February 2006, we reported results from a 16-week Phase 2 dose-ranging study with pramlintide in obese subjects. After completing 16 weeks of treatment with pramlintide in addition to lifestyle intervention, subjects on average experienced an 8.4 to 13.4 pound weight loss from baseline, compared to a 6.2 pound weight loss with placebo plus lifestyle intervention.

Pramlintide was well tolerated and showed progressive weight loss at doses up to 360 mcg. No new safety signals were observed in this study, which included higher doses than those previously studied in obese subjects. There was clear evidence of a dose response for the twice-daily regimens. Consistent with previous observations, the most common adverse effect was mild nausea. Weight loss in subjects who did not experience nausea was similar to that seen in the overall study population. In October 2006, we reported results from a continuation of this study that demonstrated that patients completing 52 weeks of pramlintide therapy experienced a 7-8% mean body weight reduction, depending upon the dose they received, compared to a 1% reduction in patients receiving placebo.

We have conducted clinical studies using pramlintide in combination with leptin and with PYY 3-36. The proof-of-concept pramlintide and metreleptin study, which we discuss below, investigated the synergy of pramlintide and metreleptin found in preclinical studies.

Metreleptin

Metreleptin is the second compound we are studying in connection with our INTO program. Metreleptin is the recombinant form of human leptin, a naturally occurring protein hormone secreted by fat cells. Leptin plays a key role in metabolism through multiple metabolic actions and appears to act primarily at the level of the hypothalamus to regulate food intake and energy expenditure. Leptin's roles in the treatment of obesity and lipodystrophy have been extensively studied, and the lead molecules have a strong safety profile. Humans suffering from lipodystrophy, a disease characterized by

loss of body fat and consequent metabolic disorders (insulin resistance, hyperglycemia, and dyslipidemia), are rendered incapable of secreting sufficient amounts of leptin due to the loss of fat cell mass.

In early 2006, we acquired the exclusive rights to the leptin molecular franchise and program (including metreleptin) from Amgen, Inc., or Amgen. Under the terms of the license agreement, we may make potential future payments related to development and regulatory milestones and will pay royalties on any product sales. Our license includes exclusive rights to the leptin intellectual property developed by Amgen as well as intellectual property Amgen originally licensed from Rockefeller University.

PYY 3-36

PYY 3-36 is the third compound we are studying in connection with our INTO program. We are developing more potent and efficacious Y-family mimetics as drug candidates, but have been utilizing the native form of PYY 3-36 for the investigation of potential treatments of obesity. Independent researchers have reported a reduction in food intake in humans using PYY 3-36. In November 2007, we announced data from a 14-day safety and tolerability Phase 1 clinical trial showing that PYY 3-36 when used in combination with pramlintide was well-tolerated. We also announced that this combination was well-tolerated with dose escalation. We intend to focus our future development of the second generation Y-family mimetic either alone or in combination with a second generation amylinomimetic.

Pramlintide-Metreleptin Combination Product Candidate

In November 2007, we announced results from a 24-week proof-of-concept study with pramlintide and metreleptin combination treatment in overweight or obese subjects. At the end of the study, the combination treatment reduced body weight on average 12.7%, significantly more than treatment with pramlintide alone (8.4%). Subjects treated with pramlintide and metreleptin lost an average of 25 pounds from the beginning of the study compared with an average of 17 pounds for subjects treated with pramlintide alone. Subjects receiving pramlintide and metreleptin continued to lose weight through the end of the study compared to those treated with pramlintide alone, whose weight loss had stabilized towards the end of the study. At the beginning of the study, the average weight of study participants was approximately 205 pounds.

Consistent with previous clinical experience with pramlintide and metreleptin as single agents, the most common side effects seen with combination treatment were injection site adverse events and nausea, which were mostly mild to moderate and transient in nature. As a result of this study we are pursuing a pramlintide-metreleptin combination product candidate. In May 2008, we announced the initiation of a six-month Phase 2B clinical study evaluating various dosing combinations of pramlintide and metreleptin and completed enrollment of this study in the third quarter of 2008. The objective of this dose-ranging study is to support dose selection for Phase 3 and to inform the ongoing development of a convenient delivery system for this combination regimen. This double-blind, placebo-controlled study has enrolled approximately 600 subjects and is expected to be completed in the second half of 2009. We plan to continue developing a delivery system that will provide both pramlintide and metreleptin in a single injection.

Second Generation Amylinomimetic (Davalintide)

In 2006, we submitted an IND application to the FDA for a second generation amylinomimetic, now known as davalintide (formerly known as AC2307). This product candidate is an amylin analog optimized for obesity with increased potency that offers the potential for enhanced efficacy and less frequent dosing, including once-weekly delivery.

During 2007, we completed three Phase 1 studies of davalintide which we believe may have some potential advantages over pramlintide for weight loss as a single agent. These advantages may include greater efficacy and improved pharmaceutical properties, such as having prolonged duration of action and being more amenable to drug delivery. These three studies included a single dose study, a twice-daily multi-dose study and a once-daily multi-dose study. In November 2007, we announced data from the twice-daily multi-dose study showing that at 3mcg/kg dosing, individuals exhibited a 996 kilocalorie reduction in intake over a 24-hour period, representing a 34% decrease in daily calories. We have moved the development of davalintide into Phase 2 with a proof-of-concept study evaluating three dosing levels to be administered to approximately 240 patients for six months. The primary efficacy endpoint of the study is body weight. We expect to have results of the study in the second half of 2009.

Research Activities

A key element of our strategy is to develop first-in-class compounds for treating metabolic diseases. To achieve this goal, we are exploring hormones with multiple mechanisms of action that will potentially lead to products that have utility in treatment of more than one disease with the potential for many product forms. To do so, we take an integrated and biological, rather than a target-driven, approach to research. Our research is centered on peptide hormones that play an important metabolic role, and which we consider more likely to have an acceptable safety profile because these hormones exist naturally in the human body. Our development path begins with identifying a particular peptide and then determining if it is a circulating hormone, a substance that travels through the bloodstream to affect bodily functions. We then attempt to understand the hormone's functionality and potential impact on a disease. Rather than starting with a known biology and targeting molecules to modify, enhance or block it, our scientists are discovering the biology of previously unknown peptides and uncovering utility that could potentially translate into a new human therapy. The conventional development process commonly used in the pharmaceutical industry emphasizes utilizing isolated cells or molecular targets to advance drug discovery. Our approach to research calls for our scientists to quickly move to *in vivo* testing using highly predictive animal models that allow us to design subsequent information-rich clinical trials in humans.

Based on a premise that every peptide hormone has a utility—and a potential therapeutic benefit—we have developed a proprietary and continually growing peptide hormone library we call PHORMOL™. PHORMOL encompasses an extensive panel of potentially valuable biologics that have been taken from nature, including human peptides not previously described. All of these have been synthesized to create a rich source of compounds for ongoing research in their functionality, utility and potential value in treating a range of human diseases.

We are also developing capabilities in delivery system research and development, focused on product presentations that enhance clinical outcomes and patient convenience. Delivery systems are selected on the basis of technical feasibility, regulatory acceptance and market preference. They include injectable sustained-release formulations such as salt complexes, lipids, biodegradable polymer and gel systems, as well as non-injectable systems such as nasal sprays, oral and transdermal systems. We are also using our resources to optimize pharmaceutical properties of peptide drugs to develop new peptide hormone analogs that may be more amenable to alternative forms of delivery.

We currently have approximately 525 full-time employees dedicated to our research and development activities. In the years ended December 31, 2008, 2007 and 2006, we incurred research and development expense of $293.1 million, $276.6 million and $222.1 million, respectively.

Strategic Relationships

We have established strategic relationships with other companies and we continue to assess additional opportunities for strategic relationships or in-licensing opportunities. For example, we

partnered with PsychoGenics, Inc. to form Psylin Neurosciences, Inc., or Psylin, a company focused on the discovery and development of peptide hormones for treatment of psychiatric disorders. In addition, we have a joint research collaboration agreement with BioSeek, Inc. that is focusing on the discovery and development of novel peptide therapeutics for inflammatory conditions. We also have a joint research collaboration agreement with Xenome Ltd. Our collaboration with Xenome is focusing on the discovery and development of novel peptide hormones for a range of metabolic and musculoskeletal diseases.

Sales, Marketing and Distribution

We have built a sales and marketing organization that focuses on healthcare providers, managed healthcare organizations, wholesalers and pharmacies, government purchasers and other third-party payors. We currently have a field force of approximately 650 people dedicated to marketing BYETTA and SYMLIN in the United States. Our field force includes a primary care sales force as well as a specialty sales force of 75 representatives who call on endocrinologists and other physicians who have large diabetes care practices and other healthcare professionals who support their practices. Our field organization also includes a managed care and government affairs organization and a medical science organization that support broad medical education programs for both BYETTA and SYMLIN. Members of our sales and marketing team have extensive industry experience from a wide range of large and small companies and have substantial experience in the field of diabetes, as well as in launching and marketing pharmaceutical products.

Lilly co-promotes BYETTA in the United States. In May 2008, we amended our United States co-promotion agreement with Lilly, resulting in a 40% increase in the total number of sales representatives promoting BYETTA beginning July 1, 2008. To achieve this increase, Lilly's existing third party sales force for Cialis® (tadafil) co-promotes BYETTA in the United States and we increased the number of sales representatives in our primary care sales force by approximately 15%. In exchange for Lilly sharing in 50% of the costs related to our additional sales representatives and paying 100% of the third party sales force discussed above, our primary care sales force co-promotes Cialis in the United States. We are currently evaluating this element of the co-promotion arrangement with Lilly.

We utilize common pharmaceutical company practices to market our products. We call on individual physicians and other healthcare professionals and other organizations and individuals involved in the prescribing, purchasing and/or distributing of human medicines. We also provide professional symposia through our extensive medical education programs. Our medical education events are conducted live, via satellite or telephone and through web-based, interactive programs. We will continue to focus on medical education efforts for both BYETTA and SYMLIN through thousands of programs across the United States organized by our medical affairs and professional education organizations. We train physicians and other healthcare professionals as speakers, so that they can in turn teach their peers about how best to incorporate BYETTA or SYMLIN into their patients' diabetes treatment regimens.

We provide customer service and other related programs for our products, such as disease and product-specific websites, insurance research services, a customer service call center and order, delivery and fulfillment services. We have programs in the United States that provide qualified uninsured and underinsured patients with our products at no charge.

We sell BYETTA and SYMLIN to wholesale distributors who in turn sell to retail pharmacies and government entities. Decisions made by these wholesalers and their customers regarding the levels of inventory they hold, and thus the amount of BYETTA and SYMLIN they purchase, may affect the level of our product sales in any particular period.

Manufacturing

We have selected manufacturers that we believe comply with current Good Manufacturing Practices, or cGMP, and other regulatory standards. Manufactured product is used commercially following established registration procedures and after applicable regulatory approvals have been granted. We have established a quality control and quality assurance program, including a set of standard operating procedures, analytical methods and specifications, designed to ensure that our products and product candidates are manufactured in accordance with applicable regulations. We require that our contract manufacturers adhere to cGMP, except for products and product candidates for toxicology and animal studies, which we require to be manufactured in accordance with current Good Laboratory Practices, or cGLP.

Although some materials for our drug products are currently available from a single-source or a limited number of qualified sources, we attempt to acquire an adequate inventory of such materials, establish alternative sources and/or negotiate long-term supply arrangements. We believe we do not have any significant issues obtaining suppliers; however, we cannot be certain that we will continue to be able to obtain long-term supplies of our manufacturing materials.

BYETTA Manufacturing

We obtain exenatide, the active ingredient contained in BYETTA, from Bachem California, or Bachem, and Mallinckrodt, Inc., or Mallinckrodt, pursuant to agreements with each company. We have agreements with Wockhardt UK (Holdings) Ltd., or Wockhardt, and Baxter Pharmaceutical Solutions LLC, a subsidiary of Baxter, Inc., or Baxter, to supply us the dosage form of exenatide in cartridges. We have an agreement with Lilly to supply pens for delivery of BYETTA in cartridges.

SYMLIN Manufacturing

We obtain pramlintide acetate, the active ingredient contained in SYMLIN, from Bachem and Lonza Ltd., or Lonza, pursuant to agreements with each company. We have a contract with Baxter for the dosage form of SYMLIN in vials. We also have an agreement with Wockhardt for the dosage form of SYMLIN in cartridges. We have an agreement with Ypsomed AG to supply pen components for the delivery of SYMLIN in cartridges. We also have an agreement with Hollister-Stier Laboratories LLC for the assembly of the SYMLIN pen components and cartridges.

Exenatide Once Weekly Manufacturing

Under the terms of our development and license agreement with Alkermes, we are responsible for manufacturing the dosing formulation of exenatide once weekly for commercial sale and will pay Alkermes milestone payments upon achievement of development milestones and royalties on sales of exenatide once weekly. Alkermes has transferred to us its technology for manufacturing exenatide once weekly and will supply us with the polymer materials required for the commercial manufacture of exenatide once weekly. We obtain bulk exenatide, the active ingredient in exenatide once weekly, from Lonza and we obtain pre-filled diluent syringes for exenatide once weekly from Vetter Pharma-Fertigung GMB & Co. KG. pursuant to long-term agreements with both companies.

We are currently building a facility in West Chester, Ohio to manufacture exenatide once weekly. Construction of this facility was substantially completed in 2008. We are working with Parsons, a group with significant experience in the design and construction of pharmaceutical manufacturing facilities, to complete the design, construction and validation of this facility. We are now manufacturing exenatide once weekly at commercial scale in this facility and we began supplying clinical trials with this material in the third quarter of 2008.

Lilly Collaboration

We entered into a collaboration agreement with Lilly in 2002 for the global development and commercialization of exenatide, including both the twice-daily version, BYETTA, and sustained-release formulations, such as exenatide once weekly. Under the terms of the agreement, Lilly made initial payments to us, and purchased approximately 1.6 million shares of our common stock. In addition, Lilly has made milestone payments to us upon the achievement of development milestones for BYETTA and exenatide once weekly and commercial milestones for BYETTA. Lilly is also obligated to make additional future commercial milestone payments to us of up to $80 million contingent upon the commercial launch of exenatide, including BYETTA and exenatide once weekly, in selected territories throughout the world. Under our co-promotion arrangement with Lilly, the parties use approximately equal efforts to co-promote BYETTA within the United States and have agreed to use approximately equal efforts to co-promote sustained-release formulations of exenatide within the United States. Lilly is responsible for commercialization efforts outside the United States. We share exenatide United States development and commercialization costs with Lilly equally and we pay Lilly 50% of the operating profits from the sale of products in the United States. Our collaboration agreement may be terminated by Lilly at any time on six months' notice.

In late 2006, BYETTA was approved in the EU and, by the end of 2008, was commercially launched in 49 countries worldwide. Lilly will pay us tiered royalties based upon the annual gross margin for all exenatide product sales, including any sustained-release formulations, outside of the United States. Royalty payments for exenatide product sales outside the United States will commence after a one-time cumulative gross margin threshold has been met. Lilly is responsible for 100% of the costs related to development of twice-daily BYETTA for sale outside of the United States. Development costs related to all other exenatide products for sale outside of the United States will continue to be allocated 80% to Lilly and 20% to us. Lilly is responsible for 100% of the costs related to commercialization of all exenatide products for sale outside the United States. We record all United States BYETTA product revenues and Lilly records all BYETTA product revenues from outside the United States.

In October 2008, we entered into an Exenatide Once Weekly Supply Agreement with Lilly pursuant to which we will supply commercial quantities of exenatide once weekly for sale in the United States, if approved by the FDA. In addition, if Lilly receives approval to market the product in jurisdictions outside the Unites States, we will be required to manufacture the product intended for commercial sale by Lilly in those jurisdictions. We have also entered into a loan agreement with Lilly pursuant to which Lilly will make a $165 million unsecured line of credit available to us that we can draw upon from time to time beginning on December 1, 2009 and ending on June 30, 2011, with maturity no later than June 30, 2014.

Competition

The biotechnology and pharmaceutical industry is highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to the products in our portfolio. A number of our largest competitors, including AstraZeneca, Bristol-Myers Squibb Company, GlaxoSmithKline, Lilly, Merck & Co., Novartis AG, Novo Nordisk, Pfizer, Sanofi-Aventis and Takeda Pharmaceuticals, are pursuing the development of or are marketing pharmaceuticals that target the same diseases that we are targeting, and it is probable that the number of companies seeking to develop products and therapies for the treatment of diabetes, obesity and other metabolic disorders will increase. Many of these and other existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. These companies may develop and introduce products and processes competitive with or superior to ours. In addition, other technologies or products may be

developed that have an entirely different approach or means of accomplishing the intended purposes of our products, which might render our technology and products noncompetitive or obsolete. For example, all of our current drug products are injectable, and may have to compete with therapies that do not require injection. We cannot be certain that we will be able to compete successfully.

SYMLIN is the only non-insulin-based drug product approved for improving blood glucose control in people with type 1 diabetes. Further, insulin and oral medications are often insufficient for many people with type 2 diabetes to achieve satisfactory glucose and weight control. BYETTA or SYMLIN may be complementary to, or competitive with, these other medications.

BYETTA and SYMLIN must compete with established therapies for market share. In addition, many companies are pursuing the development of novel pharmaceuticals that target diabetes. These companies may develop and introduce products competitive with or superior to BYETTA or SYMLIN. Such competitive products and potential products include:

- sulfonylureas;
- metformin;
- insulins (injectable and inhaled versions);
- thiazolidinediones (TZDs);
- glinides;
- dipeptidyl peptidase type IV (DPP-IV) inhibitors;
- incretin/GLP-1 agonists;
- insulin sensitizers, including PPARs;
- alpha-glucosidase inhibitors; and
- sodium-glucose transporter-2 (SGLT-2) inhibitors.

There is substantial competition in the discovery and development of treatments for obesity, as well as emerging prescription and over-the-counter treatments for this condition. Current treatments for obesity include dietary therapy, physical activity, drug therapy and surgery. Hoffmann-LaRoche and Abbott Laboratories already market oral medicines for the treatment of obesity. Glaxo Smith Kline now markets a former prescription product (orlistat-Alli) for treatment of obesity. In addition, a number of other pharmaceutical companies are developing new potential therapeutics.

Patents, Proprietary Rights, and Licenses

We believe that patents and other proprietary rights are important to our business. Our policy is to file patent applications to protect technology, inventions and improvements that may be important to the development of our business. We also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. We plan to enforce our issued patents and our rights to proprietary information and technology. We review third-party patents and patent applications, both to refine our own patent strategy and to identify useful licensing opportunities.

We have a number of patents, patent applications and rights to patents related to our compounds, products and technology, but we cannot be certain that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents. We have also filed foreign counterparts to many of these issued patents and applications.

We may obtain patents for our compounds many years before we obtain marketing approval for them. Because patents have a limited life, which may begin to run prior to the commercial sale of the

related product, the commercial value of the patent may be limited. However, we may be able to apply for patent term extensions to compensate in part for delays in obtaining marketing approval. For example, in the United States a patent term extension of 1,586 days has been granted for SYMLIN and a patent term extension of 1,287 days has been granted for BYETTA. Similar patent term extensions may be available for other products that we are developing, but we cannot be certain we will obtain them.

Included within our exenatide patent portfolio are issued patents for:

- pharmaceutical compositions containing exenatide;
- modulating gastric emptying;
- inhibiting glucagon secretion;
- stimulating insulin release; and
- reducing food intake.

These patents expire between 2013 and 2020. We do not have a composition of matter patent for the exenatide molecule.

Included within our pramlintide patent portfolio are issued patents for:

- pramlintide and other amylin agonist analogues invented by our researchers;
- amylin agonist pharmaceutical compositions, including compositions containing pramlintide; and
- methods for treating diabetes and related conditions using amylin agonists.

These patents expire between 2011 and 2018.

Our SYMLIN and BYETTA products are subject to the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which provides data exclusivity for a certain period of time. Once this exclusivity period expires, the Hatch-Waxman Act allows generic manufacturers to file Abbreviated New Drug Applications, or ANDA, with the FDA requesting approval of generic versions of previously-approved products. For example, a generic pharmaceutical manufacturer could file an ANDA for SYMLIN as early as March 2009 and for BYETTA as early as April 2009. If an ANDA is filed for one of our approved products prior to expiration of the patents covering those products, it could result in our initiating patent infringement litigation to enforce our rights.

With respect to our drug candidates, we have patents and patent applications pending, or have licensed patents and patent applications, relevant to the development and commercialization of such drug candidates. Generally, our policy is to file foreign counterpart applications in countries with significant pharmaceutical markets.

It is important that we do not infringe patents or proprietary rights of others and that we do not violate the agreements that grant proprietary rights to us. If we do infringe patents or violate these agreements, we could be prevented from developing or selling products or from using the processes covered by those patents or agreements, or we could be required to obtain a license from the third party allowing us to use their technology. We cannot be certain that, if required, we could obtain a license to any third-party technology or that we could obtain one at a reasonable cost. If we were not able to obtain a required license, we could be adversely affected. Because patent applications are confidential for at least some period of time, there may be pending patent applications from which patents will eventually issue and prevent us from developing or selling certain products unless we can obtain a license to use the patented technology.

Patents relating to pharmaceutical, biopharmaceutical and biotechnology products, compounds and processes such as those that cover our existing products, compounds and processes and those that we will likely file in the future do not always provide complete or adequate protection. Future litigation or proceedings initiated by the United States Patent and Trademark Office regarding the enforcement or validity of our existing patents or any future patents could invalidate our patents or substantially reduce their protection. In addition, statutory or regulatory changes may adversely affect our ability to obtain protection or enforce our patents. Furthermore, our pending patent applications and patent applications filed by our collaborative partners may not result in the issuance of any patents or may result in patents that do not provide adequate protection. As a result, we may not be able to prevent third parties from developing the same compounds and products that we have developed or are developing. In addition, we do not have patent protection or we may not be able to enforce our patents in certain countries. As a result, manufacturers may be able to sell generic versions of our products in those countries.

We also rely on unpatented trade secrets and improvements, unpatented internal know-how and technological innovation. We protect these rights mainly through confidentiality agreements with our corporate partners, employees, consultants and vendors. These agreements provide that all confidential information developed or made known to an individual during the course of their relationship with us will be kept confidential and will not be used or disclosed to third parties except in specified circumstances. In the case of employees, the agreements provide that all inventions made by the individual while employed by us will be our exclusive property. We cannot be certain that these parties will comply with these confidentiality agreements, that we have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by our competitors. Under some of our research and development agreements, inventions discovered in certain cases become jointly owned by us and our corporate partner and in other cases become the exclusive property of one of us. It can be difficult to determine who owns a particular invention and disputes could arise regarding those inventions.

Government Regulation

Regulation by governmental authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of pharmaceutical products. All of our potential products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical testing and clinical trials and other pre-market approval requirements by the FDA and regulatory authorities in foreign countries. Various federal, state and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of such products.

A number of steps must be taken before a pharmaceutical agent may be marketed in the United States. First, the pharmaceutical agent must undergo preclinical testing. Preclinical tests include laboratory evaluation of product chemistry and animal studies to assess the potential safety and activity of the product candidate and its formulations. The results of these studies must be submitted to the FDA as part of an IND which must be reviewed by the FDA before a proposed clinical trial can begin. Typically, clinical trials involve a three-phase process. In Phase 1, clinical trials are conducted with a small number of healthy volunteers to determine the early safety and tolerability profile and the pattern of drug distribution and metabolism. In Phase 2, clinical trials are conducted with groups of patients afflicted with a specified disease in order to determine preliminary efficacy, dosing regimens and expanded evidence of safety. In Phase 3, large-scale, multi-center, adequate and well-controlled comparative clinical trials are conducted with patients afflicted with a target disease in order to provide enough data for the statistical proof of efficacy and safety required by the FDA and others. The results of the preclinical testing and clinical trials for a pharmaceutical product are then submitted to the FDA in the form of an NDA for approval to commence commercial sales. In responding to an NDA, the

FDA may grant marketing approval, request additional information, or deny the application if it determines that the application does not satisfy its regulatory approval criteria. Once a drug is approved for marketing in the United States, the FDA requires ongoing safety monitoring to ascertain any undiscovered issues related to "real-world" use of the drug. The expanded patient exposure once a drug is introduced to the marketplace can reveal new risks (as well as new benefits) that were not detectable during clinical testing.

Among the conditions for NDA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to cGMP. In complying with cGMP, manufacturers must continue to expend time, money and effort in the area of production, quality control, and quality assurance to ensure full technical compliance. Manufacturing facilities are subject to periodic inspections by the FDA to ensure compliance.

We are also subject to various federal, state, and local laws, regulations and recommendations relating to safe working conditions; laboratory and manufacturing practices; the experimental use of animals; and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research.

The activities required before a pharmaceutical agent may be marketed in the EU are dictated by the International Conference on Harmonization and are generally similar to those established in the United States. Approval of new drugs across the EU relies on either the mutual recognition or decentralized approval procedure of the European Medicines Agency. Under the centralized procedure, the marketing application is referred for review to two review teams, each representing one of the member countries. Each reviewer then forwards an early assessment to the Committee for Medicinal Products for Human Use, or CHMP, for discussion and preparation of an initial consolidated assessment report, including a list of questions requesting clarification as well as additional information. This step initiates a series of dialogues, meetings and other communications among the CHMP, the two review teams and the applicant, leading in turn to clarification, education and refinement of the original assessment reports. Ultimately, a decision is reached to either grant marketing approval or deny the application if it is determined that the application does not satisfy the regulatory approval criteria. The clinical testing, manufacture and sale of pharmaceutical products outside of the United States and the EU are subject to regulatory approvals by other jurisdictions which may be more or less rigorous than those required by the United States or the EU.

Employees

As of December 31, 2008, we had approximately 1,800 full-time employees. A significant number of our management and professional employees have had experience with pharmaceutical, biotechnology or medical product companies. We believe that we have been highly successful in attracting skilled and experienced personnel. None of our employees is covered by collective bargaining agreements and we consider relations with our employees to be good.

Directors and Executive Officers

The names of our directors and executive officers and certain information about them as of February 15, 2009 are set forth below:

Name	Age	Position
Daniel M. Bradbury(1)	47	President, Chief Executive Officer and Director
Joseph C. Cook, Jr.(1)	67	Chairman of the Board
Adrian Adams(2)	58	Director
Steven R. Altman(2)	47	Director
Teresa Beck(3)	54	Director
Karin Eastham(2)(3)	59	Director
James R. Gavin III, M.D., Ph.D.(4)	63	Director
Ginger L. Graham(1)	53	Director
Howard E. Greene, Jr.(1)	66	Director
Jay S. Skyler, M.D., MACP(4)	62	Director
Joseph P. Sullivan(1)(3)	66	Director
James N. Wilson(2)(4)	65	Director
Craig A. Eberhard	49	Vice President, Sales
Mark G. Foletta	48	Senior Vice President, Finance and Chief Financial Officer
Mark J. Gergen	46	Senior Vice President, Corporate Development
Orville G. Kolterman, M.D.	61	Senior Vice President, Research and Development
Marcea Bland Lloyd	60	Senior Vice President, Government and Corporate Affairs, and General Counsel
Roger Marchetti	50	Senior Vice President, Human Resources and Information Management
Paul G. Marshall	49	Senior Vice President, Operations
Vincent P. Mihalik	58	Senior Vice President, Sales and Marketing and Chief Commercial Officer
Lloyd A. Rowland	52	Vice President, Governance and Compliance, and Corporate Secretary

(1) Member of the Finance Committee.

(2) Member of the Compensation and Human Resources Committee.

(3) Member of the Audit Committee.

(4) Member of the Corporate Governance Committee.

Mr. Bradbury has been our Chief Executive Officer since March 2007, serving as President since June 2006 and as Chief Operating Officer since June 2003. He has served as a director since June 2006. He previously served as Executive Vice President from June 2000 until his promotion in June 2003. He joined Amylin in 1994 and has held officer-level positions in Corporate Development and Marketing during that time. Prior to joining Amylin, Mr. Bradbury spent ten years at SmithKline Beecham Pharmaceuticals, where he held a number of sales and marketing positions. He is a member of the board of directors of Illumina, Inc. He also serves on the RAND Health Board of Advisors and as a board member for PhRMA, BIOCOM, the Keck Graduate Institute's Board of Trustees and the San Diego Regional Economic Development Corporation. Mr. Bradbury is a member of the Royal Pharmaceutical Society of Great Britain and serves on the UCSD Rady School of Management's Advisory Council. He received a Bachelor of Pharmacy from Nottingham University and a Diploma in Management Studies from Harrow and Ealing Colleges of Higher Education.

Mr. Cook has been our Chairman of the Board since March 1998 and serves on our Finance Committee. He served as Chief Executive Officer from March 1998 until September 2003. From 1994 to 1998, Mr. Cook served as a member of our Board and a consultant to us. Mr. Cook is a founder and serves as Chairman of the Board of Microbia, Inc., a privately held biotechnology company. He also serves as a director of Corcept Therapeutics Incorporated. Mr. Cook is a founder of Mountain Group Capital, LLC, Clinical Products, LLC, and Mountain Ventures, Inc. He serves on the Board of Mercy Ministries, Inc. and is past Chair of the Advisory Board of the College of Engineering, University of Tennessee. Mr. Cook retired as a Group Vice President of Eli Lilly & Company in 1993 after more than 28 years of service. Mr. Cook received a B.S. in Engineering from the University of Tennessee.

Mr. Adams has served as a director since October 2007 and serves on the Compensation and Human Resources Committee. Mr. Adams is President and Chief Executive Officer of Sepracor, Inc., a position he has held since May 2007, and serves as a member of Sepracor's board of directors. Mr. Adams joined Sepracor in March 2007 as President and Chief Operating Officer. Most recently, he was with Kos Pharmaceuticals, Inc., where he served as President and Chief Operating Officer from April 2001, prior to becoming President and Chief Executive Officer in January 2002. Mr. Adams served as President and Chief Executive Officer of Novartis-UK from 1999 until his tenure began at Kos. For the previous seven years, he was with SmithKline Beecham Pharmaceuticals, last serving as President and CEO of the company's Canadian subsidiaries. Previous assignments at SmithKline Beecham included Vice President and Director of Worldwide Marketing in the U.S., and Director and Vice President of Sales and Marketing in the United Kingdom. Mr. Adams began his career at ICI Pharmaceuticals, where he rose from research laboratory assistant to Director of Sales and Marketing. He is a graduate of Manchester University in the United Kingdom with a Bachelor of Science degree.

Mr. Altman has served as a director since March 2006 and serves on the Compensation and Human Resources Committee. He currently serves as President of QUALCOMM Incorporated, a position he has held since 2005. In 2002, Mr. Altman was named President of QUALCOMM Technology Licensing, or QTL, and previously served as QTL's Executive Vice President from 1998 to 2002 and as its Senior Vice President from 1996 to 1998. He became QTL's General Manager at the formation of the group in 1995. Mr. Altman joined QUALCOMM in 1989 as Corporate Counsel responsible for licensing and acquisitions and was appointed Vice President and General Counsel in 1992. He received his J.D. from the University of San Diego.

Ms. Beck has served as a director since March 2007 and serves on the Audit Committee. From 1998 to 1999, Ms. Beck served as President of American Stores Company, and previously served as its Chief Financial Officer from 1993 to 1998. Prior to her appointment as Chief Financial Officer, Ms. Beck served in various finance and accounting related positions with American Stores from 1982 to 1993. Before joining American Stores, Ms. Beck was the controller of Steiner Financial Corporation and she served as an audit manager for Ernst & Whinney (currently Ernst and Young LLP). Ms. Beck currently serves as a director for Questar Corporation and Lexmark International, Inc. In addition, she serves as a member of the Board of Trustees of Intermountain Healthcare, The Nature Conservancy and the Nature Conservancy of Utah. She is also Vice-Chairman of the University of Utah National Advisory Council. Ms. Beck received a B.S. and an M.B.A. from the University of Utah.

Ms. Eastham has served as a director since September 2005 and serves as the chair of the Audit Committee and on the Compensation and Human Resources Committee. From May 2004 to September 2008 she served as Executive Vice President and Chief Operating Officer, and as a member of the Board of Trustees of the Burnham Institute for Medical Research, a non-profit corporation engaged in basic biomedical research. From April 1999 to May 2004, Ms. Eastham served as Senior Vice President, Finance, Chief Financial Officer, and Secretary of Diversa Corporation. She previously held similar positions with CombiChem, Inc., a computational chemistry company, and Cytel Corporation, a biopharmaceutical company. Ms. Eastham also held several positions, including Vice

President, Finance, at Boehringer Mannheim Corporation, from 1976 to 1988. Ms. Eastham also serves as a director for Illumina, Inc. and Genoptix, Inc. Ms. Eastham received a B.S. and an M.B.A. from Indiana University and is a Certified Public Accountant and a Certified Director.

Dr. Gavin has served as a director since December 2005 and serves as chair of the Corporate Governance Committee. Dr. Gavin is CEO & Chief Medical Officer, Healing Our Village, Inc. He also serves as Clinical Professor of Medicine, Emory University School of Medicine and Clinical Professor of Medicine at the Indiana University School of Medicine. He was President of the Morehouse School of Medicine from 2002 to 2004. Dr. Gavin is a member of the board of directors of Baxter International Inc., and Anastasia Marie Laboratories, Inc. Dr. Gavin was Chairman of the board of directors of Equidyne Corporation from August 2001 to 2003. From 1991 to 2002, Dr. Gavin was a Senior Scientific Officer of the Howard Hughes Medical Institute. From 2002 until 2005, he served as National Chairman of the National Diabetes Education Program. He received his B.S. in Chemistry at Livingstone College, a Ph.D. in Biochemistry at Emory University and an M.D. at Duke University Medical School. Dr. Gavin has received numerous civic and academic awards and honors.

Ms. Graham has served as a director since November 1995 and currently serves on the Finance Committee. Ms. Graham served as President and Chief Executive Officer from September 2003 until June 2006, serving as Chief Executive Officer from June 2006 until March 2007. Prior to joining us, Ms. Graham held various positions with Guidant Corporation, including Group Chairman; Office of the President; and President of the Vascular Intervention Group and Vice President. Ms. Graham held various positions with Eli Lilly and Company from 1979 to 1992 including sales, finance, marketing and strategic planning positions. She serves on the board of directors of Genomic Health, Inc., Sierra Neuropharmaceuticals, Inc., and ICAT Managers, LLC. She also serves on the American Diabetes Research Foundation Board, the California Council on Science and Technology Board, the Health Sciences Advisory Board for the University of California, San Diego, the Advisory Board for the Kellog Center for Executive Women and the Editorial Advisory Board for the Journal of Life Sciences. Ms. Graham received an M.B.A. from Harvard University.

Mr. Greene is our co-founder and has served as a director since our inception in 1987. He serves on the Finance Committee. Mr. Greene is an entrepreneur who has participated in the founding and/or management of eleven medical technology companies over two decades, including three companies for which he served as chief executive officer. From 1987 to 1996, Mr. Greene served as our Chief Executive Officer. From 1986 until 1993, Mr. Greene was a founding general partner of Biovest Partners, a seed venture capital firm. He was Chief Executive Officer of Hybritech from 1979 until its acquisition by Eli Lilly and Company in 1986, and he was co-inventor of Hybritech's patented monoclonal antibody assay technology. Prior to joining Hybritech, he was an executive with the medical diagnostics division of Baxter Healthcare Corporation from 1974 to 1979 and a consultant with McKinsey & Company from 1967 to 1974. Mr. Greene received an M.B.A. from Harvard University.

Dr. Skyler has served as a director since August 1999 and serves on the Corporate Governance Committee. He is Professor of Medicine, Pediatrics and Psychology, in the Division of Endocrinology Diabetes and Metabolism; and Associate Director for Academic Programs at the Diabetes Research Institute; all at the University of Miami Miller School of Medicine in Florida, where he has been employed since 1976. He is also Study Chairman for the National Institute of Diabetes & Digestive & Kidney Diseases of the Type 1 Diabetes TrialNet clinical trial network, and serves on the board of directors of DexCom, Inc., and various private companies. Dr. Skyler has served as President of the American Diabetes Association and as Vice President of the International Diabetes Federation. Dr. Skyler serves on the editorial board of several diabetes and general medicine journals and the advisory panel of several pharmaceutical companies. He received his B.S. from The Pennsylvania State University, his M.D. from Jefferson Medical College, and completed postdoctoral studies at Duke University Medical Center.

Mr. Sullivan has served as a director since September 2003 and serves on the Audit Committee and as chair of the Finance Committee. Mr. Sullivan is currently Chairman of the Board of Advisors of RAND Health and Chairman of the Board of Advisors of the UCLA Medical Center. From 2000 to 2003, Mr. Sullivan served as Chairman, Chief Executive Officer and a director of Protocare, Inc. From 1993 until November 1999, he served as Chairman, Chief Executive Officer and a director of American Health Properties, Inc. For the previous twenty years, Mr. Sullivan was an investment banker with Goldman Sachs. Mr. Sullivan currently serves on the board of directors of Cymetrix Corporation, HCP, Inc. (NYSE, a real estate investment trust) and AutoGenomics, Inc. Mr. Sullivan received his M.B.A. from the Harvard Graduate School of Business Administration and his J.D. from the University of Minnesota Law School.

Mr. Wilson has served as a director since March 2002 and is our lead independent director. He serves as the chair of the Compensation and Human Resources Committee and on the Corporate Governance Committee. He is a director and Chairman of the Board of both Corcept Therapeutics Inc. and NuGEN, Inc. From 1996 to 2001, Mr. Wilson was Chairman of the Board of Amira Medical, Inc. From 1990 to 1994, Mr. Wilson served as President and Chief Operating Officer of Syntex Corporation. Prior to 1990, he served in various senior management positions, including Chief Executive Officer for Neurex Corporation and LifeScan, Inc. Mr. Wilson received his B.A. and M.B.A. from the University of Arizona.

Mr. Eberhard has served as Vice President, Sales since May 2003. Prior to joining us, Mr. Eberhard was Regional Vice President, Sales, at Pharmacia Corporation, for which he had worked for 21 years. During his career with Pharmacia Corporation and its related pre-merger companies, he held positions in sales, sales management, corporate training, sales operations, and managed care before assuming the Vice President, Sales position. Mr. Eberhard received a B.S. in Biology from California Lutheran University.

Mr. Foletta has served as Senior Vice President, Finance and Chief Financial Officer since March 2006 and he previously served as Vice President, Finance and Chief Financial Officer from March 2000 to March 2006. Mr. Foletta previously served as a Principal of Triton Group Management, Inc. from 1997 to 2000. From 1986 to 1997, Mr. Foletta held a number of management positions with Intermark, Inc. and Triton Group Ltd., the most recent of which was Senior Vice President, Chief Financial Officer and Corporate Secretary. From 1982 to 1986, Mr. Foletta was with Ernst & Young, most recently serving as an Audit Manager. He is a director of Anadys Pharmaceuticals, Inc. Mr. Foletta received a B.A. in Business Economics from the University of California, Santa Barbara. He is a Certified Public Accountant and a member of the Financial Executives Institute.

Mr. Gergen has served as Senior Vice President, Corporate Development since August 2006 and previously served as Vice President of Business Development from May 2005 to August 2006. Prior to joining us, Mr. Gergen was an independent consultant to biotech and medical technology companies for strategy, financing and corporate development. From 2003 to 2005, Mr. Gergen was Executive Vice President at CardioNet, Inc. He held various positions at Advanced Tissue Sciences, Inc. from 2000 to 2003 most recently as Chief Restructuring Officer and Acting CEO. He also served as Senior Vice President, Chief Financial and Development Officer and Vice President, Development, General Counsel and Secretary. From 1999 to 2000, Mr. Gergen was employed at Premier, Inc. and from 1994 to 1999 he held various positions with Medtronic, Inc. From 1990 to 1994 he held various corporate development positions at Jostens, Inc. and from 1986 to 1990, he practiced law at various law firms. Mr. Gergen serves on the Board of Directors of a privately held company. Mr. Gergen received a B.A. in Administration from Minot State University and a J.D. from the University of Minnesota Law School.

Dr. Kolterman has served as Senior Vice President, Research and Development since May 2008 and previously served as Senior Vice President, Clinical and Regulatory Affairs from 2005 to 2008. He

also served as Senior Vice President, Clinical Affairs from February 1997 to August 2005, Vice President, Medical Affairs from 1993 to 1997, and Director, Medical Affairs from 1992 to 1993. From 1983 to 1992, he was Program Director of the General Clinical Research Center and Medical Director of the Diabetes Center, at the University of California, San Diego Medical Center. Since 1989, he has been Adjunct Professor of Medicine at the University of California, San Diego. From 1978 to 1983, he was Assistant Professor of Medicine in the Endocrinology and Metabolism Division at the University of Colorado School of Medicine, Denver. He was a member of the Diabetes Control and Complications Trial Study Group and presently serves as a member of the Epidemiology of Diabetes Intervention and Complications Study. He is also a past-president of the California Affiliate of the American Diabetes Association. Dr. Kolterman received his M.D. from Stanford University School of Medicine.

Ms. Lloyd has served as our Senior Vice President, Legal and Corporate Affairs, and General Counsel since February 2007. Prior to joining us, Ms. Lloyd served as Group Senior Vice President, Chief Administrative Officer, General Counsel and Secretary of VHA Inc. from November 2004 to February 2007. Previously, she served as VHA's General Counsel and Secretary from May 1999 to November 2004. From 1993 to April 1999, Ms. Lloyd was Vice President and Assistant General Counsel of Medtronic, Inc. and served as Medtronic's Assistant General Counsel from 1991 to 1993. From 1978 to 1991, Ms. Lloyd held various legal positions with Medtronic. Prior to joining Medtronic, Ms. Lloyd served as counsel to Pillsbury Company and Montgomery Ward & Co. and she taught Business Law at the University of Minnesota Business School. Ms. Lloyd is a member of the board of the California Healthcare Institute and is an associate of the Women Business Leaders of the United States Health Care Industry Foundation. She received a B.S./B.A. from Knox College and a J.D. from Northwestern University.

Mr. Marchetti has served as our Senior Vice President, Human Resources and Information Management since July 2007 and previously served as Senior Vice President, Human Resources and Corporate Services from November 2005 to July 2007. Prior to joining us, he served as Vice President, Human Resources for Guidant Corporation from July 2002 to October 2005. Prior to this role, he served as Vice President, Finance and Information Systems, Guidant Europe, Middle East, Africa, and Canada, since the beginning of 2001. From 1999 through 2000, he served as Vice President, Human Resources for Guidant's Vascular Intervention group, and served as Guidant's Corporate Controller and Chief Accounting Officer from 1994 to 1999. He joined Eli Lilly and Company's Medical Devices and Diagnostics division in 1988. In 1992, he became Financial Manager of Lilly's pharmaceutical manufacturing operations in Indianapolis. From 1980 to 1986, he was with Touche Ross & Co. (currently Deloitte). He received a B.S. from LaSalle University in Philadelphia and an M.B.A. from the Ross School of Business at the University of Michigan. He is a Certified Public Accountant.

Mr. Marshall has served as Senior Vice President, Operations since December 2008. He previously served as Vice President Operations from December 2006 to December 2008. Prior to joining us, he was Vice President of Corporate Manufacturing at Amgen, Inc. From 2002 to 2005, Mr. Marshall served as President of Manufacturing at Recombinant Proteins at the Bioscience Division of Baxter International. From 1999 to 2002, he was Site Head of the Baxter International Thousand Oaks facility. He joined Creative BioMolecules in 1992, first as Head of Process Development and Clinical Manufacturing and then as Head of Operations. From 1988 to 1992, Mr. Marshall held various management positions with Welgen Manufacturing Partnership (now Amgen, Rhode Island), Repligen Corporation and Damon Biotech. Mr. Marshall received a B.S. and an M.S. in Biology from the University of Massachusetts at Dartmouth and completed three years of post-graduate work concentrating in hematology and coagulation research at Brown University.

Mr. Mihalik has served as Senior Vice President, Sales and Marketing and Chief Commercial Officer since January 2009. Before joining us, Mr. Mihalik served as Vice President of Global Brand Development Diabetes and Endocrine Platform Team Leader for Lilly since 2004. Previously, he was Business Unit Head of Diabetes Care for Lilly U.S. from 2001 to 2004. From 1990 to 2001 he served in

various senior management positions at other healthcare companies including Roche Diagnostics Corporation, Boehringer Mannheim Group and Baxter Healthcare Inc. He has a B.S. degree in Biology from Pennsylvania State University and completed the Northwestern University Masters in Management-Executive Program.

Mr. Rowland has served as our Vice President, Governance and Compliance, Secretary, and Chief Compliance Officer since February 2007. He previously served as our Vice President, Legal, Secretary and General Counsel from September 2001 to February 2007. Prior to joining us, Mr. Rowland served in various positions at Alliance Pharmaceutical Corp., including as Vice President, General Counsel and Secretary, beginning in 1993. Earlier, Mr. Rowland served as Vice President and Senior Counsel, Finance and Securities, at Imperial Savings Association for four years. For the previous eight years, he was engaged in the private practice of corporate law with the San Diego, California law firm of Gray, Cary, Ames & Fry, and the Houston, Texas law firm of Bracewell & Patterson. He received a J.D. from Emory University.

Item 1A. ***Risk Factors***

CAUTIONARY FACTORS THAT MAY AFFECT FUTURE RESULTS

Except for the historical information contained herein or incorporated by reference, this annual report on Form 10-K and the information incorporated by reference contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results may differ materially from those discussed here. Factors that could cause or contribute to differences in our actual results include those discussed in the following section, as well as those discussed in Part II, Item 7 entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this annual report on Form 10-K and in any other documents incorporated by reference into this report. You should consider carefully the following risk factors, together with all of the other information included or incorporated in this annual report on Form 10-K. Each of these risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock. There may be additional risks that we do not presently know of or that we currently believe are immaterial which could also impair our business and financial position.

We have a history of operating losses, anticipate future losses and may never become profitable.

We have experienced significant operating losses since our inception in 1987, including losses of $315.4 million in 2008, $211.1 million in 2007 and $218.9 million in 2006. As of December 31, 2008, we had an accumulated deficit of approximately $1.7 billion. The extent of our future losses and the timing of potential profitability are uncertain, and we may never achieve profitable operations. We have been engaged in discovering and developing drugs since inception, which has required, and will continue to require, significant research and development expenditures. We derived substantially all of our revenues prior to 2005 from development funding, fees and milestone payments under collaborative agreements and from interest income. BYETTA and SYMLIN may not be as commercially successful as we expect and we may not succeed in commercializing any of our other drug candidates. We may incur substantial operating losses for at least the next few years. These losses, among other things, have had and will have an adverse effect on our stockholders' equity and working capital. Even if we become profitable, we may not remain profitable.

We began selling, marketing and distributing our first products, BYETTA and SYMLIN, in 2005 and we will depend heavily on the success of those products in the marketplace.

Prior to the launch of BYETTA and SYMLIN in 2005, we had never sold or marketed our own products. Our ability to generate product revenue for the next few years will depend solely on the success of these products. The ability of BYETTA and SYMLIN to generate revenue at the levels we expect will depend on many factors, including the following:

- the ability of patients in the current uncertain economic climate to be able to afford our medications or obtain health care coverage that covers our products;
- acceptance of and ongoing satisfaction with these first-in-class medicines in the United States and foreign markets by the medical community, patients receiving therapy and third party payers;
- a satisfactory efficacy and safety profile as demonstrated in a broad patient population;
- successfully expanding and sustaining manufacturing capacity to meet demand;
- safety concerns in the marketplace for diabetes therapies;
- the competitive landscape for approved and developing therapies that will compete with the products; and
- our ability to expand the indications for which we can market the products.

If we encounter safety issues with BYETTA or SYMLIN or any other drugs we market or fail to comply with extensive continuing regulations enforced by domestic and foreign regulatory authorities, it could cause us to discontinue marketing those drugs, reduce our revenues and harm our ability to generate future revenues, which would negatively impact our financial position.

BYETTA and SYMLIN, in addition to any other of our drug candidates that may be approved by the FDA, will be subject to continual review by the FDA, and we cannot assure you that newly discovered or developed safety issues will not arise. With the use of any of our marketed drugs by a wide patient population, serious adverse events may occur from time to time that initially do not appear to relate to the drug itself, and only if the specific event occurs with some regularity over a period of time does the drug become suspect as having a causal relationship to the adverse event. Some patients taking BYETTA have reported developing pancreatitis. We are working to better understand the relationship between BYETTA and pancreatitis described in some spontaneously reported cases. In keeping with our focus on patient safety, we continue to pursue our drug safety program that includes thorough investigation of individual spontaneous case reports along with clinical and epidemiologic studies. Within the detection limits of an initial epidemiology study which we provided to the FDA, we have not observed an increased incidence of pancreatitis associated with BYETTA compared to other treatments for diabetes and thus believe a definite causal relationship between BYETTA and pancreatitis has not been proved. Any safety issues could cause us to suspend or cease marketing of our approved products, cause us to modify how we market our approved products, subject us to substantial liabilities, and adversely affect our revenues and financial condition.

Moreover, the marketing of our approved products will be subject to extensive regulatory requirements administered by the FDA and other regulatory bodies, including adverse event reporting requirements and the FDA's general prohibition against promoting products for unapproved uses. The manufacturing facilities for our approved products are also subject to continual review and periodic inspection and approval of manufacturing modifications. Manufacturing facilities that manufacture drug products for the United States market, whether they are located inside or outside the United States, are subject to biennial inspections by the FDA and must comply with the FDA's current good manufacturing practice, or cGMP, regulations. The FDA stringently applies regulatory standards for manufacturing. Failure to comply with any of these post-approval requirements can, among other

things, result in warning letters, product seizures, recalls, fines, injunctions, suspensions or revocations of marketing licenses, operating restrictions and criminal prosecutions. Any of these enforcement actions, any unanticipated changes in existing regulatory requirements or the adoption of new requirements, or any safety issues that arise with any approved products, could adversely affect our ability to market products and generate revenues and thus adversely affect our ability to continue our business.

The manufacturers of our products and drug candidates also are subject to numerous federal, state, local and foreign laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and hazardous substance disposal. In the future, our manufacturers may incur significant costs to comply with those laws and regulations, which could increase our manufacturing costs and reduce our ability to operate profitably.

We currently do not manufacture our own drug products or some of our drug candidates and may not be able to obtain adequate supplies, which could cause delays, subject us to product shortages, or reduce product sales.

The manufacturing of sufficient quantities of newly-approved drug products and drug candidates is a time-consuming and complex process. We currently have no manufacturing capabilities. In order to successfully commercialize our products, including BYETTA and SYMLIN, and continue to develop our drug candidates, including exenatide once weekly, we rely on various third parties to provide the necessary manufacturing.

There are a limited number of manufacturers that operate under the FDA's cGMP regulations capable of manufacturing for us. In addition, there are a limited number of bulk drug substance suppliers, cartridge manufacturers and disposable pen manufacturers. If we are not able to arrange for and maintain third-party manufacturing on commercially reasonable terms, or we lose one of our sole source suppliers used for our existing products or for some components of our manufacturing processes for our products or drug candidates, we may not be able to market our products or complete development of our drug candidates on a timely basis, if at all.

Reliance on third-party suppliers limits our ability to control certain aspects of the manufacturing process and therefore exposes us to a variety of significant risks, including, but not limited to, risks to our ability to commercialize our products or conduct clinical trials, risks of reliance on the third-party for regulatory compliance and quality assurance, third-party refusal to supply on a long-term basis, or at all, the possibility of breach of the manufacturing agreement by the third-party and the possibility of termination or non-renewal of the agreement by the third-party, based on its business priorities, at a time that is costly or inconvenient for us. In addition, reliance on single-source suppliers subjects us to the risk of price increases by these suppliers which could negatively impact our operating margins. If any of these risks occur, our product supply will be interrupted resulting in lost or delayed revenues and delayed clinical trials. Our reliance on third-party manufacturers for the production of our two commercial products is described in more detail below.

We rely on Bachem and Mallinckrodt to manufacture our long-term commercial supply of bulk exenatide, the active ingredient in BYETTA. In addition, we rely on single-source manufacturers for some of our raw materials used by Bachem and Mallinckrodt to produce bulk exenatide. We also rely on Wockhardt and Baxter to manufacture the dosage form of BYETTA in cartridges. We are further dependent upon Lilly to supply pens for delivery of BYETTA in cartridges.

We rely on Bachem and Lonza to manufacture our commercial supply of bulk pramlintide acetate, the active ingredient contained in SYMLIN. In addition, we rely on Baxter to manufacture the dosage form of SYMLIN in vials. We recently received FDA approval of a disposable pen for the delivery of SYMLIN in cartridges. We rely on Wockhardt for the dosage form of SYMLIN in cartridges and Ypsomed AG to manufacture the components for the SYMLIN disposable pen. We also rely on Hollister-Stier Laboratories LLC for the assembly of the SYMLIN pen.

If any of our existing or future manufacturers cease to manufacture or are otherwise unable to timely deliver sufficient quantities of BYETTA or SYMLIN, in either bulk or dosage form, or other product components, including pens for the delivery of these products, it could disrupt our ability to market our products, subject us to product shortages, reduce product sales and/or reduce our profit margins. Any delay or disruption in the manufacturing of bulk product, the dosage form of our products or other product components, including pens for delivery of our products, could also harm our reputation in the medical and patient communities. In addition, we may need to engage additional manufacturers so that we will be able to continue our commercialization and development efforts for these products or drug candidates. The cost and time to establish these new manufacturing facilities would be substantial.

Our manufacturers have produced BYETTA and SYMLIN for commercial use for approximately four years, however, unforeseeable risks related to environmental, economic, technical or other issues may be encountered as we, together with our manufacturers, continue to develop familiarity and experience with regard to manufacturing our products. Furthermore, we and the other manufacturers used for our drug candidates may not be able to produce supplies in commercial quantities if our drug candidates are approved. While we believe that business relations between us and our manufacturers are generally good, we cannot predict whether any of the manufacturers that we may use will meet our requirements for quality, quantity or timeliness for the manufacture of bulk exenatide or pramlintide acetate, dosage form of BYETTA or SYMLIN, or pens. Therefore, we may not be able to obtain necessary supplies of products with acceptable quality, on acceptable terms or in sufficient quantities, if at all. Our dependence on third parties for the manufacture of products may also reduce our gross profit margins and our ability to develop and deliver products in a timely manner.

In order to manufacture exenatide once weekly on a commercial scale, if it is approved by the FDA, we must complete construction of and commission a new facility and validate the manufacturing process. We are dependent on Alkermes and Parsons to assist us in the construction and commissioning of the manufacturing facility. We have never established, validated, and operated a manufacturing facility and cannot assure you that we will be able to successfully establish or operate such a facility in a timely or economical manner, or at all. In addition, we are dependent on Alkermes to successfully develop and transfer to us its technology for manufacturing exenatide once weekly and to supply us with commercial quantities of the polymer required to manufacture exenatide once weekly. We also will need to obtain sufficient supplies of diluents, solvents, devices, packaging and other components necessary for commercial manufacture of exenatide once weekly. Although we are working diligently to qualify the commercial-scale manufacturing process at this facility, we cannot be assured that we will be able to demonstrate comparability of product manufactured at development scale and product manufactured at commercial scale. If we are unable to demonstrate comparability of product, we may not be able to commercially launch exenatide once weekly in a timely manner or at all.

Our ability to generate revenues will be diminished if we fail to obtain acceptable prices or an adequate level of reimbursement for our products from third-party payers.

The continuing efforts of government, private health insurers and other third-party payers to contain or reduce the costs of health care through various means, including efforts to increase the amount of patient co-pay obligations, may limit our commercial opportunity. In the United States, we expect that there will continue to be a number of federal and state proposals to implement government control over the pricing of prescription pharmaceuticals. In addition, increasing emphasis on managed care in the United States will continue to put pressure on the rate of adoption and pricing of pharmaceutical products.

Significant uncertainty exists as to the reimbursement status of health care products. Third-party payers, including Medicare, are challenging the prices charged for medical products and services. Government and other third-party payers increasingly are attempting to contain health care costs by

limiting both coverage and the level of reimbursement for new drugs and by refusing to provide coverage for uses of approved products for disease indications for which the FDA has not granted labeling approval. Third-party insurance coverage may not be available to patients for BYETTA and/or SYMLIN or any other products we discover and develop. If government and other third-party payers do not provide adequate coverage and reimbursement levels for our products, the market acceptance of these products may be reduced.

Competition in the biotechnology and pharmaceutical industries may result in competing products, superior marketing of other products and lower revenues or profits for us.

There are many companies that are seeking to develop products and therapies for the treatment of diabetes and other metabolic disorders. Our competitors include multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. A number of our largest competitors, including AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Lilly, Merck & Co., Novartis, Novo Nordisk, Pfizer, Sanofi-Aventis and Takeda Pharmaceuticals, are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting, and it is possible that the number of companies seeking to develop products and therapies for the treatment of diabetes, obesity and other metabolic disorders will increase. Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. In addition, many of these competitors have significantly greater experience than we do in undertaking preclinical testing and human clinical studies of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA approval for superior products. Furthermore, now that we have received FDA approval for BYETTA and SYMLIN, we may also be competing against other companies with respect to our manufacturing and product distribution efficiency and sales and marketing capabilities, areas in which we have limited or no experience as an organization.

Our target patient population for BYETTA includes people with diabetes who have not achieved adequate glycemic control using metformin, sulfonylurea and/or a TZD, three common oral therapies for type 2 diabetes. Our target population for SYMLIN is people with either type 2 or type 1 diabetes whose therapy includes multiple mealtime insulin injections daily. Other products are currently in development or exist in the market that may compete directly with the products that we are developing or marketing. Various other products are available or in development to treat type 2 diabetes, including:

- sulfonylureas;
- metformin;
- insulins, including injectable and inhaled versions;
- TZDs;
- glinides;
- DPP-IV inhibitors;
- incretin/GLP-1 agonists;
- PPARs; and
- alpha-glucosidase inhibitors.

In addition, several companies are developing various approaches, including alternative delivery methods, to improve treatments for type 1 and type 2 diabetes. We cannot predict whether our products will have sufficient advantages to cause health care professionals to adopt them over other products or that our products will offer an economically feasible alternative to other products. Our products could become obsolete before we recover expenses incurred in developing these products.

Delays in the conduct or completion of our clinical trials, the analysis of the data from our clinical trials or our manufacturing scale-up activities may result in delays in our planned filings for regulatory approvals, and may adversely affect our ability to enter into new collaborative arrangements.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical studies that will cause us to delay or suspend our ongoing and planned clinical studies, delay the analysis of data from our completed or ongoing clinical studies or perform additional clinical studies prior to receiving necessary regulatory approvals. We also cannot predict whether we will encounter delays or an inability to create manufacturing processes for drug candidates that allow us to produce drug product in sufficient quantities to be economical, otherwise known as manufacturing scale-up.

If the results of our ongoing or planned clinical studies for our drug candidates are not available when we expect or if we encounter any delay in the analysis of data from our clinical studies or if we encounter delays in our ability to scale-up our manufacturing processes:

- we may be unable to complete our development programs for exenatide once weekly or our obesity clinical trials;
- we may have to delay or terminate our planned filings for regulatory approval;
- we may not have the financial resources to continue research and development of any of our drug candidates; and
- we may not be able to enter into, if we chose to do so, any additional collaborative arrangements.

In addition, Lilly can terminate our collaboration for the development and commercialization of BYETTA and sustained-release formulations of exenatide at any time on six months' notice.

Any of the following could delay the completion of our ongoing and planned clinical studies:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in enrolling volunteers;
- lower than anticipated retention rate of volunteers in a clinical trial;
- negative results of clinical studies;
- insufficient supply or deficient quality of drug candidate materials or other materials necessary for the performance of clinical trials;
- our inability to reach agreement with Lilly regarding the scope, design, conduct or costs of clinical trials with respect to BYETTA, exenatide once weekly or nasal exenatide; or
- serious side effects experienced by study participants relating to a drug candidate.

We are substantially dependent on our collaboration with Lilly for the development and commercialization of BYETTA and dependent on Lilly and Alkermes for the development of exenatide once weekly.

We have entered into a collaborative arrangement with Lilly, who currently markets diabetes therapies and is developing additional diabetes drug candidates, to commercialize BYETTA and further develop sustained-release formulations of BYETTA, including exenatide once weekly. We entered into this collaboration in order to:

- fund some of our research and development activities;
- assist us in seeking and obtaining regulatory approvals; and

- assist us in the successful commercialization of BYETTA and exenatide once weekly.

In general, we cannot control the amount and timing of resources that Lilly may devote to our collaboration. If Lilly fails to assist in the further development of exenatide once weekly or the commercialization of BYETTA, or if Lilly's efforts are not effective, our business may be negatively affected. We are relying on Lilly to obtain regulatory approvals for and successfully commercialize BYETTA and exenatide once weekly outside the United States. Our collaboration with Lilly may not continue or result in additional successfully commercialized drugs. Lilly can terminate our collaboration at any time upon six months' notice. If Lilly ceased funding and/or developing and commercializing BYETTA or exenatide once weekly, we would have to seek additional sources for funding and may have to delay, reduce or eliminate one or more of our commercialization and development programs for these compounds. If Lilly does not successfully commercialize BYETTA outside the United States we may receive limited or no revenues from them. In addition, we are dependent on Alkermes to successfully develop and transfer to us its technology for manufacturing exenatide once weekly. If Alkermes' technology is not successfully developed to effectively deliver exenatide in a sustained release formulation, or Alkermes does not devote sufficient resources to the collaboration, our efforts to develop sustained release formulations of exenatide could be delayed or curtailed.

If our patents are determined to be unenforceable or if we are unable to obtain new patents based on current patent applications or for future inventions, we may not be able to prevent others from using our intellectual property. If we are unable to obtain licenses to third party patent rights for required technologies, we could be adversely affected.

We own or hold exclusive rights to many issued United States patents and pending United States patent applications related to the development and commercialization of exenatide, including BYETTA and exenatide once weekly, SYMLIN and our other drug candidates. These patents and applications cover composition-of-matter, medical indications, methods of use, formulations and other inventive results. We have issued and pending applications for formulations of BYETTA and exenatide once weekly, but we do not have a composition-of-matter patent covering exenatide. We also own or hold exclusive rights to various foreign patent applications that correspond to issued United States patents or pending United States patent applications.

Our success will depend in part on our ability to obtain patent protection for our products and drug candidates and technologies both in the United States and other countries. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Alternatively, a third party may successfully challenge or circumvent our patents. Our rights under any issued patents may not provide us with sufficient protection against competitive products or otherwise cover commercially valuable products or processes. For example, our SYMLIN and BYETTA products are subject to the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the "Hatch-Waxman Act," which provides data exclusivity for a certain period of time. Once this exclusivity period expires, the Hatch-Waxman Act allows generic manufacturers to file Abbreviated New Drug Applications, or ANDAs, with the FDA requesting approval of generic versions of previously-approved products. For example, a generic pharmaceutical manufacturer could file an ANDA for SYMLIN as early as March 2009 and for BYETTA as early as April 2009. If an ANDA is filed for one of our approved products prior to expiration of the patents covering those products, it could result in our initiating patent infringement litigation to enforce our rights. We can provide no assurances that we would prevail in such an action or in any challenge related to our patent rights.

In addition, because patent applications in the United States are maintained, in general, in secrecy for 18 months after the filing of the applications, and publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we cannot be sure that the inventors of subject matter covered by our patents and patent applications were the first to invent or the first to file patent applications for these inventions. Third parties have filed, and in the future are likely to file, patent

applications on inventions similar to ours. From time-to-time we have participated in, and in the future are likely to participate in, interference proceedings declared by the United States Patent and Trademark Office to determine priority of invention, which could result in a loss of our patent position. We have also participated in, and in the future are likely to participate in, opposition proceedings against our patents in other jurisdictions, such as Europe and Australia. Furthermore, we may not have identified all United States and foreign patents that pose a risk of infringement.

We also rely upon licensing opportunities for some of our technologies. We cannot be certain that we will not lose our rights to certain patented technologies under existing licenses or that we will be able to obtain a license to any required third-party technology. If we lose our licensed technology rights or if we are not able to obtain a required license, we could be adversely affected.

We may be unable to obtain regulatory clearance to market our drug candidates in the United States or foreign countries on a timely basis, or at all.

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. The process of obtaining FDA and other regulatory approvals is costly, time-consuming, uncertain and subject to unanticipated delays. Regulatory authorities may refuse to approve an application for approval of a drug candidate if they believe that applicable regulatory criteria are not satisfied. Regulatory authorities may also require additional testing for safety and efficacy. Moreover, if the FDA grants regulatory approval of a product, the approval may be limited to specific indications or limited with respect to its distribution, and expanded or additional indications for approved drugs may not be approved, which could limit our revenues. Foreign regulatory authorities may apply similar limitations or may refuse to grant any approval. Unexpected changes to the FDA or foreign regulatory approval process could also delay or prevent the approval of our drug candidates.

The data collected from our clinical trials may not be sufficient to support approval of our drug candidates or additional or expanded indications by the FDA or any foreign regulatory authorities. Biotechnology stock prices have declined significantly in certain instances where companies have failed to meet expectations with respect to FDA approval or the timing for FDA approval. If the FDA's or any foreign regulatory authority's response is delayed or not favorable for any of our drug candidates, our stock price could decline significantly.

Moreover, manufacturing facilities operated by us or by the third-party manufacturers with whom we may contract to manufacture our unapproved drug candidates may not pass an FDA or other regulatory authority preapproval inspection. Any failure or delay in obtaining these approvals could prohibit or delay us or any of our business partners from marketing these drug candidates.

Consequently, even if we believe that preclinical and clinical data are sufficient to support regulatory approval for our drug candidates, the FDA and foreign regulatory authorities may not ultimately approve our drug candidates for commercial sale in any jurisdiction. If our drug candidates are not approved, our ability to generate revenues may be limited and our business will be adversely affected.

Litigation regarding patents and other proprietary rights may be expensive, cause delays in bringing products to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties and preventing others from infringing our patents. Challenges by pharmaceutical companies against the patents of competitors are common. Legal standards relating to the validity of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents are still developing. As a result, our ability to obtain and enforce patents is uncertain and involves complex legal and factual questions. Third parties may challenge, in courts or through patent

office proceedings, or infringe upon, existing or future patents. In the event that a third party challenges a patent, a court or patent office may invalidate the patent or determine that the patent is not enforceable. Proceedings involving our patents or patent applications or those of others could result in adverse decisions about:

- the patentability of our inventions, products and drug candidates; and/or
- the enforceability, validity or scope of protection offered by our patents.

The manufacture, use or sale of any of our products or drug candidates may infringe on the patent rights of others. If we are unable to avoid infringement of the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to successfully defend an infringement action or have infringing patents declared invalid, we may:

- incur substantial monetary damages;
- encounter significant delays in bringing our drug candidates to market; and/or
- be precluded from participating in the manufacture, use or sale of our products or drug candidates or methods of treatment requiring licenses.

We are subject to "fraud and abuse" and similar laws and regulations, and a failure to comply with such regulations or prevail in any litigation related to noncompliance could harm our business.

Upon approval of BYETTA and SYMLIN by the FDA, we became subject to various health care "fraud and abuse" laws, such as the Federal False Claims Act, the federal anti-kickback statute and other state and federal laws and regulations. Pharmaceutical companies have faced lawsuits and investigations pertaining to violations of these laws and regulations. We cannot guarantee that measures that we have taken to prevent such violations, including our corporate compliance program, will protect us from future violations, lawsuits or investigations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our financial results will fluctuate, and these fluctuations may cause our stock price to fall.

Forecasting future revenues is difficult, especially since we launched our first products in 2005 and the level of market acceptance of these products may change rapidly. In addition, our customer base is highly concentrated with four customers accounting for most of our net product sales. Fluctuations in the buying patterns of these customers, which may result from seasonality, wholesaler buying decisions or other factors outside of our control, could significantly affect the level of our net sales on a period to period basis. As a result, it is reasonably likely that our financial results will fluctuate to an extent that may not meet with market expectations and that also may adversely affect our stock price. There are a number of other factors that could cause our financial results to fluctuate unexpectedly, including:

- product sales;
- cost of product sales;
- achievement and timing of research and development milestones;
- collaboration revenues;
- cost and timing of clinical trials, regulatory approvals and product launches;
- marketing and other expenses;

- manufacturing or supply issues; and
- potential acquisitions of businesses and technologies and our ability to successfully integrate any such acquisitions into our existing business.

We may require additional financing in the future, which may not be available to us on favorable terms, or at all.

We intend to use our available cash for:

- Commercialization of BYETTA and SYMLIN;
- Establishment of additional manufacturing sources, including our Ohio manufacturing facility;
- Development of exenatide once weekly and other pipeline candidates;
- Executing our INTO strategy;
- Our other research and development activities;
- Other operating expenses;
- Potential acquisitions or investments in complementary technologies or businesses; and
- Other general corporate purposes.

We may also be required to use our cash to pay principal and interest on outstanding debt, including a $125 million term loan due in 2010, referred to as the Term Loan, and $775 million in outstanding principal amount of convertible senior notes, of which $200 million is due in 2011, referred to as the 2004 Notes and $575 million is due in 2014, referred to as the 2007 Notes.

If we require additional financing in the future, we cannot assure you that it will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through our debt and equity securities offerings, there can be no assurance that we will be able to so in the future, especially given the current adverse economic and credit conditions.

Our investments in marketable debt securities are subject to credit and market risks that may adversely affect their fair value.

We maintain a portfolio of investments in marketable debt securities which are recorded at fair value. Although we have established investment guidelines relative to diversification and maturity with the objective of maintaining safety of principal and liquidity, credit rating agencies may reduce the credit quality of our individual holdings which could adversely affect their value. Lower credit quality and other market events, such as increases in interest rates, and further deterioration in the credit markets may have an adverse effect on the fair value of our investment holdings and cash position.

Our business has a substantial risk of product liability claims, and insurance may not be adequate to cover these claims.

Our business exposes us to potential product liability risks that are inherent in the testing, manufacturing and marketing of human therapeutic products. For example, we are currently involved in seven product liability cases, four of which have been stayed pending the U.S. Supreme Court's decision on federal preemption of such cases in *Wyeth v. Levine.* We have also been notified of additional claimants who may file product liability complaints. Product liability claims could result in the imposition of substantial defense costs and liability on us, a recall of products, or a change in the indications for which they may be used. We currently have limited product liability insurance coverage. We cannot assure you that our insurance will provide adequate coverage against potential liabilities.

Our ability to enter into and maintain third-party relationships is important to our successful development and commercialization of BYETTA, SYMLIN and our other drug candidates and to our potential profitability.

With respect to sales, marketing and distribution outside the United States, we will be substantially dependent on Lilly for activities relating to BYETTA and sustained-release formulations of BYETTA, including exenatide once weekly. We believe that we will likely need to enter into marketing and distribution arrangements with third parties for, or find a corporate partner who can provide support for, the development and commercialization of SYMLIN or our other drug candidates outside the United States. We may also enter into arrangements with third parties for the commercialization of SYMLIN or any of our other drug candidates within the United States.

With respect to BYETTA and, if approved, exenatide once weekly, Lilly is co-promoting within the United States. If Lilly ceased commercializing BYETTA or, if approved, exenatide once weekly, for any reason, we would likely need to either enter into a marketing and distribution arrangement with a third party for those products or significantly increase our internal sales and commercialization infrastructure.

We may not be able to enter into marketing and distribution arrangements or find a corporate partner for SYMLIN or our other drug candidates as we deem necessary. If we are not able to enter into a marketing or distribution arrangement or find a corporate partner who can provide support for commercialization of our drug candidates as we deem necessary, we may not be able to successfully perform these marketing or distribution activities. Moreover, any new marketer or distributor or corporate partner for our drug candidates, including Lilly, with whom we choose to contract may not establish adequate sales and distribution capabilities or gain market acceptance for our products, if any.

We have a significant amount of indebtedness. We may not be able to make payments on our indebtedness, and we may incur additional indebtedness in the future, which could adversely affect our operations.

In April 2004, we issued $200 million of the 2004 Notes and in June 2007, we issued $575 million of the 2007 Notes. In December 2007, we entered into the $125 million Term Loan due in December 2010. Our ability to make payments on our debt, including the 2004 and 2007 Notes and the Term Loan, will depend on our future operating performance and ability to generate cash and may also depend on our ability to obtain additional debt or equity financing. During each of the last five years, our operating cash flows were negative and insufficient to cover our fixed charges. We may need to use our cash to pay principal and interest on our debt, thereby reducing the funds available to fund our research and development programs, strategic initiatives and working capital requirements. Our ability to generate sufficient operating cash flow to service our indebtedness, including the 2004 and 2007 Notes and the Term Loan, and fund our operating requirements will depend on our ability, alone or with others, to successfully develop, manufacture, obtain required regulatory approvals for and market our drug candidates, as well as other factors, including general economic, financial, competitive, legislative and regulatory conditions, some of which are beyond our control. Our debt service obligations increase our vulnerabilities to competitive pressures, because many of our competitors are less leveraged than we are. If we are unable to generate sufficient operating cash flow to service our indebtedness and fund our operating requirements, we may be forced to reduce or defer our development programs, sell assets or seek additional debt or equity financing, which may not be available to us on satisfactory terms or at all. Our level of indebtedness may make us more vulnerable to economic or industry downturns. If we incur new indebtedness, the risks relating to our business and our ability to service our indebtedness will intensify.

We may be required to redeem our convertible senior notes upon a designated event or repay the Term Loan upon an event of default.

Holders of the 2004 and 2007 Notes may require us to redeem all or any portion of their notes upon the occurrence of certain designated events which generally involve a change in control of our company. The lenders under the Term Loan may require us to repay outstanding principal and accrued interest due under the Term Loan upon the occurrence of an event of default, which could include, among other things, nonpayment of principle and interest, violation of covenants and a change in control. We recently received notices from each of Icahn Partners LP and certain of its affiliates (the "Icahn Group") and Eastbourne Capital Management, L.L.C. ("Eastbourne") and certain of its affiliates, announcing their intent to each nominate five individuals for election to our Board of Directors at the 2009 annual meeting and, in the case of the Icahn Group, to submit a proposal for shareholder approval requesting that we reincorporate in the state of North Dakota. If as a result of this potential proxy contest a majority of our Board of Directors ceases to be composed of the existing directors or other individuals approved by a majority of the existing directors, then a "change of control" under the Term Loan and a "fundamental change" under the indenture for 2007 Notes will be triggered. If triggered, the lenders under the Term Loan may terminate their commitments and accelerate our outstanding debt and the holders of our 2007 Notes may require us to repurchase the notes. We may not have the liquidity or financial resources to do so at the times required or at all.

We may not have sufficient cash funds to redeem the notes upon a designated event or repay the Term Loan upon an event of default. We may elect, subject to certain conditions, to pay the redemption price for the 2004 Notes in our common stock or a combination of cash and our common stock. We may be unable to satisfy the requisite conditions to enable us to pay some or all of the redemption price for the 2004 Notes in our common stock. If we are prohibited from redeeming the 2004 or 2007 Notes, we could seek consent from our lenders to redeem the 2004 or 2007 notes. If we are unable to obtain their consent, we could attempt to refinance the 2004 or 2007 Notes. If we were unable to obtain a consent or refinance, we would be prohibited from redeeming the 2004 or 2007 Notes. If we were unable to redeem the 2004 or 2007 Notes upon a designated event, it would result in an event of default under the indentures governing the 2004 or 2007 Notes. An event of default under the indentures could result in a further event of default under our other then-existing debt, including the Term Loan. In addition, the occurrence of a designated event may be an event of default under our other debt. Further, an event of default under the Term Loan could result in an event of default under the indentures governing the 2004 or 2007 Notes.

If our research and development programs fail to result in additional drug candidates, the growth of our business could be impaired.

Certain of our research and development programs for drug candidates are at an early stage and will require significant research, development, preclinical and clinical testing, manufacturing scale-up activities, regulatory approval and/or commitments of resources before commercialization. We cannot predict whether our research will lead to the discovery of any additional drug candidates that could generate additional revenues for us.

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

We are highly dependent on our chief executive officer, and the other principal members of our executive and scientific teams. The unexpected loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives. Recruiting and retaining qualified sales, marketing, regulatory, scientific and other personnel and consultants will also be critical to our success. We may not be able to attract and retain these personnel and consultants on

acceptable terms given the competition between numerous pharmaceutical and biotechnology companies. We do not maintain "key person" insurance on any of our employees.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our corporate partners, employees, consultants, manufacturers, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information.

Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Our research and development activities and planned manufacturing activities involve the use of hazardous materials, which subject us to regulation, related costs and delays and potential liabilities.

Our research and development and our planned manufacturing activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our research and development safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. In addition, as part of the development of our planned manufacturing activities, we will need to develop additional safety procedures for the handling and disposing of hazardous materials. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of these laws or regulations.

We are exposed to potential risks from legislation requiring companies to evaluate internal control over financial reporting.

The Sarbanes-Oxley Act requires that we report annually on the effectiveness of our internal control over financial reporting. Among other things, we must perform systems and processes evaluation and testing. We must also conduct an assessment of our internal control to allow management to report on, and our independent registered public accounting firm to attest to, our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. In connection with our Section 404 compliance efforts, we have incurred or expended, and expect to continue to incur or expend, substantial accounting and other expenses and significant management time and resources. We have implemented certain remediation activities resulting from our ongoing assessment of internal control over financial reporting. Our future assessment, or the future assessments by our independent registered public accounting firm, may reveal material weaknesses in our internal control. If material weaknesses are identified in the future we would be required to conclude that our internal control over financial reporting are ineffective and we could be subject to sanctions or investigations by the SEC, the NASDAQ Stock Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our common stock.

We have implemented anti-takeover provisions that could discourage or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and as a result our management may become entrenched and hard to replace.

Provisions in our certificate of incorporation and bylaws could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions include:

- allowing our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors;
- allowing our board of directors to issue, without stockholder approval, up to 5.5 million shares of preferred stock with terms set by the board of directors;
- limiting the ability of holders of our outstanding common stock to call a special meeting of our stockholders; and
- preventing stockholders from taking actions by written consent and requiring all stockholder actions to be taken at a meeting of our stockholders.

Each of these provisions, as well as selected provisions of Delaware law, could discourage potential takeover attempts, could adversely affect the trading price of our securities and could cause our management to become entrenched and hard to replace. In addition to provisions in our charter documents and under Delaware law, an acquisition of our company could be made more difficult by our employee benefits plans and our employee change in control severance plan, under which, in connection with a change in control and termination of employment, stock options held by our employees may become vested and our officers may receive severance benefits. We also have implemented a stockholder rights plan, also called a poison pill, which could make it uneconomical for a third party to acquire us on a hostile basis.

Our executive officers, directors and major stockholders control approximately 66% of our common stock.

As of December 31, 2008, executive officers, directors and holders of 5% or more of our outstanding common stock, in the aggregate, owned or controlled approximately 66% of our outstanding common stock. As a result, these stockholders are able to influence all matters requiring approval by our stockholders, including the election of directors and the approval of corporate transactions. This concentration of ownership may also delay, deter or prevent a change in control of our company and may make some transactions more difficult or impossible to complete without the support of these stockholders.

We could be negatively affected as a result of a threatened proxy fight and other actions of activist shareholders

If a proxy contest results from one or both notices received from the Icahn Group or Eastbourne announcing their intent to each nominate five individuals for election to our Board of Directors at the 2009 annual meeting and, in the case of the Icahn Group, to submit a proposal for shareholder approval requesting that we reincorporate in the state of North Dakota, our business could be adversely affected because:

- responding to proxy contests and other actions by activist stockholders can be costly and time-consuming, disrupting our operations and diverting the attention of management and our employees;
- if a majority of our Board of Directors ceases to be composed of the existing directors or other individuals approved by a majority of the existing directors, we may be required to repay $575 million under our 2007 Notes, $125 million under our Term Loan and any amounts that

may be outstanding under our $15 million revolving credit facility, and if a cross-default is triggered, $200 million under our 2004 Notes;

- perceived uncertainties as to our future direction may impact our existing and potential collaborations or strategic relationships and in-licensing opportunities and may make it more difficult to attract and retain qualified personnel; and
- if individuals are elected to our Board of Directors with a specific agenda, it may adversely affect our ability to effectively and timely implement our strategic plan.

Substantial future sales of our common stock by us or our existing stockholders or the conversion of our convertible senior notes to common stock could cause the trading price of our common stock to fall.

Sales by existing stockholders of a large number of shares of our common stock in the public market or the perception that additional sales could occur could cause the trading price of our common stock to drop. Likewise, the issuance of shares of common stock upon conversion of our convertible notes or redemption of our convertible notes upon a designated event, or upon additional convertible debt or equity financings or other share issuances by us, including shares issued in connection with potential future strategic alliances, could adversely affect the trading price of our common stock. Our convertible notes are currently convertible into a total of up to 15.2 million shares. In addition, the existence of these notes may encourage short selling of our common stock by market participants.

Significant volatility in the market price for our common stock could expose us to litigation risk.

The market prices for securities of biopharmaceutical and biotechnology companies, including our common stock, have historically been highly volatile, and the market from time to time has experienced significant price and volume fluctuations that are unrelated to the quarterly operating performance of these biopharmaceutical and biotechnology companies. Since January 1, 2007, the high and low sales price of our common stock varied significantly, as shown in the following table:

	High	Low
Year ending December 31, 2009		
First Quarter (through February 10, 2009)	$14.13	$10.16
Year ending December 31, 2008		
Fourth Quarter	$20.47	$ 5.50
Third Quarter	$35.00	$18.55
Second Quarter	$33.22	$25.30
First Quarter	$37.38	$23.75
Year ended December 31, 2007		
Fourth Quarter	$51.10	$35.83
Third Quarter	$53.25	$40.86
Second Quarter	$46.93	$36.91
First Quarter	$42.45	$35.55

Given the uncertainty of our future funding, whether BYETTA and SYMLIN will meet our expectations, and the regulatory approval of our other drug candidates, we may continue to experience volatility in our stock price for the foreseeable future. In addition, the following factors may significantly affect the market price of our common stock:

- our financial results and/or fluctuations in our financial results;
- safety issues with BYETTA, SYMLIN or our product candidates;
- clinical study results;

- determinations by regulatory authorities with respect to our drug candidates;
- our ability to complete our Ohio manufacturing facility and the commercial manufacturing process for exenatide once weekly;
- developments in our relationships with current or future collaborative partners;
- our ability to successfully execute our commercialization strategies;
- developments in our relationships with third-party manufacturers of our products and other parties who provide services to us;
- technological innovations or new commercial therapeutic products by us or our competitors;
- developments in patent or other proprietary rights; and
- governmental policy or regulation, including with respect to pricing and reimbursement.

Broad market and industry factors also may materially adversely affect the market price of our common stock, regardless of our actual operating performance. Periods of volatility in the market price of our common stock expose us to securities class-action litigation, and we may be the target of such litigation as a result of market price volatility in the future.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

Our primary administrative offices and research laboratories are located in San Diego, California. As of December 31, 2008, we had leases for approximately 830,000 square feet of office and laboratory space. Our leases on a majority of these properties expire between 2015 and 2019. We have also entered into short-term leases and other agreements for small offices in Beachwood, Ohio, Laguna Niguel, California and Washington, D.C.

Our wholly-owned subsidiary, Amylin Ohio LLC, owns two buildings and 44.4 acres of land in West Chester, Ohio. The buildings, once built out for the manufacture of exenatide once weekly, will have approximately 565,000 square feet of manufacturing and office space.

Item 3. ***Legal Proceedings***

From time-to-time we become involved in various lawsuits, claims and proceedings relating to the conduct of our business, including those pertaining to product liability, patent infringement and employment claims. For example, we are currently involved in seven product liability cases, four of which have been stayed pending the U.S Supreme Court's decision on federal preemption of such cases in *Wyeth v. Levine.* We have also been notified of additional claimants who may file product liability complaints. While we cannot predict the outcome of any lawsuit, claim or proceeding, we believe the disposition of the current lawsuits is not likely to have a material effect on our financial condition or liquidity.

Item 4. ***Submission of Matters to a Vote of Security Holders***

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is traded on The NASDAQ Global Market under the symbol "AMLN." The following table sets forth, for the periods indicated, the reported high and low sales price per share of our common stock on The NASDAQ Global Market:

	High	Low
Year Ended December 31, 2008		
Fourth Quarter	$20.47	$ 5.50
Third Quarter	$35.00	$18.55
Second Quarter	$33.22	$25.30
First Quarter	$37.38	$23.75
Year Ended December 31, 2007		
Fourth Quarter	$51.10	$35.83
Third Quarter	$53.25	$40.86
Second Quarter	$46.93	$36.91
First Quarter	$42.45	$35.55

The last reported sale price of our common stock on The NASDAQ Global Market on February 10, 2009 was $13.05. As of February 10, 2009, there were approximately 620 shareholders of record of our common stock.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings for funding growth and, therefore, do not anticipate paying any cash dividends in the foreseeable future.

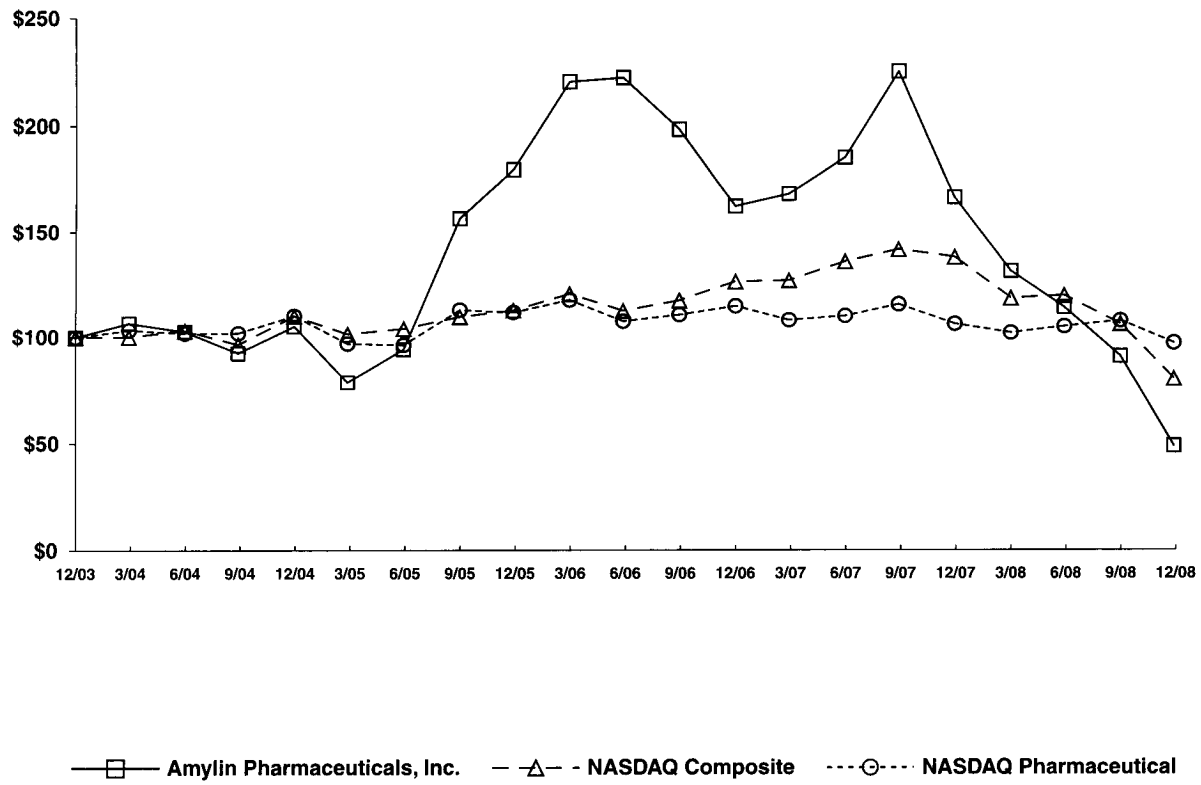
For information concerning prior stockholder approval of and other matters relating to our equity incentive plans, see "Equity Compensation Plan Information" under Item 12 in this annual report on Form 10-K.

PERFORMANCE MEASUREMENT COMPARISON

The material in this section is not "soliciting material," is not deemed "filed" with the Securities and Exchange Commission, and is not to be incorporated by reference into any filing of Amylin under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

The following graph compares total stockholder returns of Amylin for the past five years to two indices: the NASDAQ CRSP Total Return Index for the NASDAQ Stock Market (U.S. companies), or the NASDAQ-US, and the NASDAQ Pharmaceutical Index, or the NASDAQ-Pharmaceutical. The total return for our common stock and for each index assumes the reinvestment of dividends, although dividends have never been declared on our common stock, and is based on the returns of the component companies weighted according to their capitalizations as of the end of each monthly period. The NASDAQ-US tracks the aggregate price performance of equity securities of U.S. companies traded on the NASDAQ National Market System, or the NMS. The NASDAQ-Pharmaceutical tracks the aggregate price performance of equity securities of pharmaceutical companies traded on the NMS.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Amylin Pharmaceuticals, Inc., The NASDAQ Composite Index
And The NASDAQ Pharmaceutical Index



*$100 invested on 12/31/03 in stock & index-including reinvestment of dividends.
Fiscal year ending December 31.

Item 6. ***Selected Financial Data***

Please read the following selected financial data in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the Consolidated Financial Statements and related notes included elsewhere in this annual report on Form 10-K.

	Years Ended December 31				
	2008	2007	2006	2005	2004
	(in thousands, except for per share amounts)				
Consolidated Statements of Operations Data:					
Net product sales	$ 765,342	$ 701,450	$ 474,038	$ 86,713	$ —
Revenues under collaborative agreements	74,767	79,547	36,837	53,761	34,268
Total revenues	840,109	780,997	510,875	140,474	34,268
Costs and expenses:					
Cost of goods sold	91,596	65,457	50,073	14,784	—
Selling, general and administrative	395,112(1)	390,982(1)	281,950(1)	171,520	66,958
Research and development	293,095(2)	276,600(2)	222,053(2)	132,128	119,558
Collaborative profit-sharing	302,600	290,934	194,191	31,359	—
Restructuring	54,926(3)	—	—	—	—
Total costs and expenses	1,137,329	1,023,973	748,267	349,791	186,516
Make-whole payment on debt redemption	—	—	(7,875)	—	—
Net interest and other income (expense)	(3,242)	31,840	26,411	2,485	(4,909)
Loss on impairment of investments	(14,943)	—	—	—	—
Net loss	(315,405)	(211,136)	(218,856)	(206,832)	(157,157)
Net loss per share—basic and diluted	$ (2.30)	$ (1.59)	$ (1.78)	$ (1.96)	$ (1.67)
Shares used in calculating net loss per share—basic and diluted	137,006	132,621	122,647	105,532	94,054
Consolidated Balance Sheets Data:					
Cash, cash equivalents and short-term investments	$ 816,838	$ 1,130,415	$ 767,331	$ 443,423	$ 293,756
Working capital	$ 722,290	$ 1,049,024	$ 702,930	$ 415,134	$ 282,421
Total assets	$ 1,712,629	$ 1,774,211	$ 1,060,386	$ 566,962	$ 357,800
Long-term obligations, excluding current portion	$ 1,047,977	$ 934,109	$ 221,208	$ 399,112	$ 403,233
Accumulated deficit	$(1,749,725)	$(1,434,320)	$(1,223,184)	$(1,004,328)	$(797,496)
Total stockholders' equity (deficit)	$ 350,874	$ 552,818	$ 635,291	$ 69,264	$ (87,370)

(1) Selling, general and administrative expenses for the years ended December 31, 2008, 2007 and 2006 include approximately $34.0 million, $35.4 million, and $29.0 million, respectively, of employee stock-based compensation expense pursuant to the provisions of Statement of Financial Accounting Standards No. 123R *"Share-Based Payment"* which the Company adopted on January 1, 2006.

(2) Research and development expenses for the years ended December 31, 2008, 2007 and 2006 include approximately $21.1 million, $23.6 million, and $22.9 million, respectively, of employee stock-based compensation expense pursuant to the provisions of Statement of Financial Accounting Standards No. 123R *"Share-Based Payment"* which the Company adopted on January 1, 2006.

(3) Restructuring charge for the year ended December 31, 2008 included $0.8 million of employee stock-based compensation expense pursuant to the provisions of Statement of Financial Accounting Standards No. 123R *"Share-Based Payment"* which the Company adopted on January 1, 2006

Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations*

Overview

We are a biopharmaceutical company committed to improving the lives of people with diabetes, obesity and other diseases through the discovery, development and commercialization of innovative medicines. We have developed and gained approval for two first-in-class medicines to treat diabetes, BYETTA® (exenatide) injection and SYMLIN® (pramlintide acetate) injection, both of which were commercially launched in the United States during the second quarter of 2005. BYETTA was approved in the European Union, or EU, in 2006 and our collaboration partner, Lilly has commercially launched BYETTA in 49 countries as of December 31, 2008. Our near-term business strategy is to create value for patients and our stockholders by capitalizing on market drivers, such as the ADA's recent inclusion of BYETTA as the only new addition to their treatment guidelines. Our focus remains on increasing BYETTA and SYMLIN revenue, submitting a New Drug Application, or NDA, for exenatide once weekly, significantly improving operating results and progressing toward positive operating cash flow by the end of 2010. Our long-term strategy is focused on making prudent investment decisions based on strong clinical data to advance our obesity program. We intend to finalize our obesity funding and development strategy by the end of 2009.

BYETTA is the first and only approved medicine in a new class of compounds called glucagon-like peptide-1, or GLP-1, receptor agonists. We began selling BYETTA in the United States in June 2005. BYETTA is approved in the United States for the treatment of patients with type 2 diabetes who have not achieved adequate glycemic control and are using metformin, a sulfonylurea and/or a TZD, three common oral therapies for type 2 diabetes. In October 2008, the ADA and the European Association for the Study of Diabetes, or EASD, updated their type 2 diabetes treatment guidelines, placing the GLP-1 receptor agonist class, of which BYETTA is the only approved product, as a secondary treatment option for type 2 diabetes patients. In August 2008, the FDA updated a prior alert for BYETTA referencing pancreatitis. Prescriptions declined in the second half of 2008. During that time period we committed our field resources to educating the medical community on the facts about BYETTA, pancreatitis, and the product's safety profile. We believe the decline in BYETTA prescriptions and demand for the products stabilized at the end of the fourth quarter of 2008. Net product sales of BYETTA were $678.5 million, $636.0 million, and $430.2 million for the years ended December 31, 2008, 2007, and 2006, respectively.

We have an agreement with Lilly for the global development and commercialization of exenatide. This agreement includes BYETTA and any sustained-release formulations of exenatide such as exenatide once weekly, our once weekly formulation of exenatide for the treatment of type 2 diabetes. Under the terms of the agreement, operating profits from products sold in the United States are shared equally between Lilly and us. The agreement provides for tiered royalties payable to us by Lilly based upon the annual gross margin for all exenatide product sales, including any long-acting release formulations, outside of the United States. Royalty payments for exenatide product sales outside of the United States will commence after a one-time cumulative gross margin threshold amount has been met. We expect royalty payments to commence in 2010. Lilly is responsible for 100% of the costs related to development of twice-daily BYETTA for sale outside of the United States. Development costs related to all other exenatide products for sale outside of the United States will continue to be allocated 80% to Lilly and 20% to us. Lilly will continue to be responsible for commercialization and all of the costs related to commercialization of all exenatide products for sale outside of the United States.

SYMLIN is the first and only approved medicine in a new class of compounds called amylinomimetics. We began selling SYMLIN in the United States in April 2005. Symlin is approved in the United States for the treatment of patients with either type 1 or type 2 diabetes who are treated with mealtime insulin but who have not achieved adequate glycemic control. In early 2008, we commercially launched the SymlinPen® 120 and SymlinPen® 60 pen injector devices in the United

States. These new pre-filled pen-injector devices feature simple, fixed dosing to improve mealtime glucose control. Net product sales of SYMLIN were $86.8 million, $65.5 million and $43.8 million for the years ended December 31, 2008, 2007 and 2006 respectively.

We have a field force of approximately 650 people dedicated to marketing BYETTA and SYMLIN in the United States. Our field force includes our specialty and primary care sales forces, a managed care and government affairs organization, a medical science organization and diabetes care specialists. In addition, Lilly co-promotes BYETTA in the United States. In May 2008, we amended our United States co-promotion agreement with Lilly, resulting in a 40% increase in the total number of sales representatives promoting BYETTA beginning July 1, 2008. To achieve this increase, Lilly's existing third party sales force for Cialis® (tidalafil) co-promotes BYETTA in the United States and we increased the number of sales representatives in its existing primary care sales force by approximately 15%. In exchange for Lilly sharing in 50% of the costs related to our additional sales representatives and paying 100% of the costs of the third party sales force discussed above, our primary care sales force co-promotes Cialis in the United States. We are currently evaluating this element of the co-promotion arrangement with Lilly.

In addition to our marketed products, we are working with Lilly and Alkermes to develop exenatide once weekly. We are also working with Parsons on the construction of a manufacturing facility for exenatide once weekly in Ohio. We substantially completed the construction of this facility in 2008. We are now manufacturing exenatide once weekly at commercial scale in this facility and we began supplying clinical trials with this material in the third quarter of 2008. In October 2008 we entered into a commercial supply agreement with Lilly, pursuant to which we will supply exenatide once weekly for sale in the United States, if approved. In addition we will supply Lilly with commercial quantities of exenatide once weekly for sale by Lilly outside of the United States, if approved. Under the terms of this agreement, Lilly made a $125 million cash payment to us in October 2008 representing an amount to compensate us for our cost of carrying Lilly's share of the capital investment in our exenatide once weekly manufacturing facility in Ohio. In addition to the $125 million cash payment, we will recover Lilly's share of the over $500 million capital investment in the facility through an allocation of depreciation to cost of goods sold in accordance with our collaboration agreement with Lilly. The total amount that will ultimately be recovered from Lilly will be dependent upon the proportion of product supplied for sale in the United States, the cost of which is shared equally by the parties, and the proportion of the product supplied for sale outside the United States, the cost of which is paid for 100% by Lilly. We also entered into a loan agreement with Lilly under which we may borrow up to $165 million beginning on December 1, 2009 and ending on June 30, 2011, with maturity no later than June 30, 2014.

During the second quarter of 2008, we held our pre-NDA meeting with the FDA to discuss open items for our exenatide once weekly regulatory submission. Based on the pre-NDA meeting and our ongoing dialog with the FDA, we continue to believe that the pacing item for an NDA submission is to collect sufficient data to demonstrate the comparability between material manufactured by Alkermes in its facility and used in previous clinical studies and the commercial scale material produced in our Ohio facility. In December 2008, we announced that the FDA has indicated that data from an ongoing extension of our DURATION-1 study could be used to demonstrate comparability. Acceptance by the FDA of the comparability data is dependent upon the DURATION-1 study extension results that we expect to have in early 2009. Although we believe that our exenatide once weekly NDA submission is on track to be completed in the first half of 2009, if we are required to initiate a new clinical study to demonstrate comparability, the timing of the NDA submission would depend on the parameters of the new study, and our submission could be delayed.

In 2009, we will continue to focus on building a superior profile for exenatide once weekly by conducting three clinical trials that will compare exenatide once weekly against competing products.

The objective of these studies is to support the launch of exenatide once weekly and demonstrate superiority and the transformational nature of our exenatide once weekly therapy.

In November 2008, we announced a strategic restructuring and workforce reduction that reduced the size of our San Diego workforce by approximately 25%, or 330 employees. The goal of the restructuring was to better align our cost structure with anticipated revenues and is part of our business plan to achieve positive operating cash flow by the end of 2010. We believe we have the appropriate resources to market BYETTA and SYMLIN, bring exenatide once weekly to market as soon as possible, and continue to advance our obesity programs.

Our long-term growth strategy is focused on making prudent investment decisions based on strong clinical data to advance our obesity program and includes our INTO strategy. In November 2007, we announced that overweight or obese subjects in a 24-week proof-of-concept study treated with a combination of pramlintide, an analog of human amylin and the same active ingredient in SYMLIN, and metreleptin, an analog of human leptin, lost an average of 25 pounds from baseline, resulting in reduced body weight on average of 12.7%. In 2009 we plan to continue the development of a potential obesity medicine that is a combination of pramlintide and metreleptin and the development of a second generation amylinomimetic, now known as davalintide (formerly known as AC2307), which we have now moved into Phase 2 clinical trials. By the end of 2009, we intend to finalize our obesity funding and development strategy.

Although our efforts will remain primarily focused on our near-term opportunities including BYETTA, SYMLIN and exenatide once weekly and select investments in our obesity programs, we also maintain an active discovery research program focused on novel peptide and protein therapeutics and are actively seeking to in-license additional drug candidates. We have also made a number of strategic investments and collaborations for the potential development of additional drug candidates.

Since our inception in September 1987, we have devoted substantially all of our resources to our research and development programs and, more recently, to the commercialization of our products. All of our revenues prior to May 2005 were derived from fees and expense reimbursements under our BYETTA collaboration agreement with Lilly, previous SYMLIN collaborative agreements, and previous co-promotion agreements. During the second quarter of 2005, we began to derive revenues from product sales of BYETTA and SYMLIN. At December 31, 2008, our accumulated deficit was approximately $1.7 billion.

At December 31, 2008, we had $816.8 million in cash, cash equivalents and short-term investments. Additionally we have future availability of $165 million beginning December 1, 2009 pursuant to the loan agreement with Lilly. Although we may not generate positive operating cash flows for the next few of years, we intend to improve our operating results and reduce our use of cash for operating activities from current levels to achieve our goal to be operating cash flow positive by the end of 2010. Additionally, we expect that our use of cash for capital expenditures will decrease significantly from 2008 levels following the substantial completion of our manufacturing facility in Ohio in 2008. Refer to the discussions under the headings "*Liquidity and Capital Resources*" below and "*Cautionary Factors That May Affect Future Results*" in Part I, Item 1A for further discussion regarding our anticipated future capital requirements.

Recent Developments

Diabetes

BYETTA

- Communicated the addition of GLP-1 receptor agonist class, of which BYETTA is the only approved product, to the ADA and EASD treatment guidelines as a secondary treatment option for type 2 diabetes patients.

- Initiated co-promotion of BYETTA with third party Lilly primary care sales force, increasing the sales force promoting BYETTA by 40% effective July 1, 2008.

Exenatide Once Weekly

- Announced that the ongoing extension of the DURATION-1 study is appropriate to use as the basis for demonstrating comparability between intermediate-scale clinical trial material made in Alkermes' manufacturing facility, and commercial-scale drug product made at Amylin's manufacturing facility based on feedback from the U.S. Food and Drug Administration (FDA) and reaffirmed plans for exenatide once weekly NDA submission to the FDA by the end of the first half of 2009.
- Completed enrollment of DURATION-2 and DURATION-3, the second and third studies in a planned program of superiority clinical studies of exenatide once weekly. Results for DURATION-2, comparing exenatide once-weekly against a TZD and a dipeptidyl peptidase-4 (DPP-4) inhibitor on a background of metformin therapy, are expected in the second quarter of 2009. Results for DURATION-3, comparing exenatide once weekly to insulin glargine in patients using oral diabetes medications are expected in the third quarter of 2009.
- Initiated DURATION-4, the fourth study in a planned program of superiority clinical studies of exenatide once weekly. Results for DURATION-4, comparing exenatide once weekly as a monotherapy treatment to either metformin, a TZD or a DPP-4 inhibitor are expected in 2010.
- Executed an exenatide once weekly supply agreement with Lilly, under which Lilly made an initial payment of $125 million to Amylin in the fourth quarter of 2008. In addition, Lilly extended a $165 million line of credit to Amylin. These agreements underscore Amylin's and Lilly's commitment to the successful commercialization of exenatide once weekly, strengthen Amylin's balance sheet and provide additional financial flexibility.
- Announced results from a 52-week open-label clinical study that showed the durable efficacy of exenatide once weekly. Patients taking exenatide once weekly experienced an average A1C decline of 2.0 percent with 9.5 pound weight loss, and over the course of one year, sustained a similar improvement in glucose control compared to those receiving treatment for 30 weeks.

SYMLIN

- Published data showing that the use of mealtime SYMLIN with basal insulin therapy for 24 weeks resulted in more patients with type 2 diabetes achieving improved glucose control, without weight gain or hypoglycemia compared to the use of rapid-acting insulin with basal insulin.
- Commercially launched the SymlinPen 120 and the SymlinPen 60 pen-injector devices for administering SYMLIN in the United States in January 2008. These new pre-filled pen-injector devices feature simple, fixed dosing to improve mealtime glucose control.

Obesity programs

- Presented novel data on Amylin's promising obesity pipeline at The Obesity Society's Scientific Conference that supported the therapeutic potential of the integrated neurohormonal approach to obesity pharmacotherapy.
- Completed enrollment of a phase 2B study to evaluate different dosing combinations of pramlintide and metreleptin. The objective of this dose-ranging study is to support dose selection for phase 3, and to guide the development of a delivery system for this combination regimen. Results from this study are expected in the second half of 2009.

- Completed enrollment of a phase 2 clinical study of davalintide, our second generation amylinomimetic. Results from this study are expected in the second half of 2009

Financial and Operational

- Implemented a strategic restructuring that reduced our San Diego workforce by approximately 25% and announced our business plan to achieve positive operating cash flow by the end of 2010.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates, including those related to revenue recognition, stock-based compensation, inventory costs, research and development expenses and income taxes. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect the significant judgments and estimates used in the preparation of our consolidated financial statements (see Note 1 to our consolidated financial statements on page F-6).

Revenue Recognition

We recognize revenue from the sale of our products, license fees and milestones earned and for reimbursement of development costs based on contractual arrangements.

Net Product Sales

We sell our products primarily to wholesale distributors, who in turn, sell to retail pharmacies, pharmacy benefit managers and government entities. Decisions made by these wholesalers and their customers regarding the level of inventories they hold, and thus the amount of product they purchase, can materially affect the level of our product sales in any particular period.

We recognize revenue from the sale of our products when delivery has occurred, title has transferred to the customer, the selling price is fixed or determinable, collectability is reasonably assured and the Company has no further obligations. The Company records allowances for product returns, rebates and wholesaler chargebacks, wholesaler discounts and prescription vouchers. We are required to make significant judgments and estimates in determining some of these allowances. If actual results differ from our estimates, we will be required to make adjustments to these allowances in the future.

Product Returns

We do not offer our wholesale customers a general right of return. However, we will accept returns of products that are damaged or defective when received by the wholesale customer or for any unopened product during the period beginning six months prior to and up to 12 months subsequent to its expiration date. We estimate product returns based on our historical returns experience. Additionally, we consider several other factors in our estimation process including our internal sales

forecasts, the expiration dates of product shipped and third party data to assist us in monitoring estimated channel inventory levels and prescription trends. Actual returns could exceed our historical experience and our estimates of expected future returns due to factors such as wholesaler and retailer stocking patterns and inventory levels and/or competitive changes. To date actual returns have not differed materially from our estimates.

Rebates and Wholesaler Chargebacks

Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and contracted discounts with commercial payors. Rebates are amounts owed after the final dispensing of the product by a pharmacy to a benefit plan participant and are based upon contractual agreements or legal requirements with private sector and public sector (e.g. Medicaid) benefit providers. The allowance for rebates is based on contractual discount rates, expected utilization under each contract and our estimate of the amount of inventory in the distribution channel that will become subject to such rebates. Our estimates for expected utilization for rebates are based on historical rebate claims and to a lesser extent third party market research data. Rebates are generally invoiced and paid quarterly in arrears so that our accrual consists of an estimate of the amount expected to be incurred for the current quarter's activity, plus an accrual for prior quarters' unpaid rebates and an accrual for inventory in the distribution channel.

Wholesaler chargebacks are discounts that occur when contracted customers purchase directly from an intermediary wholesale purchaser. Contracted customers, which currently consist primarily of Federal government entities purchasing off the Federal Supply Schedule, generally purchase the product at its contracted price, plus a mark-up from the wholesaler. The wholesaler, in-turn, charges back to the Company the difference between the price initially paid by the wholesaler and the contracted price paid to the wholesaler by the customer. The allowance for wholesaler chargebacks is based on expected utilization of these programs and reported wholesaler inventory levels. Actual rebates and wholesaler chargebacks could exceed historical experience and our estimates of future participation in these programs. To date, actual rebate claims and wholesaler chargebacks have not differed materially from our estimates.

Wholesaler Discounts

Wholesaler discounts consist of prompt payment discounts and distribution service fees. We offer all of our wholesale customers a 2% prompt-pay discount within the first 30 days after the date of the invoice. Distribution service fees arise from contractual agreements with certain of our wholesale customers for distribution services they provide to us and are generally a fixed percentage of their purchases of our products in a given period. Prompt payment discounts and distribution service fees are recorded as a reduction to gross sales in the period the sales occur. The allowance for wholesaler discounts is based upon actual data of product sales to wholesale customers and not on estimates.

Prescription Vouchers

Prescription vouchers result in amounts owed to pharmacies that have redeemed vouchers for a free prescription. We provide prescription vouchers to physicians, who in turn distribute them to patients. Patients may redeem a voucher at a pharmacy for a free prescription. We reimburse the pharmacy for the price it paid the wholesaler for the medicine and record this reimbursement as a reduction to gross sales. The allowance for prescription vouchers is based on the number of unredeemed vouchers in circulation, and the estimated utilization rate. The estimated utilization rate is based on our historical utilization rates experience with prescription vouchers. The allowance for prescription vouchers could exceed historical experience and our estimates of future utilization rates. To date, actual prescription voucher utilization has not differed materially from our estimates.

Revenues under collaborative agreements

Amounts received for upfront product and technology license fees under multiple-element arrangements are deferred and recognized over the period of such services or performance if such arrangements require on-going services or performance. Non-refundable amounts received for substantive milestones are recognized upon achievement of the milestone and the expiration of stock conversion rights, if any, associated with such payments. Amounts received for equalization of development expenses are recognized in the period in which the related expenses are incurred. Any amounts received prior to satisfying our revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets.

Valuation of Stock-Based Compensation

We account for stock-based compensation to employees in accordance with SFAS No. 123R, "*Share-Based Payment.*" SFAS No. 123R requires us to expense the estimated fair value of non-cash, stock-based payments to employees.

We estimate the fair value of stock-based payments to employees using the Black-Scholes model. This estimate is affected by our stock price as well as assumptions regarding a number of inputs that require us to make significant estimates and judgments. These inputs include the expected volatility of our stock price, the expected term of employee stock options, the risk-free interest rate and expected dividends.

We estimate volatility based upon the historical volatility of our common stock for a period corresponding to the expected term of our employee stock options and the implied volatility of market-traded options on our common stock with various maturities between six months and two years, consistent with the guidance in SFAS No. 123R and the SEC's Staff Accounting Bulletin, or SAB, No. 107. Prior to the adoption of SFAS No. 123R, we estimated volatility based on the historical volatility of our common stock for a period corresponding to the expected term of our employee stock options. The determination to use implied volatility in addition to historical volatility was based upon the availability of data related to actively traded options on our common stock and our assessment that the addition of implied volatility is more representative of future stock price trends than historical volatility alone.

The expected life of our employee stock options represents the weighted-average period of time that options granted are expected to be outstanding in consideration of historical exercise patterns and the assumption that all outstanding options will be exercised at the mid-point of the then current date and their maximum contractual term.

The risk-free interest rates are based on the yield curve of United States Treasury strip securities in effect at the time of grant for periods corresponding with the expected life of our employee stock options. We have never paid dividends and do not anticipate doing so for the foreseeable future. Accordingly, we have assumed no dividend yield for purposes of estimating the fair value of our stock-based payments to employees.

If factors underlying the above assumptions change in future periods, the associated estimated non-cash, stock-based compensation expense that we record may differ significantly from what we have recorded in the current period.

Inventories and Related Reserves

Inventories consist of raw materials, work-in-process and finished goods for SYMLIN and BYETTA. We maintain inventory reserves primarily for production failures and potential product expiration. The manufacturing processes for our products are complex. Deviations in the manufacturing process may result in production failures and additional inventory reserves. Obsolete inventory due to

expiration may also result in additional inventory reserves. In estimating inventory obsolescence reserves, we analyze the shelf life, expiration dates and internal sales forecasts, each on a product-by-product basis.

Research and Development Expenses

Research and development costs are expensed as incurred and include: salaries, benefits, bonus, stock-based compensation, license fees, milestones under license agreements, costs paid to third-party contractors to perform research, conduct clinical trials, and develop drug materials and delivery devices; and associated overhead expenses and facilities costs. Clinical trial costs are a significant component of research and development expenses and include costs associated with third-party contractors. Invoicing from third-party contractors for services performed can lag several months. We accrue the costs of services rendered in connection with third-party contractor activities based on our estimate of management fees, site management and monitoring costs and data management costs. Differences between actual clinical trial costs from estimated clinical trial costs have historically not been material and are adjusted for in the period in which they become known.

Income Taxes

We have net deferred tax assets relating primarily to net operating loss carry forwards and research and development tax credits. Subject to certain limitations, these deferred tax assets may be used to offset taxable income in future periods. Since we have been unprofitable since inception and the likelihood of future profitability is not assured, we have reserved for most of these deferred tax assets in our consolidated balance sheets at December 31, 2008 and 2007, respectively. If we determine that we are able to realize a portion or all of these deferred tax assets in the future, we will record an adjustment to increase their recorded value and a corresponding adjustment to increase income in that same period.

We adopted the provisions of FASB Interpretation Number 48, or FIN 48 and FASB Staff Position, or FSP, FIN 48-1 effective January 1, 2007. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS No. 109, *"Accounting for Income Taxes,"* and prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. We had no cumulative effect adjustment related to the adoption due to a full valuation allowance against deferred tax assets. We provide estimates for unrecognized tax benefits. These unrecognized tax benefits relate primarily to issues common among corporations in our industry. We apply a variety of methodologies in making these estimates which include advice from industry and subject experts, evaluation of public actions taken by the Internal Revenue Service and other taxing authorities, as well as our own industry experience. If our estimates are not representative of actual outcomes, our results could be materially impacted.

Recently Issued Accounting Pronouncements

In May 2008, the FASB issued FSP No. APB 14-1 *"Accounting for Convertible Debt Instruments that may be Settled in Cash Upon Conversion (Including Partial Cash Settlement)."* FSP No. APB 14-1 establishes that the liability and equity components of convertible debt instruments within the scope of FSP APB No. 14-1 shall be separately accounted for in a manner that will reflect the entity's nonconvertible debt borrowing rate when interest cost is recognized in subsequent periods. The carrying amount of the liability component of the convertible debt instrument will be determined by measuring the fair value of a similar liability that does not have an associated equity component. The carrying value of the equity component will be determined by deducting the fair value of the liability component from the initial proceeds ascribed to the convertible debt instrument as a whole. Related transaction

costs shall be allocated to the liability and equity components in proportion to the allocation of proceeds and accounted for as debt issuance costs and equity issuance costs, respectively. The excess of the principal amount of the liability component over its carrying amount shall be amortized to interest cost using the interest method. FSP No. APB 14-1 is effective for us on January 1, 2009 and shall be applied retrospectively to all periods presented with the cumulative effect of the change in accounting principle on periods prior to those presented recognized as of the beginning of the first period presented. Early adoption is not permitted. We expect that the adoption of FSP No. APB 14-1 will have a material impact on interest expense reported in our consolidated financial statements.

In March 2008, the FASB issued SFAS No. 161, *"Disclosures about Derivative Instruments and Hedging Activities, an amendment of FASB Statement No. 133,"* which requires additional disclosures about the objectives of using derivative instruments, the method by which the derivative instruments and related hedged items are accounted for under FASB Statement No.133 and its related interpretations, and the effect of derivative instruments and related hedged items on financial position, financial performance and cash flows. SFAS No. 161 also requires disclosure of the fair values of derivative instruments and their gains and losses in a tabular format. SFAS No. 161 is effective for us on January 1, 2009 . We do not expect that the adoption of SFAS No. 161 will have a material impact on our financial statement disclosures.

In December 2007, the FASB issued SFAS No. 141 (revised 2007), or SFAS No. 141R, *"Business Combinations"* and SFAS 160, *"Noncontrolling Interests in Consolidated Financial Statements, an amendment of Accounting Research Bulletin No. 51."* SFAS 141R will change how business acquisitions are accounted for and will impact financial statements both on the acquisition date and in subsequent periods. SFAS No. 160 will change the accounting and reporting for minority interests, which will be recharacterized as noncontrolling interests and classified as a component of equity. SFAS No. 141R and SFAS No. 160 are effective for us on January 1, 2009. Early adoption is not permitted. We do not expect that the adoption of SFAS No. 141R and SFAS No. 160 will have will have a material impact on our consolidated financial statements.

In December 2007, the FASB ratified the consensuses reached in Emerging Issues Task Force, or EITF, Issue No. 07-1, "Collaborative Arrangements". EITF Issue No. 07-1 defines collaborative arrangements and establishes reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangements and third parties. Under EITF Issue No. 07-1, payments between participants pursuant to a collaborative arrangement that are within the scope of other authoritative accounting literature on income statement classification should be accounted for using the relevant provisions of that literature. If the payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments should be based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 also provides disclosure requirements and is effective for us on January 1, 2009. The effect of applying EITF Issue No. 07-1 will be reported as a change in accounting principle through retrospective applications to all prior periods presented for all collaborative arrangements existing as of the effective date, unless it is impracticable. We do not expect that the adoption of EITF Issue No. 07-1 will have a material impact on our consolidated financial statements.

Results of Operations

Net Product Sales

Net product sales for the years ended December 31, 2008, 2007 and 2006 were $765.3 million, $701.5 million and $474.0 million, respectively, and consisted of sales of BYETTA and SYMLIN, less allowances for product returns, rebates and wholesaler chargebacks, wholesaler discounts, and prescription vouchers.

The following table provides information regarding net product sales (in millions):

	Year ended December 31,		
	2008	2007	2006
BYETTA	$678.5	$636.0	$430.2
SYMLIN	86.8	65.5	43.8
	$765.3	$701.5	$474.0

The increases in net product sales for BYETTA and SYMLIN for the year ended December 31, 2008 as compared to the same period in 2007 and the increases in net product sales for BYETTA and SYMLIN for the year ended December 31, 2007 as compared to the same period in 2006 primarily reflect continued growth in patient demand and the impact of price increases. Sales of our products in future periods may be impacted by numerous factors, including potential competition, the potential approval of additional products including exenatide once weekly, regulatory matters, including potential label changes for BYETTA, economic factors and other environmental factors.

Revenues under Collaborative Agreements

The following table summarizes the components of revenues under collaborative agreements for the years ended December 31, 2008, 2007 and 2006 (in millions):

	Year ended December 31,		
	2008	2007	2006
Amortization of up-front payments	$ 4.3	$ 4.3	$ 4.3
Recognition of milestone payments	—	15.0	—
Cost-sharing payments	70.5	60.2	32.5
	$74.8	$79.5	$36.8

Substantially all of the revenue recorded in these periods consists of amounts earned pursuant to our BYETTA collaboration agreement with Lilly and consists primarily of the continued amortization of up-front payments, milestone payments and cost-sharing payments to equalize development expenses for BYETTA and exenatide once weekly.

The $4.7 million decrease in revenues under collaborative agreements in 2008, as compared to 2007, primarily reflects increased cost-sharing payments partially offset by a reduction in milestone payments. The increase in cost-sharing payments in 2008, as compared to 2007, reflects Lilly's reimbursement to us for increased development expenses for exenatide one weekly. There were no milestone payments in 2008, compared to $15 million in milestone payments in 2007 earned primarily upon Lilly's launch of BYETTA in the European Union in 2007. The $42.7 million increase in revenues under collaborative agreements in 2007, as compared to 2006, primarily reflects increases in milestone payments due to the recognition of $15 million in milestone payments discussed above and increased cost-sharing payments. The increase in cost-sharing payments in 2007, as compared to 2006, primarily reflects Lilly's reimbursement for increased development expenses incurred by us for exenatide once weekly.

In future periods, we expect that revenues under collaborative agreements will consist of ongoing cost-sharing payments from Lilly for sharing of development costs, possible future milestone payments, continued amortization of the $30 million portion of the up-front payment received from Lilly upon signing of our collaboration agreement in 2002 and, following the commercial launch of exenatide once-weekly, the amortization of a portion of the $125 million cash payment received in connection with the exenatide once weekly supply agreement discussed above. The amount of cost-sharing revenue recorded will be dependent on the timing, extent and relative proportion of total development costs for

the exenatide once weekly and BYETTA development programs incurred by us and by Lilly. The receipt and recognition as revenue of future milestone payments is subject to the achievement of performance requirements underlying such milestone payments.

Cost of Goods Sold

Cost of goods sold was $91.6 million, representing a gross margin of 88%, $65.5 million, representing a gross margin of 91%, and $50.1 million, representing a gross margin of 89%, for the years ended December 31, 2008, 2007 and 2006, respectively. Cost of goods sold is comprised primarily of manufacturing costs associated with BYETTA and SYMLIN sales during the period. The decrease in gross margin in 2008, as compared to 2007, primarily reflects increased production costs for BYETTA due to lower production volumes, increases in inventory reserves and product mix, including the introduction of the SymlinPen, partially offset by higher net sales prices per unit for BYETTA and SYMLIN. The improvement in gross margin in 2007, as compared to 2006, primarily reflects a higher average net sales price per unit for BYETTA and lower unit costs for BYETTA resulting from higher production volumes. Annual fluctuations in gross margins may be influenced by production volumes, product mix, pricing and the level of sales allowances.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $395.1 million, $391.0 million and $282.0 million in the years ended December 31, 2008, 2007 and 2006, respectively.

The $4.1 million increase in 2008 as compared to 2007 reflects slight increases in promotional spending for BYETTA and SYMLIN and business infrastructure. We expect selling, general and administrative expenses to decrease in 2009 due our reduced cost structure following our strategic restructuring and workforce reduction implemented during the quarter ended December 31, 2008, discussed below and in Note 5 to the accompanying financial statements.

The $109.0 million increase in 2007 as compared to 2006 reflects the full annual effect of the expansion of our sales force during the fourth quarter of 2006, increased promotional expenses for BYETTA and SYMLIN, increased business infrastructure to support our growth and an increase in stock-based compensation including costs associated with the adoption of our employee stock ownership plan, or ESOP, and increased expense from stock options due to growth in our number of employees.

We, along with Lilly, are jointly responsible for the co-promotion of BYETTA within the United States, and share equally in sales force costs and external marketing expenses. Accordingly, our selling, general and administrative expenses include our 50% share of these costs in the United States.

Research and Development Expenses

Currently, our research and development efforts are focused on programs for the treatment of diabetes and obesity in various stages of development. From inception through 1998, we devoted substantially all of our research and development efforts to SYMLIN. Beginning in 1999, our research and development costs started to include costs for our other drug candidates, primarily BYETTA and exenatide once weekly. In 2004 we initiated our program for the treatment of obesity with pramlintide and in 2006 we commenced our INTO clinical research program for obesity.

The drug development process in the United States includes a series of steps defined by the FDA. The process begins with discovery and preclinical evaluation leading up to the submission of an IND to the FDA, which allows for the initiation of the clinical evaluation of a potential drug candidate in humans. Clinical evaluation is typically comprised of three phases of study: Phase 1, Phase 2 and Phase 3. Generally, the majority of a drug candidate's total development costs are incurred during

Phase 3, which consists of trials that are typically both the longest and largest conducted during the drug development process. Successful completion of Phase 3 clinical testing is followed by the submission of an NDA to the FDA for marketing approval. It is not uncommon for the FDA to request additional data following its review of an NDA, which can significantly increase the drug development timeline and expenses. Following initial regulatory approval for a drug candidate, companies generally initiate additional clinical trials aimed at expanding product labeling and market potential.

The timing and costs to complete the successful development of any of our drug candidates are highly uncertain, and therefore difficult to estimate.

Our research and development costs are comprised of salaries and bonuses, benefits, non-cash stock-based compensation; license fees, milestones under license agreements, costs paid to third-party contractors to perform research, conduct clinical trials, and develop drug materials and delivery devices; and associated overhead expenses and facilities costs. We charge direct internal and external program costs to the respective development programs. We also incur indirect costs that are not allocated to specific programs because such costs benefit multiple development programs and allow us to increase our pharmaceutical development capabilities. These consist primarily of facilities costs and other internal shared resources related to the development and maintenance of systems and processes applicable to all of our programs.

The following table sets forth information regarding our research and development expenses for our major projects for the years ended December 31, 2008, 2007 and 2006 (in millions):

	Year ended December 31,		
	2008	2007	2006
Diabetes(1)	$152.7	$150.2	$104.5
Obesity	55.3	51.5	43.9
Research and early-stage programs	31.5	29.3	40.8
Indirect costs	53.6	45.6	32.9
	$293.1	$276.6	$222.1

(1) Research and development expenses consist primarily of costs associated with Byetta and exenatide once weekly which are shared by Lilly pursuant to our collaboration agreement. Cost-sharing payments received by Lilly are included in revenues under collaborative agreements. Increased expenditures for our diabetes development programs are generally partially offset by an increase in cost-sharing payments from Lilly. Cost-sharing payments were $70.5 million, $60.2 million and $32.5 million for the years ended December 31, 2008, 2007 and 2006, respectively

Research and development expenses increased to $293.1 million for the year ended December 31, 2008 from $276.6 million for the year ended December 31, 2007. The $16.5 million increase in 2008 as compared to 2007 primarily reflects continued investments in exenatide once weekly, including manufacturing scale up at our Ohio manufacturing facility and costs associated with the ongoing DURATION clinical trials discussed above, and continued investment in our obesity development programs, including costs associated with the ongoing Phase 2B study evaluating pramlintide and metreleptin discussed above. We expect that research and development expenses will decrease in 2009 due to our lower cost structure following the restructuring we implemented in the quarter ended December 31, 2008, discussed below and in Note 5 to the accompanying financial statements.

Research and development expenses increased to $276.6 million for the year ended December 31, 2007 from $222.1 million for the year ended December 31, 2006. The $54.5 million increase in 2007 as

compared to 2006 primarily reflects increased expenses associated with our diabetes programs. The increase in expenses for our diabetes programs primarily reflects increased expenses for exenatide once weekly associated with manufacturing scale-up at third-party manufacturers and our manufacturing facility in Ohio and expenses associated with a 30-week comparator study of exenatide once-weekly injection and BYETTA taken twice daily in patients with type 2 diabetes we completed in the fourth quarter of 2007.

Collaborative Profit-Sharing

Collaborative profit-sharing was $302.6 million, $290.9 million and $194.2 million for the years ended December 31, 2008, 2007 and 2006, respectively, and consists of Lilly's 50% share of the gross margin for BYETTA sales in the United States.

Restructuring

In November 2008 we announced a strategic restructuring and workforce reduction that reduced the size of our San Diego workforce by approximately 25%, or 330 employees. The goal of the restructuring was to better align our cost structure with anticipated revenues and is part of our business plan to be operating cash flow positive by the end of 2010. We believe we have appropriate resources to grow product sales from BYETTA and SYMLIN and bring exenatide once weekly to market as soon as possible.

In addition, we also consolidated our San Diego facilities and have sub-leased or intend to sublease exited facilities. In connection with the restructuring, we recorded a charge of $54.9 million for the year ended December 31, 2008. This charge consists primarily of expenses related to facility leases for exited facilities, including impairments of related tenant improvements and employee separation benefits.

The following table sets forth the components of the restructuring charge (in millions):

	Year ended December 31, 2008
Facility related charges	$31.3
Employee separation costs	13.9
Asset impairments	8.8
Other restructuring charges	0.9
	$54.9

We have substantially completed all of the above activities included in the restructuring plan and all costs associated with the restructuring were incurred during the year ended December 31, 2008.

Make-whole Payment on Debt Redemption

In July 2006, we called for the redemption on August 24, 2006 of all our outstanding convertible senior notes due June 2008, or the 2003 Notes, under a provisional redemption based upon the market price of our common stock exceeding certain thresholds. All holders elected to convert their 2003 Notes into shares of our common stock. In connection with the conversion, we issued approximately 5.6 million shares, including 180,005 shares as a make-whole payment, representing $112.94 per $1,000 principal amount of the 2003 Notes converted less interest actually paid. In connection with this make-whole payment, we recorded a non-cash, non-operating charge of $7.9 million during the third quarter of 2006.

Interest and Other Income and Expense

Interest and other income consist primarily of interest income from investment of cash and investments. Interest and other income was $26.6 million in 2008, $47.0 million in 2007 and $34.9 million in 2006. The decrease in 2008 compared to 2007 primarily reflects lower average investment balances and lower interest rates in 2008 as compared to 2007. The increase in 2007 compared to 2006 primarily reflects higher average investment balances due to net proceeds of $558.7 million from the sale of the 2007 Notes.

Interest and other expense consist primarily of interest expense resulting from our long-term debt obligations and includes interest payments and the amortization of debt issuance costs. Interest and other expense was $29.8 million in 2008, $15.1 million in 2007 and $8.5 million in 2006. The increase in 2008 compared to 2007 primarily reflects additional interest expense for our 2007 notes and $125 million long-term note payable entered into in December 2007. The increase in 2007 compared to 2006 primarily reflects an increase in additional interest expense for our 2007 Notes.

Loss on Impairment of Investments

We recognized a loss on impairment of investments of $14.9 million for the year ended December 31, 2008. This primarily represents a recognized $9.0 million other-than-temporary impairment loss on an equity investment in a privately held entity based upon our assessment of the entity's financial and technical performance and the entity's ability to raise additional capital in significantly deteriorated financial markets to fund ongoing operations. We also recognized a $5.9 million other-than-temporary impairment loss on a corporate debt security in our investment portfolio based upon our assessment of the impact of bankruptcy proceedings of the issuer on the recoverability of our investment. At December 31, 2008, gross unrealized losses on our short-term investments were $9.0 million, all of which we determined to be temporary.

Net Loss

Our net loss for the year ended December 31, 2008 was $315.4 million compared to $211.1 million in 2007 and $218.9 million in 2006. The increase in our net loss in 2008 compared to 2007 primarily reflects the increased expenses, including the restructuring charge, partially offset by the increased net product sales discussed above. The decrease in our net loss in 2007 compared to 2006 primarily reflects increased net product sales and revenues under collaborative agreements, partially offset by increased selling, general, and administrative expenses, increased research and development expenses and increased collaborative profit-sharing discussed above.

We may incur operating losses for the next few years. In November 2008 we announced our restructuring and our business plan to become operating cash flow positive by the end of 2010. However, our ability to reach profitability in the future will be heavily dependent upon the amount of product sales that we achieve for BYETTA, SYMLIN and exenatide once weekly, if approved and our ability to control our operating expenses, including ongoing expenses associated with the continued commercialization of BYETTA and SYMLIN, costs associated with the development and commercialization of exenatide once weekly, if approved, and expenses associated with our research and development programs, including our obesity and our early-stage development programs and related support infrastructure. Our operating results may fluctuate from quarter to quarter as a result of differences in the timing of expenses incurred and revenues recognized.

Liquidity and Capital Resources

Since our inception, we have financed our operations primarily through public sales and private placements of our common and preferred stock, debt financings, payments received pursuant to our BYETTA collaboration with Lilly, reimbursement of SYMLIN development expenses through earlier

collaboration agreements, and since the second quarter of 2005, through product sales of BYETTA and SYMLIN.

At December 31, 2008, we had $816.8 million in cash, cash equivalents and short-term investments, compared to $1.1 billion at December 31, 2007 and we have future availability of $165 million beginning December 1, 2009 pursuant to the loan agreement with Lilly. In November 2008, following our restructuring, we announced our business plan to be operating cash flow positive by the end of 2010. Additionally, we expect that our use of cash for capital expenditures will decrease significantly following the substantial completion of our manufacturing facility in Ohio in 2008. Therefore our current business plan does not contemplate a need to raise additional funds from outside sources however, we will continue to evaluate the performance of our business and strategic opportunities which may require us to raise additional funds from outside sources in the future. If we require additional financing in the future, we cannot assure you that it will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through our debt and equity securities offerings, there can be no assurance that we will be able to so in the future, especially given the current adverse economic and credit conditions.

We used cash of $19.5 million, $125.2 million and $126.0 million for our operating activities in the years ended December 31, 2008, 2007 and 2006, respectively. Our cash used for operating activities reflect a source of cash due to the $125 million cash payment received from Lilly in connection with exenatide once-weekly supply agreement signed in October 2008. In addition, our cash used for operating activities in 2008 included uses of cash due to increases in other current assets and inventories of $13.0 million and $15.6 million, respectively and a decrease in payable to collaborative partner of $5.6 million. The increase in other current assets reflects prepayments for raw material inventory and the increase in inventories reflects inventory purchases in accordance with contractual agreements. The decrease in payable to collaborative partner primarily reflects lower gross profit on BYETTA sales, of which 50% is payable to Lilly, in the quarter ending December 31, 2008 as compared to the same period in 2007. Our cash used for operating activities in 2008 included sources of cash for increases in our current liabilities, including an increase of $8.6 million in accounts payable and accrued liabilities, an increase of $4.9 million in accrued compensation, an increase of $46.7 million in accrued restructuring costs, of which $24.2 million is classified as current, and a decrease in accounts receivable of $11.2 million. The increase in accounts payable and accrued liabilities primarily reflects growth in our expenses generally, and accounts payable timing differences. The increase in accrued compensation primarily reflects an increased accrual for our ESOP, which will be funded with shares of our common stock in the quarter ending March 31, 2009. The increase in accrued restructuring costs reflects accrued expenses associated with our recent restructuring and consists primarily of the fair value of net cash payments related to facility lease losses.

Our investing activities used cash of $182.2 million, $296.1 million and $425.9 million in the years ended December 31, 2008, 2007 and 2006, respectively. Investing activities in all three years consisted primarily of purchases and sales of short-term investments and purchases of property, plant and equipment. Purchases of property, plant and equipment increased to $295.1 million in 2008, from $268.7 million in 2007 and $97.9 million in 2006. The increases in 2008 and 2007 primarily reflect costs associated with our manufacturing facility for exenatide once weekly and, to a lesser extent, purchases of tenant improvements, computer software, office equipment and scientific equipment to support our growth. We expect that our capital expenditures will decrease significantly in 2009 following the substantial completion of our Ohio manufacturing facility in 2008. Through December 31, 2008, we had expended in excess of $522.5 million associated with the construction of this facility which includes costs associated with the construction of the facility, purchase and installation of equipment and capitalized labor and materials required to validate the facility. We will continue to evaluate potential additional investments in our Ohio manufacturing facility during the product lifecycle for exenatide once weekly.

Financing activities provided cash of $16.7 million, $776.9 million and $546.5 million in the years ended December 31, 2008, 2007 and 2006, respectively. Financing activities in 2008 include proceeds from the exercise of stock options and proceeds from our employee stock purchase plan. Financing activities for 2007 included proceeds from the exercise of stock options, proceeds from our employee stock purchase plan and $559 million in net proceeds from the issuance of the 2007 Notes. Financing activities for 2006 included proceeds from the exercise of stock options, proceeds from our employee stock purchase plan and $508 million in net proceeds from a public offering of 11.5 million shares of our common stock in April 2006.

At December 31, 2008, we had $200 million in aggregate principal amount of the 2004 Notes due 2011 and $575 million of the 2007 Notes due 2014 outstanding. The 2004 Notes are currently convertible into a total of up to 5.8 million shares of our common stock at approximately $34.35 per share and are not redeemable at our option. The 2007 Notes are currently convertible into a total of up to 9.4 million shares of our common stock at approximately $61.07 per share and are not redeemable at our option.

In December 2007, we entered into a $140 million credit agreement. The credit agreement provides for a $125 million term loan and a $15 million revolving credit facility. The revolving credit facility also provides for the issuance of letters of credit and foreign exchange hedging up to the $15 million borrowing limit. The term loan is repayable on a quarterly basis, with no payments due quarters one through four, 6.25% of the outstanding principal due quarters five through eleven, and 56.25% of the outstanding principal due in quarter twelve. At December 31, 2008 we had an outstanding balance of $125 million under the term loan and had issued $5.6 million of standby letters of credit under the revolving credit facility. Both loans have a final maturity date of December 21, 2010. Interest on the term loan is payable quarterly in arrears at a rate equal to 1.75% above the London Interbank Offered Rate, or LIBOR, of either one, two, three or six months LIBOR term at our election. We have entered into an interest rate swap agreement which resulted in a fixed interest rate of 5.717% under the term loan. The interest rate on the credit facility is LIBOR plus 1.0% or the Bank of America prime rate, at our election.

In October 2008, we entered into a loan agreement with Lilly pursuant to which Lilly will make available to us a $165 million unsecured line of credit that we can draw upon from time to time beginning on December 1, 2009 and ending on June 30, 2011. Any interest due under this credit facility will bear interest at the five-day average three-month LIBOR rate immediately prior to the date of the advance plus 5.25% and shall be due and payable quarterly in arrears on the first business day of each quarter. All outstanding principal, together with all accrued and unpaid interest, shall be due and payable the earlier of 36 months following the date on which the loan commitment is fully advanced or June 30, 2014.

The following table summarizes our contractual obligations and maturity dates as of December 31, 2008 (in thousands).

Contractual Obligations	Payments Due by Period				
	Total	Less than 1 year	2-3 years	4-5 years	After 5 years
Long-term convertible debt	$ 775,000	$ —	$200,000	$ —	$575,000
Interest on long-term convertible debt	107,375	22,250	42,000	34,500	8,625
Long-term note payable	125,000	31,250	93,750	—	—
Interest on long-term note payable, net of swap transactions(1)	11,166	6,476	4,690	—	—
Inventory purchase obligations(2)	384,128	107,034	131,159	145,935	—
Construction contracts	38,900	38,900	—	—	—
Operating leases	210,862	23,422	46,928	49,485	91,027
Total(3)	$1,652,431	$229,332	$518,527	$229,920	$674,652

(1) The interest payments shown were calculated using a rate of 5.717%, the net rate from the term loan and interest rate swap, on the outstanding principal balance of the term loan.

(2) Includes $42.2 million of outstanding purchase orders, cancelable by us upon 30 days' written notice, subject to reimbursement of costs incurred through the date of cancellation. Also includes $311.8 million of commitments for exenatide once weekly that are contingent upon FDA approval of exenatide once weekly.

(3) Excludes long-term obligation of $6.3 million related to deferred compensation, the payment of which is subject to elections made by participants that are subject to change.

In addition, under certain license and collaboration agreements we are required to pay royalties and/or milestone payments upon the successful development and commercialization of related products. We expect to make development milestone payments up to $1.8 million associated with licensing agreements in the next 12 months. Additional milestones of up to approximately $301.7 million could be paid over the next ten to fifteen years if development and commercialization of all our early stage programs continue and are successful. The significant majority of these milestones relate to potential future regulatory approvals and subsequent sales thresholds. Given the inherent risk in pharmaceutical development, it is highly unlikely that we will ultimately make all of these milestone payments; however, we would consider these payments as positive because they would signify that the related products are moving successfully through development and commercialization.

Our future capital requirements will depend on many factors, including: the amount of product sales we and Lilly achieve for BYETTA and we achieve for SYMLIN and exenatide once weekly, if approved; costs associated with the continued commercialization of BYETTA and SYMLIN; costs associated with the establishment of our exenatide once weekly manufacturing facility; costs of potential licenses or acquisitions; the potential need to repay existing indebtedness; costs associated with an increase in our infrastructure; our ability to receive or need to make milestone payments; our ability, and the extent to which we establish collaborative arrangements for SYMLIN or any of our product candidates; progress in our research and development programs and the magnitude of these programs; costs involved in preparing, filing, prosecuting, maintaining, enforcing or defending our patents; competing technological and market developments; and costs of manufacturing, including costs associated with establishing our own manufacturing capabilities or obtaining and validating additional manufacturers of our products; and scale-up costs for our drug candidates.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that are currently or reasonably likely to be material to our consolidated financial position or results of operations.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

We invest our excess cash primarily in United States Government securities, asset-backed securities, and debt instruments of financial institutions and corporations with investment-grade credit ratings. These instruments have various short-term maturities. We do not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions in any material fashion. Accordingly, we believe that, while the instruments held are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive investments. Our debt is not subject to significant swings in valuation as interest rates on our debt are fixed. The fair value of our 2004 Notes and 2007 Notes at December 31, 2008 was approximately $150 million and $260 million, respectively. We have entered into an interest rate swap in connection with our $125 million term loan. The fair value of the interest rate swap at December 31, 2008 was a liability of $5.0 million. A hypothetical 1% adverse move in interest rates along the entire interest rate yield curve would not materially affect the fair value of our financial instruments that are exposed to changes in interest rates.

Item 8. ***Financial Statements and Supplementary Data***

The financial statements and supplemental data required by this item are set forth at the pages indicated in Part IV, Item 15(a)(1) of this annual report.

Item 9. ***Changes In and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

Item 9A. ***Controls and Procedures***

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2008.

Our management does not expect that our disclosure controls and procedures or our internal controls over financial reporting will prevent all potential error and fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, or misstatements due to error, if any, within the Company have been detected. While we believe that our disclosure controls and procedures and internal control over financial reporting are and have been effective, we intend to continue to examine and refine our disclosure controls and procedures and internal control over financial reporting and to monitor ongoing developments in these areas.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in *Internal Control—Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2008. The effectiveness of our internal control over financial reporting as of December 31, 2008 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Changes in Internal Control Over Financial Reporting

There has been no change in our internal control over financial reporting in our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm on Internal Control Over Financial Reporting

The Board of Directors and Stockholders of Amylin Pharmaceuticals, Inc.

We have audited Amylin Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Amylin Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Amylin Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the accompanying consolidated balance sheets of Amylin Pharmaceuticals, Inc. as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2008 of Amylin Pharmaceuticals, Inc. and our report dated February 23, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California
February 23, 2009

PART III

Item 9B. ***Other Information***

None.

Item 10. ***Directors, Executive Officers and Corporate Governance***

The information required by this item with respect to executive officers and directors is incorporated by reference from the information under the captions "Election of Directors," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Business Conduct and Ethics" contained in the proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with our 2009 annual meeting of stockholders.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference to the information under the captions "Compensation of Directors," "Executive Compensation," "Report of the Compensation Committee of the Board of Directors on Executive Compensation," and "Compensation Committee Interlocks and Insider Participation" contained in the proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with our 2009 annual meeting of stockholders.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters***

The information required by this item is incorporated by reference to the information under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" contained in the proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with our 2009 annual meeting of stockholders.

Item 13. ***Certain Relationships and Related Transactions, and Director Independence***

The information required by this item is incorporated by reference to the information under the captions "Election of Directors" and "Certain Transactions" contained in the proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with our 2009 annual meeting of stockholders.

Item 14. ***Principal Accountant Fees and Services***

The information required by this item is incorporated by reference to the information under the caption contained in "Ratification of Selection of Independent Registered Public Accounting Firm" contained in the proxy statement to be filed with the SEC pursuant to Regulation 14A in connection with our 2009 annual meeting of stockholders.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a)(1) **Index to Consolidated Financial Statements**

The financial statements required by this item are submitted in a separate section beginning on page F-1 of this annual report.

(a)(2) **Financial Statement Schedules:** The following Schedule is filed as part of this annual report on Form 10-K:

	Page Number
II. Valuation Accounts	F-38

All other schedules have been omitted because they are not applicable or required, or the information required to be set forth therein is included in the Consolidated Financial Statements or notes thereto.

(a)(3) **Index to Exhibits**—See Item 15(b) below.

(b) **Exhibits**

Exhibit Footnote	Exhibit Number	
(1)	3.1	Amended and Restated Certificate of Incorporation of the Registrant.
(5)	3.2	Fourth Amended and Restated Bylaws of the Registrant.
(11)	3.3	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.
(31)	3.4	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.
	4.1	Reference is made to Exhibits 3.1 - 3.4.
(15)(2)	4.2	Registration Rights Agreement dated September 19, 2002, between the Registrant and Eli Lilly and Company.
(14)	4.3	Rights Agreement dated June 17, 2002, between the Registrant and American Stock Transfer & Trust Company.
(14)	4.4	Certificate of Designation of Series A Junior Participating Preferred Stock.
(20)	4.5	First Amendment to Rights Agreement dated December 13, 2002, between the Registrant and American Stock Transfer & Trust Company.
(8)	4.6	Indenture, dated as of April 6, 2004, between Registrant and J.P. Morgan Trust Company, National Association (as Trustee).
(8)	4.7	Form of 2.50% Convertible Senior Note due 2011.
(30)	4.8	Indenture, dated as of June 8, 2007, between Registrant and The Bank of New York Trust Company, N.A. (as Trustee).
(30)	4.9	Registration Rights Agreement, dated as of June 8, 2007, among Registrant, Goldman Sachs & Co. and Morgan Stanley & Co. Incorporated.
(1)	10.1	Form of Indemnity Agreement entered into between the Registrant and its directors and officers.†
(12)	10.2	Registrant's 1991 Stock Option Plan, as amended.†
(4)	10.3	Form of Incentive Stock Option Agreement under the 1991 Stock Option Plan.†
(1)	10.4	Form of Supplemental Stock Option Agreement under the 1991 Stock Option Plan.†
(1)	10.5	Form of Supplemental Stock Option Agreement not granted under the 1991 Stock Option Plan with related schedule.†

Exhibit Footnote	Exhibit Number	
(29)	10.6	Registrant's Amended and Restated 2001Employee Stock Purchase Plan.†
(16)	10.7	Registrant's Non-Employee Directors' Stock Option Plan (the "Directors' Plan").†
(3)	10.8	Phantom Stock Unit Agreement, dated January 4, 1995, between the Registrant and Farview Management Co., L.P.†
(6)(2)	10.9	Patent and Technology License Agreement, Consulting Agreement and Nonstatutory Stock Option Agreement dated October 1, 1996, between the Registrant and Dr. John Eng.
(7)	10.10	Registrant's Directors' Deferred Compensation Plan.†
(17)	10.11	Registrant's Directors' Plan Stock Option Agreement, as amended. †
(9)	10.12	Special Form of Incentive Stock Option Agreement the 1991 Stock Option Plan of the Registrant.†
(10)	10.13	Stock Option Agreement dated March 25, 1998, between the Registrant and Joseph C. Cook, Jr.†
(13)(2)	10.14	Development and License Agreement dated May 15, 2000, between the Registrant and Alkermes Controlled Therapeutics II, Inc.
	10.15	Registrant's Amended and Restated Officer Change in Control Severance Benefit Plan. †
(26)	10.16	Registrant's Amended and Restated 2001 Equity Incentive Plan.†
(15)(2)	10.17	Collaboration Agreement dated September 19, 2002, between the Registrant and Eli Lilly and Company.
(15)(2)	10.18	U.S. Co-Promotion Agreement dated September 19, 2002, between the Registrant and Eli Lilly and Company.
(15)	10.19	Milestone Conversion Agreement dated September 19, 2002, between the Registrant and Eli Lilly and Company.
(18)(2)	10.20	Device Development and Manufacturing Agreement dated July 1, 2003, between Registrant and Eli Lilly and Company.
(17)	10.21	Form of Registrant's 2001 Equity Incentive Plan Officer Stock Option Agreement, as amended. †
(17)	10.22	Form of Registrant's 2001 Equity Incentive Plan Stock Option Agreement, as amended. †
(19)(2)	10.23	Manufacturing Agreement dated May 12, 2003, between Registrant and UCB S.A.
(21)(2)	10.24	Exenatide Manufacturing Agreement dated October 21, 2003, between Registrant and Mallinckrodt Inc.
(21)(2)	10.25	Commercial Supply Agreement for Exenatide dated December 23, 2003, between Registrant and Bachem, Inc.
(22)(2)	10.26	Commercial Supply Agreement dated February 14, 2005 between Registrant and Baxter Pharmaceutical Solutions LLC.
(22)(2)	10.27	Commercial Supply Agreement dated March 2, 2005 between Registrant and Baxter Pharmaceutical Solutions LLC.
	10.28	Summary Description of Registrant's Named Executive Officer Oral At-Will Employment Agreements. †
(23)	10.29	Description of Registrant's Executive Cash Bonus Plan. †
(25)(2)	10.30	Amendment to Development and License Agreement dated October 24, 2005, between Registrant and Alkermes Controlled Therapeutics II.
(24)(2)	10.31	Commercial Supply Agreement dated June 28, 2005, between Registrant and Bachem, Inc.

Exhibit Footnote	Exhibit Number	
(27)(2)	10.32	Commercial Supply Agreement dated October 12, 2006 between Registrant and Wockhardt UK (Holdings) Ltd.
(27)(2)	10.33	Amendment to Collaboration Agreement dated October 31, 2006 between Registrant and Eli Lilly and Company.
(28)	10.34	Employment Agreement, dated March 7, 2007, by and between Registrant and Daniel M. Bradbury. †
(32)	10.35	Registrant's 2001 Non-Qualified Deferred Compensation Plan. †
(32)	10.36	Credit Agreement, dated as of December 21, 2007, among Registrant, The Bank of America, N.A. (as Administrative Agent) and the other lenders set forth therein.
(33)	10.37	First Amendment to Exenatide Manufacturing Agreement dated January 6, 2006, between Registrant and Mallinckrodt Inc.
(33)(2)	10.38	Amended and Restated Commercial Supply Agreement dated April 1, 2008, between Registrant and Wockhardt UK (Holdings) Ltd.
(33)(2)	10.39	Addendum to U.S. Co-Promotion Agreement dated May 8, 2008, between Registrant and Eli Lilly and Company
(33)	10.40	Consulting Agreement dated June 1, 2008, between Registrant and Alain Baron
(33)(2)	10.41	Third Amendment to Supply Agreement dated January 1, 2008, between Registrant and Mallinckrodt Inc.
(5)	10.42	Amendment to Employment Agreement dated December 3, 2008, between Registrant and Daniel M. Bradbury †
	10.43	Exenatide Once Weekly Supply Agreement dated October 16, 2008, between Registrant and Eli Lilly and Company*
	10.44	Loan Agreement dated October 16, 2008, between Registrant and Eli Lilly and Company
	10.45	First Amendment to Credit Agreement dated October 27, 2008, among Registrant, the Bank of America, N.A. (as Administrative Agent) and other lenders set forth therein
	10.46	Amendment to Commercial Supply Agreement dated December 8, 2008, between Registrant and Baxter Pharmaceutical Solutions LLC*
	10.47	Amendment to the Amended and Restated Commercial Supply Agreement dated January 23, 2009, between Registrant and Wockhardt UK (Holdings) Ltd.*
	21.1	Subsidiaries of Registrant.
	23.1	Consent of Independent Registered Public Accounting Firm.
	24.1	Power of Attorney. Reference is made to page 71.
	31.1	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
	31.2	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended.
	32.1	Certifications Pursuant to U.S.C. Section 1350, As Adopted Pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002.

† Indicates management or compensatory plan or arrangement required to be identified pursuant to Item 15(c).

* Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

(1) Filed as an exhibit to the Registrant's Registration Statement on Form S-1 (No. 33-44195) or amendments thereto and incorporated herein by reference.

(2) Confidential Treatment has been granted by the Securities and Exchange Commission with respect to portions of this agreement.

(3) Filed as an exhibit to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 1994, and incorporated herein by reference.

(4) Filed as an exhibit to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 1995, and incorporated herein by reference.

(5) Filed as an exhibit on Form 8-K dated December 8, 2008, and incorporated herein by reference.

(6) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 1996, and incorporated herein by reference.

(7) Filed as an exhibit to the Registrant's Registration Statement on Form S-8 (No. 333-61660) or amendments thereto and incorporated herein by reference.

(8) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004, and incorporated herein by reference.

(9) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 1998, and incorporated herein by reference.

(10) Filed as an exhibit to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 1998, and incorporated herein by reference.

(11) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001, and incorporated herein by reference.

(12) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999, and incorporated herein by reference.

(13) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2000, and incorporated herein by reference.

(14) Filed as an exhibit on Form 8-K dated June 18, 2002, and incorporated herein by reference.

(15) Filed as an exhibit on Form 8-K dated October 3, 2002, and incorporated herein by reference.

(16) Filed as an exhibit to Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2001, and incorporated herein by reference.

(17) Filed as an exhibit to Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003, and incorporated herein by reference .

(18) Filed as an exhibit to Amendment 1 to Registrant's Quarterly Report on Form 10-Q/A for the quarter ended June 30, 2003, and incorporated herein by reference .

(19) Filed as an exhibit to Amendment 1 to Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003, and incorporated herein by reference.

(20) Filed as an exhibit to Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2002, and incorporated herein by reference.

(21) Filed as an exhibit to Amendment 1 to Registrant's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2003, and incorporated herein by reference.

(22) Filed as an exhibit to Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2004, and incorporated herein by reference.

(23) Filed on Form 8-K dated December 7, 2007, and incorporated herein by reference.

(24) Filed as an exhibit to Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2005, and incorporated herein by reference.

(25) Filed as an exhibit to Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2005, and incorporated herein by reference.

(26) Filed as an exhibit on Form 8-K dated May 30, 2008 and incorporated herein by reference.

(27) Filed as an exhibit to Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2006, and incorporated herein by reference.

(28) Filed as an exhibit to Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2007, and incorporated herein by reference.

(29) Filed as an exhibit on Form 8-K dated May 29, 2007, and incorporated herein by reference.

(30) Filed as an exhibit on Form 8-K dated June 8, 2007, and incorporated herein by reference.

(31) Filed as an exhibit to Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2007, and incorporated herein by reference.

(32) Filed as an exhibit to Registrant's Annual report on Form 10-K for the fiscal year ended December 31, 2007, and incorporated herein by reference.

(33) Filed as an exhibit to Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2008, and incorporated herein by reference.

SIGNATURES

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

AMYLIN PHARMACEUTICALS, INC.

Date: February 27, 2009

By: /s/ DANIEL M. BRADBURY
Daniel M. Bradbury,
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Daniel M. Bradbury and Mark G. Foletta, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments to this Report, and any other documents in connection therewith, and to file the same, with all exhibits thereto, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substituted, may lawfully do or cause to be done by virtue hereof.

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

Signatures	Title	Date
/s/ DANIEL M. BRADBURY Daniel M. Bradbury	President and Chief Executive Officer *(Principal Executive Officer)*	February 27, 2009
/s/ MARK G. FOLETTA Mark G. Foletta	Senior Vice President, Finance and Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 27, 2009
/s/ JOSEPH C. COOK, JR. Joseph C. Cook, Jr.	Chairman of the Board	February 27, 2009

Signatures	Title	Date
/s/ ADRIAN ADAMS Adrian Adams	Director	February 27, 2009
/s/ STEVEN R. ALTMAN Steven R. Altman	Director	February 27, 2009
/s/ TERESA BECK Teresa Beck	Director	February 27, 2009
/s/ KARIN EASTHAM Karin Eastham	Director	February 27, 2009
/s/ JAMES R. GAVIN III, M.D., PHD. James R. Gavin III, M.D., PhD.	Director	February 27, 2009
/s/ GINGER L. GRAHAM Ginger L. Graham	Director	February 27, 2009
/s/ HOWARD E. GREENE, JR. Howard E. Greene, Jr.	Director	February 27, 2009
/s/ JAY S. SKYLER, M.D. Jay S. Skyler, M.D., MACP	Director	February 27, 2009
/s/ JOSEPH P. SULLIVAN Joseph P. Sullivan	Director	February 27, 2009
/s/ JAMES N. WILSON James N. Wilson	Director	February 27, 2009

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Amylin Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Amylin Pharmaceuticals, Inc. as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2008. Our audits also included the financial statement schedule listed in the Index at Item 15(a)(2). These financial statements and schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Amylin Pharmaceuticals, Inc., at December 31, 2008 and 2007, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly, in all material respects, the information set forth therein.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Amylin Pharmaceuticals, Inc's internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 23, 2009 expressed an unqualified opinion thereon.

/S/ ERNST & YOUNG LLP

San Diego, California
February 23, 2009

AMYLIN PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except per share data)

	December 31, 2008	December 31, 2007
ASSETS		
Current assets:		
Cash and cash equivalents	$ 237,263	$ 422,232
Short-term investments	579,575	708,183
Accounts receivable, net	62,369	73,579
Inventories, net	115,823	100,214
Other current assets	41,038	32,100
Total current assets	1,036,068	1,336,308
Property, plant and equipment, net	636,922	390,301
Other long-term assets	23,755	28,082
Debt issuance costs	15,884	19,520
	$ 1,712,629	$ 1,774,211
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 39,467	$ 37,530
Accrued compensation	65,145	56,428
Payable to collaborative partner	60,470	66,116
Other current liabilities	90,125	122,924
Restructuring liability, current portion	24,235	—
Notes payable, current portion	31,250	—
Deferred revenue, current portion	3,086	4,286
Total current liabilities	313,778	287,284
Deferred revenue, net of current portion	—	3,086
Long-term deferred credit	125,000	—
Restructuring liability, net of current portion	22,503	—
Other long-term obligations, net of current portion	31,724	31,023
Notes payable, net of current portion	93,750	125,000
Convertible senior notes	775,000	775,000
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $.001 par value, 7,500 shares authorized, none issued and outstanding at December 31, 2008 and 2007	—	—
Common stock, $.001 par value, 450,000 shares authorized, 137,623 and 135,044 issued and outstanding at December 31, 2008 and 2007	138	135
Additional paid-in capital	2,111,473	1,987,453
Accumulated deficit	(1,749,725)	(1,434,320)
Accumulated other comprehensive loss	(11,012)	(450)
Total stockholders' equity	350,874	552,818
	$ 1,712,629	$ 1,774,211

See accompanying notes to consolidated financial statements.

AMYLIN PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Year ended December 31,		
	2008	2007	2006
Revenues:			
Net product sales	$ 765,342	$ 701,450	$ 474,038
Revenues under collaborative agreements	74,767	79,547	36,837
Total revenues	840,109	780,997	510,875
Costs and expenses:			
Cost of goods sold	91,596	65,457	50,073
Selling, general and administrative	395,112	390,982	281,950
Research and development	293,095	276,600	222,053
Collaborative profit-sharing	302,600	290,934	194,191
Restructuring	54,926	—	—
Total costs and expenses	1,137,329	1,023,973	748,267
Operating loss	(297,220)	(242,976)	(237,392)
Make-whole payment on debt redemption	—	—	(7,875)
Interest and other income	26,561	46,969	34,903
Interest and other expense	(29,803)	(15,129)	(8,492)
Loss on impairment of investments	(14,943)	—	—
Net loss	$ (315,405)	$ (211,136)	$(218,856)
Net loss per share—basic and diluted	$ (2.30)	$ (1.59)	$ (1.78)
Shares used in computing net loss per share, basic and diluted	137,006	132,621	122,647

See accompanying notes to consolidated financial statements.

AMYLIN PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

For the years ended December 31, 2008, 2007 and 2006

(in thousands)

	Common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive (loss) income	Total stockholders' equity
	Shares	Amount				
Balance at December 31, 2005	110,531	$111	$1,073,948	$(1,004,328)	$ (467)	$ 69,264
Comprehensive loss:						
Net loss	—	—	—	(218,856)	—	(218,856)
Unrealized gain on available-for-sale securities	—	—	—	—	1,618	1,618
Comprehensive loss						(217,238)
Issuance of common stock upon exercise of options, net	2,405	2	31,635	—	—	31,637
Issuance of common stock for other employee benefit plans	457	—	10,296	—	—	10,296
Employee stock-based compensation	—	—	51,485	—	—	51,485
Issuance of common stock for restricted stock awards	8	—	353	—	—	353
Conversion of convertible senior notes, net of debt issuance costs	5,377	5	172,972	—	—	172,977
Issuance of common stock for make-whole payment	180	—	7,875	—	—	7,875
Issuance of common stock in public offering, net	11,500	12	507,518	—	—	507,530
Non-employee stock-based compensation	—	—	1,112	—	—	1,112
Balance at December 31, 2006	130,458	130	1,857,194	(1,223,184)	1,151	635,291
Comprehensive loss:						
Net loss	—	—	—	(211,136)	—	(211,136)
Unrealized loss on available-for-sale securities	—	—	—	—	(1,601)	(1,601)
Comprehensive loss						(212,737)
Issuance of common stock upon exercise of options, net	2,547	3	37,396	—	—	37,399
Issuance of common stock upon exercise of warrants	1,604	2	18,370	—	—	18,372
Issuance of common stock for other employee benefit plans	435	—	14,735	—	—	14,735
Employee stock-based compensation	—	—	59,064	—	—	59,064
Non-employee stock-based compensation	—	—	694	—	—	694
Balance at December 31, 2007	135,044	135	1,987,453	(1,434,320)	(450)	552,818
Comprehensive loss:						
Net loss	—	—	—	(315,405)	—	(315,405)
Unrealized loss on available-for-sale securities	—	—	—	—	(10,562)	(10,562)
Comprehensive loss						(325,967)
Issuance of common stock upon exercise of options, net	528	—	7,260	—	—	7,260
Issuance of common stock upon milestone conversion	790	1	29,999	—	—	30,000
Issuance of common stock for other employee benefit plans	578	1	13,717	—	—	13,718
Issuance of common stock for employee stock ownership plan	683	1	16,995	—	—	16,996
Employee stock-based compensation	—	—	55,901	—	—	55,901
Non-employee stock-based compensation	—	—	148	—	—	148
Balance at December 31, 2008	137,623	$138	$2,111,473	$(1,749,725)	$(11,012)	$ 350,874

See accompanying notes to consolidated financial statements.

AMYLIN PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Years ended December 31,		
	2008	2007	2006
Operating activities:			
Net loss	$ (315,405)	$(211,136)	$(218,856)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	33,348	21,563	16,228
Stock-settled compensation accruals	25,109	21,696	5,869
Employee stock-based compensation	55,115	59,064	51,838
Loss on impairment of investments	14,943	—	—
Restructuring (including $786 of employee stock-based compensation)	9,483	—	—
Make-whole payment on debt redemption	—	—	7,875
Other non-cash expenses	5,718	3,028	1,247
Changes in operating assets and liabilities:			
Accounts receivable, net	11,210	(15,490)	(32,389)
Inventories, net	(15,609)	(40,915)	(32,549)
Other current assets	(13,005)	(10,016)	(3,995)
Accounts payable and accrued liabilities	8,641	28,101	38,293
Accrued compensation	4,888	1,300	7,071
Payable to collaborative partner	(5,646)	13,778	35,660
Deferred revenue	111,498	(4,286)	(4,286)
Deferred collaborative profit sharing	9,216	—	—
Restructuring liabilities	46,738	—	—
Other assets and liabilities, net	(5,752)	8,153	1,987
Net cash used in operating activities	(19,510)	(125,160)	(126,007)
Investing activities:			
Purchases of short-term investments	(1,015,811)	(392,155)	(714,772)
Sales and maturities of short-term investments	1,132,017	383,076	386,840
Purchases of property, plant and equipment	(295,060)	(268,674)	(97,925)
Increase in other long-term assets	(3,299)	(18,348)	(33)
Net cash used in investing activities	(182,153)	(296,101)	(425,890)
Financing activities:			
Proceeds from issuance of common stock, net	16,694	64,687	546,511
Proceeds from issuance of convertible debt, net	—	558,670	—
Proceeds from long-term note payable	—	123,496	—
Proceeds from contingent share settled obligation	—	30,000	—
Principal payments on capital leases	—	—	—
Net cash provided by financing activities	16,694	776,853	546,511
Increase (decrease) in cash and cash equivalents	(184,969)	355,592	(5,386)
Cash and cash equivalents at beginning of year	422,232	66,640	72,026
Cash and cash equivalents at end of year	$ 237,263	$ 422,232	$ 66,640
Supplemental disclosures of cash flow information:			
Interest paid, net of interest capitalized	$ 17,701	$ 9,477	$ 6,409
Interest capitalized	$ 11,867	$ 4,483	$ 560
Property, plant and equipment additions in other current liabilities at year end	$ 6,057	$ 15,559	$ 21,219
Common stock issued upon conversion of senior convertible notes	$ —	$ —	$ 175,000
Reclassification of debt issuance costs to additional paid-in capital upon conversion of convertible senior notes	$ —	$ —	$ 1,980
Non-cash financing activities:			
Issuance of common stock upon milestone conversion	$ 30,000	$ —	$ —
Shares contributed as employer 401(k) match	$ 4,284	$ 5,819	$ 2,811
Issuance of common stock for employee stock ownership plan	$ 16,996	$ —	$ —

See accompanying notes to consolidated financial statements.

1. Summary of Significant Accounting Policies

Organization

Amylin Pharmaceuticals, Inc., referred to as the Company or Amylin, was incorporated in Delaware on September 29, 1987. Amylin is a biopharmaceutical company engaged in the discovery, development and commercialization of drug candidates for the treatment of diabetes, obesity and other diseases.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Amylin Ohio, LLC, and Amylin Investments, LLC. All significant intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

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

Revenue Recognition

Net Product Sales

The Company sells BYETTA® (exenatide) injection for the treatment of type 2 diabetes and SYMLIN® (pramlintide acetate) injection for the treatment of type 1 and type 2 diabetes primarily to wholesale distributors, who, in turn, sell to retail pharmacies and government entities. Product sales are recognized when delivery of the products has occurred, title has passed to the customer, the selling price is fixed or determinable, collectability is reasonably assured and the Company has no further obligations. The Company records allowances for product returns, rebates, wholesaler chargebacks, wholesaler discounts, and prescription vouchers at the time of sale and reports product sales net of such allowances. The Company must make significant judgments in determining these allowances. If actual results differ from the Company's estimates, the Company will be required to make adjustments to these allowances in the future.

The Company records all United States BYETTA and SYMLIN product sales. With respect to BYETTA, the Company has determined that it is qualified as a principal under the criteria set forth in Emerging Issues Task Force (EITF), Issue 99-19, *"Reporting Gross Revenue as a Principal vs. Net as an Agent,"* based on the Company's responsibilities under its contracts with Eli Lilly and Company, or Lilly, which include manufacture of product for sale in the United States, responsibility for establishing pricing in the United States, distribution, ownership of product inventory and credit risk from customers.

Revenues Under Collaborative Agreements

Amounts received for upfront product and technology license fees under multiple-element arrangements are deferred and recognized over the period of such services or performance if such arrangements require on-going services or performance. Non-refundable amounts received for

1. Summary of Significant Accounting Policies (Continued)

substantive milestones are recognized upon achievement of the milestone. Amounts received for sharing of development expenses are recognized in the period in which the related expenses are incurred. Any amounts received prior to satisfying these revenue recognition criteria are recorded as deferred revenue.

Collaborative Profit-Sharing

Collaborative profit-sharing represents Lilly's 50% share of the gross margin for Byetta sales in the United States (see Note 4).

Shipping and Handling Costs

Shipping and handling costs incurred for product shipments are included in cost of goods sold in the accompanying consolidated statements of operations.

Research and Development Expenses

Research and development costs are expensed as incurred and include salaries and bonuses, benefits, non-cash stock-based compensation, license fees, milestones under license agreements, costs paid to third-party contractors to perform research, conduct clinical trials, and develop drug materials and delivery devices; and associated overhead expenses and facilities costs. Clinical trial costs, including costs associated with third-party contractors, are a significant component of research and development expenses. Invoicing from third-party contractors for services performed can lag several months. The Company accrues the costs of services rendered in connection with such activities based on its estimate of management fees, site management and monitoring costs, and data management costs. Actual clinical trial costs may differ from estimates and are adjusted in the period in which they become known.

Concentrations of Risk

The Company relies on third-party manufacturers for the production of its products and drug candidates. If the Company's third-party manufacturers are unable to continue manufacturing its products and/or drug candidates, or if the Company loses one of its sole source suppliers used in its manufacturing processes, the Company may not be able to meet market demand for its products and could be materially and adversely affected.

Lilly provides funding for 50% of the development and commercialization expenses for BYETTA and exenatide once weekly and 55% of exenatide once weekly manufacturing development expenses in the United States pursuant to a global development and commercialization agreement between the parties. Lilly co-promotes the product with the Company in the United States and manufactures pen devices for the administration of BYETTA. If Lilly is unable to perform these activities the Company may be unable to meet market demand for its products and could be materially and adversely affected.

The Company is also subject to credit risk from its accounts receivable related to product sales. The Company sells its products in the United States primarily to wholesale distributors. The top four of the Company's customers represented approximately 95% of net product sales in 2008 and 95% of the accounts receivable balance at December 31, 2008. The Company evaluates the credit worthiness of its

1. Summary of Significant Accounting Policies (Continued)

customers and generally does not require collateral. The Company has not experienced any material losses on uncollectible accounts receivable to date.

Net product sales for the years ended December 31, 2008, 2007 and 2006 were $765.3 million, $701.5 million and $474.0 million, respectively, and consisted of sales of BYETTA and SYMLIN, less allowances for product returns, rebates and wholesaler chargebacks, wholesaler discounts, and prescription vouchers.

The following table provides information regarding net product sales by product (in millions):

	Year ended December 31,		
	2008	2007	2006
BYETTA	$678.5	$636.0	$430.2
SYMLIN	86.8	65.5	43.8
	$765.3	$701.5	$474.0

Three of the Company's customers each accounted for more than 10% of total revenues for the year ended December 31, 2008, and two of the Company's customers each accounted for more than 10% of total revenues for the years ended December 31, 2007 and 2006, respectively. The following table summarizes the percent of the Company's total revenues that were attributed to each of these three customers (as a % of total revenues):

	Year ended December 31,		
	2008	2007	2006
Medco Health Solutions	11%	*	*
McKesson Corporation	35%	37%	36%
Cardinal Health, Inc.	33%	32%	34%

* *Less than 10%*

The Company invests its excess cash in U.S. Government securities, securities of agencies sponsored by the U.S. Government, asset-backed securities, mortgage-backed securities, and debt instruments of financial institutions and corporations with investment-grade credit ratings. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. The primary goal of these guidelines is to safeguard principal and they are periodically reviewed. These guidelines prohibit investments in auction rate securities. Financial instruments that potentially subject the Company to significant credit risk consist principally of cash equivalents and short-term investments.

Cash and Cash Equivalents

The Company considers instruments with a maturity date of less than 90 days from the date of purchase to be cash equivalents. Cash and cash equivalents include certificates of deposits underlying letters of credit and cash collateral for derivative financial instruments of $3.5 million at December 31, 2008 and 2007, respectively.

1. Summary of Significant Accounting Policies (Continued)

Fair Value Measurements

Statement of Financial Accounting Standards (SFAS) No. 157, "*Fair Value Measurements*," provides a framework for measuring fair value and requires expanded disclosures regarding fair value measurements. SFAS No. 157 defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact. SFAS No. 157 prioritizes the inputs used in measuring fair value into the following hierarchy:

Level 1	Quoted prices (unadjusted) in active markets for identical assets or liabilities;
Level 2	Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable; and
Level 3	Unobservable inputs in which little or no market activity exists, therefore requiring an entity to develop its own assumptions about the assumptions that market participants would use in pricing.

Short-Term Investments

The Company's short-term investments, consisting principally of debt securities, are classified as available-for-sale and are stated at fair value based upon observed market prices (Level 1 in the fair value hierarchy). Unrealized holding gains or losses on these securities are included in other comprehensive loss. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. For investments in mortgage-backed securities, amortization of premiums and accretion of discounts are recognized in interest income using the interest method, adjusted for anticipated prepayments as applicable. Estimates of expected cash flows are updated periodically and changes are recognized in the calculated effective yield prospectively as appropriate. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in impairment loss on investments. In assessing potential impairment of its short-term investments, the Company evaluates the impact of interest rates, potential prepayments on mortgage-backed securities, changes in credit quality, the length of time and extent to which the market value has been less than cost, and the Company's intent and ability to retain the security in order to allow for an anticipated recovery in fair value. The cost of securities sold is based on the specific-identification method.

Accounts Receivable

Trade accounts receivable are recorded net of allowances for cash discounts for prompt payment, doubtful accounts, product returns and chargebacks. Allowances for rebate discounts and distribution fees are included in other current liabilities in the accompanying consolidated balance sheets. Estimates for allowances for doubtful accounts are determined based on existing contractual obligations, historical payment patterns and individual customer circumstances. The allowance for doubtful accounts was $0.6 million and $0.2 million at December 31, 2008 and December 31, 2007, respectively.

1. Summary of Significant Accounting Policies (Continued)

Inventories, net

Inventories are stated at the lower of cost (FIFO) or market and net of a valuation allowance for potential excess and/or obsolete material of $5.1 million and $5.3 million at December 31, 2008 and December 31, 2007, respectively. Raw materials consists of bulk drug material for BYETTA and SYMLIN, work-in-process consists of in-process BYETTA cartridges, in-process SYMLIN cartridges and in-process SYMLIN vials, and finished goods consists of BYETTA drug product in a disposable pen/cartridge delivery system, finished SYMLIN drug product in vials for syringe administration and finished SYMLIN drug product in a disposable pen/cartridge delivery system.

Property, plant and Equipment

Property, plant and equipment, consists of construction in process, leasehold improvements, computer software, office equipment and furniture, laboratory equipment, production equipment, land, and building and is recorded at cost. Depreciation of software and equipment is computed using the straight-line method, over three to fifteen years. Leasehold improvements are amortized on a straight-line basis over the shorter of the estimated useful lives of the assets or the remaining term of the lease. Depreciation of buildings is computed using the straight-line method, over fifteen or thirty years. Construction in progress includes costs associated with the Company's manufacturing facility for exenatide once weekly, which is currently under construction in Ohio (see Note 4). The Company recorded depreciation expense of $29.2 million, $19.0 million, and $14.3 million in the years ended December 31, 2008, 2007 and 2006, respectively.

The Company records impairment losses on property, plant and equipment used in operations when events and circumstances indicate that assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amount of those assets. The Company also records the assets to be disposed of at the lower of their carrying amount or fair value less cost to sell. For the year ended December 31, 2008, the Company recorded $8.8 million in asset impairments related to impaired leasehold improvements associated with facility leases the Company will no longer use in its operations as part of its restructuring discussed in Note 5. While the Company's current and historical operating and cash flow losses are indicators of impairment, the Company believes the future cash flows to be received support the carrying value of its long-lived assets and accordingly, the Company has not recognized any impairment losses, with the exception of those discussed above, as of December 31, 2008.

FDA validation costs, which to date relate to the Company's manufacturing facility for exenatide once weekly, are capitalized as part of the effort required to acquire and construct long-lived assets, including readying them for their initial intended use, and are amortized over the estimated useful life of the asset.

Computer Software Costs for Internal Use

The Company records the costs of computer software for internal use in accordance with AICPA Statement of Position (SOP) 98-1, *"Accounting for the Costs of Computer Software Developed or Obtained for Internal Use."* SOP 98-1 requires that certain internal-use computer software costs be capitalized. Capitalized costs are amortized on a straight-line basis over the estimated useful life of software, generally three years and included in depreciation expense.

1. Summary of Significant Accounting Policies (Continued)

Investments in Unconsolidated Entities

The Company uses the equity method of accounting for investments in other companies that are not controlled by the Company and in which the Company's interest is generally between 20% and 50% of the voting shares or the Company has significant influence over the entity, or both. The Company's share of the income or losses of these entities are included in interest and other expense, and the investments, which have a net book value of $4.7 million and $15.7 million at December 31, 2008 and December 31, 2007, respectively, are included in other long-term assets. The Company recorded $4.5 million and $1.8 million of equity method investee losses during the years ended December 31, 2008 and 2007, respectively. The Company recognized an impairment loss of $9.0 million in 2008 on one of its equity method investments after assessing the financial and technical performance of the entity in which the investment was made as well as the entity's ability to raise additional capital in significantly deteriorated financial markets to fund ongoing operations.

Patents

The Company has filed a number of patent applications with the United States Patent and Trademark Office and in foreign countries. Certain legal and related costs incurred in connection with pending patent applications have been capitalized. Costs related to successful patent applications are amortized over the lesser of the remaining useful life of the related technology or the remaining patent life, commencing on the date the patent is issued. Gross capitalized patent costs were approximately $5.5 million and $4.9 million at December 31, 2008 and 2007, respectively. Accumulated amortization was approximately $2.6 million and $2.2 million at December 31, 2008 and 2007, respectively. Patents are classified as other long-term assets in the accompanying consolidated balance sheets. The Company recorded patent amortization expense of $0.4 million in the year ended December 31, 2008, and $0.3 million in each of the years ended December 31, 2007 and 2006. Capitalized costs related to patent applications are expensed as a selling, general and administrative expense in the period during which a determination not to pursue such applications is made. Such expenses were not material in the years ended December 31, 2008, 2007 and 2006, respectively.

Net Loss Per Share

Basic and diluted net loss applicable to common stock per share is computed using the weighted average number of common shares outstanding during the period. Common stock equivalents from stock options and warrants of approximately 3.0 million, 6.8 million and 8.0 million were excluded from the calculation of net loss per share for the years ended December 31, 2008, 2007 and 2006, respectively, because the effect would be antidilutive. In addition, common stock equivalents from shares underlying the Company's convertible senior notes of 15.2 million, 11.1 million, and 5.8 million were excluded from the net loss per share for the years ended December 31, 2008, 2007 and 2006, respectively, because the effect would be antidilutive. In future periods, if the Company reports net income and the common share equivalents for the Company's convertible senior notes are dilutive, the common stock equivalents will be included in the weighted average shares computation and interest expense related to the notes will be added back to net income to calculate diluted earnings per share.

1. Summary of Significant Accounting Policies (Continued)

Derivative Financial Instruments

The Company mitigates certain financial exposures, including currency risk and interest rate risk, through a controlled program of risk management that includes the use of derivative financial instruments. Derivatives are recorded on the balance sheet at fair value, with changes in value being recorded in interest and other income and interest and other expense. The fair value of the Company's derivative financial instruments was a net liability of $4.8 million and $0.4 million at December 31, 2008 and 2007, respectively. The Company has determined that its derivative financial instruments are defined as Level 2 in the fair value hierarchy. The Company recognized unrealized losses on derivative financial instruments of $4.9 million and $0.1 million for the years ended December 31, 2008 and 2007, respectively. The Company did not have any derivative financial instruments for the year ended December 31, 2006.

Comprehensive Loss

SFAS No. 130, *"Reporting Comprehensive Income"* requires that all components of comprehensive loss be reported in the financial statements in the period in which they are recognized. Comprehensive income is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Net loss and other comprehensive loss, including unrealized gains and losses on investments, shall be reported, net of their related tax effect, to arrive at comprehensive loss.

Accounting for Stock-Based Compensation

Effective January 1, 2006, the Company adopted the fair value method of accounting for stock-based compensation arrangements in accordance with Financial Accounting Standards Board (FASB) SFAS No. 123R, *"Share-Based Payment,"* which establishes accounting for non-cash, stock-based awards exchanged for employee services and requires companies to expense the estimated fair value of these awards over the requisite employee service period, which for the Company is generally the vesting period. The Company adopted SFAS No. 123R using the modified prospective method. Under the modified prospective method, prior periods are not revised for comparative purposes. The valuation provisions of SFAS No. 123R apply to new awards and to awards that are outstanding on the effective date and subsequently modified or cancelled. Estimated non-cash, compensation expense for awards outstanding at the effective date will be recognized over the remaining service period using the compensation cost calculated for pro-forma disclosure purposes under SFAS No. 123, *"Accounting for Stock-Based Compensation."*

The Company uses the Black-Scholes model to estimate the value of non-cash, stock-based payments granted to employees under SFAS No. 123R.

The weighted-average estimated fair value of employee stock options and employee stock purchase rights granted during the year ended December 31, 2008 was $10.43 and $7.14 per share, respectively, and the weighted-average estimated fair value of employee stock options and employee stock purchase

1. Summary of Significant Accounting Policies (Continued)

rights granted during the year ended December 31, 2007 was $18.01 and $10.01 per share, respectively using the following weighted-average assumptions:

	Years ended December 31,		
	2008	2007	2006
Stock option plans			
Volatility	46.5%	44.2%	52.4%
Expected life in years	4.2	5.4	5.4
Risk-free interest rate	3.4%	4.7%	4.8%
Dividend yield	—%	—%	—%
Employee stock purchase plan			
Volatility	56.8%	27.9%	43.2%
Expected life in years	0.5	0.5	0.5
Risk-free interest rate	1.9%	4.9%	4.9%
Dividend yield	—%	—%	—%

The Company estimates volatility based upon the historical volatility of its common stock for a period corresponding to the expected term of its employee stock options and the implied volatility of market-traded options on its common stock with various maturities between six months and two years, consistent with the guidance in SFAS No. 123R and the Securities and Exchange Commission's Staff Accounting Bulletin (SAB) No. 107. The determination to use implied volatility in addition to historical volatility was based upon the availability of actively traded options on the Company's common stock and the Company's assessment that the addition of implied volatility is more representative of future stock price trends than historical volatility alone.

The expected life of the Company's employee stock options represents the weighted-average period of time that options granted are expected to be outstanding in consideration of historical exercise patterns and the assumption that all outstanding options will be exercised at the mid-point of the then current date and their maximum contractual term.

The risk-free interest rates are based on the yield curve of U.S. Treasury strip securities in effect at the time of grant for periods corresponding with the expected life of the Company's employee stock options. The Company has never paid dividends and does not anticipate doing so for the foreseeable future. Accordingly, the Company has assumed no dividend yield for purposes of estimating the fair value of its stock-based payments to employees.

Stock-based compensation expense recognized in accordance with SFAS No. 123R is based on awards ultimately expected to vest, and therefore is reduced by expected forfeitures. The Company estimates forfeitures based upon historical forfeiture rates, and will adjust its estimate of forfeitures if actual forfeitures differ, or are expected to differ, from such estimates. Changes in estimated forfeitures will be recognized through a cumulative adjustment in the period of the change and will also impact the amount of stock-based compensation expense in future periods

The Company recorded $55.9 million, or $0.41 per share, and $59.1 million, or $0.45 per share, and $51.8 million, or $0.42 per share, of total employee non-cash, stock-based compensation expense for the years ended December 31, 2008, 2007 and 2006, respectively, as required by the provisions of

1. Summary of Significant Accounting Policies (Continued)

SFAS No. 123R. Stock-based compensation expense capitalized as part of inventory and fixed assets was negligible and there was no impact on the Company's reported cash flows for the years ended December 31, 2008 and 2007. The breakdown of total employee non-cash, stock-based compensation expense by operating statement classification is presented below (in thousands):

	Year ended December 31,		
	2008	2007	2006
Selling, general and administrative expenses	$33,977	$35,420	$28,966
Research and development expenses	21,138	23,644	22,872
Restructuring	786	—	—
	$55,901	$59,064	$51,838

In addition to the stock-based compensation discussed above, the Company also recorded $20.2 million and $17.3 million of expense associated with its Employee Stock Ownership Plan, or ESOP, for the years ended December 31, 2008 and 2007, respectively. There was no expense for the ESOP in 2006 as the plan was not adopted until 2007. The breakdown of non-cash ESOP expense by operating statement classification is presented below (in thousands):

	Year ended December 31,	
	2008	2007
Selling, general and administrative expenses	$11,267	$10,022
Research and development expenses	8,529	7,269
Restructuring	417	—
	$20,213	$17,291

Recently Issued Accounting Standards

In May 2008, the FASB issued FASB Staff Position , or FSP, No. APB 14-1, "*Accounting for Convertible Debt Instruments that may be Settled in Cash Upon Conversion (Including Partial Cash Settlement).*" FSP No. APB 14-1 establishes that the liability and equity components of convertible debt instruments within the scope of FSP APB No. 14-1 shall be separately accounted for in a manner that will reflect the entity's nonconvertible debt borrowing rate when interest cost is recognized in subsequent periods. The carrying amount of the liability component of the convertible debt instrument will be determined by measuring the fair value of a similar liability that does not have an associated equity component. The carrying value of the equity component will be determined by deducting the fair value of the liability component from the initial proceeds ascribed to the convertible debt instrument as a whole. Related transaction costs shall be allocated to the liability and equity components in proportion to the allocation of proceeds and accounted for as debt issuance costs and equity issuance costs, respectively. The excess of the principal amount of the liability component over its carrying amount shall be amortized to interest cost using the interest method. FSP No. APB 14-1 is effective for the Company on January 1, 2009 and shall be applied retrospectively to all periods presented with the cumulative effect of the change in accounting principle on periods prior to those presented recognized as of the beginning of the first period presented. Early adoption is not permitted. The Company

1. Summary of Significant Accounting Policies (Continued)

expects that the adoption of FSP No. APB 14-1 will have a material impact on interest expense reported in its consolidated financial statements.

In March 2008, the FASB issued SFAS No. 161, *"Disclosures about Derivative Instruments and Hedging Activities, an amendment of FASB Statement No. 133,"* which requires additional disclosures about the objectives of using derivative instruments, the method by which the derivative instruments and related hedged items are accounted for under FASB Statement No.133 and its related interpretations, and the effect of derivative instruments and related hedged items on financial position, financial performance and cash flows. SFAS No. 161 also requires disclosure of the fair values of derivative instruments and their gains and losses in a tabular format. SFAS No. 161 will be effective for the Company on January 1, 2009. The Company does not expect that the adoption of SFAS No. 161 will have a material impact on its consolidated financial statement disclosures.

In December 2007, the FASB issued SFAS No. 141 (revised 2007), or SFAS No. 141R, *"Business Combinations"* and SFAS No. 160, *"Noncontrolling Interests in Consolidated Financial Statements, an amendment of Accounting Research Bulletin No. 51."* SFAS 141R will change how business acquisitions are accounted for and will impact financial statements both on the acquisition date and in subsequent periods. SFAS No. 160 will change the accounting and reporting for minority interests, which will be recharacterized as noncontrolling interests and classified as a component of equity. SFAS No. 141R and SFAS No. 160 are effective for the Company on January 1, 2009. Early adoption is not permitted. The Company does not expect that the adoption of SFAS No. 141R and SFAS No. 160 will have a material impact on its consolidated financial statements, but will change the manner in which potential future acquisitions and direct costs of acquisitions are reported.

In December 2007, the FASB ratified the consensuses reached in Emerging Issue Task Force, or EITF, Issue No. 07-1, *"Collaborative Arrangements"*. EITF Issue No. 07-1 defines collaborative arrangements and establishes reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangements and third parties. Under EITF Issue No. 07-1, payments between participants pursuant to a collaborative arrangement that are within the scope of other authoritative accounting literature on income statement classification should be accounted for using the relevant provisions of that literature. If the payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments should be based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 also provides disclosure requirements and is effective for the Company on January 1, 2009. The effect of applying EITF Issue No. 07-1 will be reported as a change in accounting principle through retrospective applications to all prior periods presented for all collaborative arrangements existing as of the effective date, unless it is impracticable. The Company does not expect that the impact that the adoption of EITF Issue No. 07-1 will have a material impact on its consolidated financial statements.

2. Investments

The following is a summary of short-term investments as of December 31, 2008 and 2007 (in thousands):

	Available-for-Sale Securities			
	Amortized Cost	Gross Unrealized Gains(1)	Gross Unrealized Losses(1)	Estimated Fair Value
December 31, 2008				
U.S. Treasury securities	$130,193	$ 449	$ —	$130,642
Obligations of U.S. Government-sponsored enterprises	129,197	656	(1,494)	128,359
Corporate debt securities	294,805	175	(4,090)	290,890
Asset backed securities	33,081	4	(3,401)	29,684
Total	$587,276	$1,284	$(8,985)	$579,575
December 31, 2007				
U.S. Treasury securities	$ 80,282	$ 385	$ (19)	$ 80,648
Obligations of U.S. Government-sponsored enterprises	82,640	441	(141)	82,940
Corporate debt securities	408,020	101	(1,576)	406,545
Asset backed securities	138,447	258	(655)	138,050
Total	$709,389	$1,185	$(2,391)	$708,183

(1) Other comprehensive loss included an unrealized loss of $3.3 million and an unrealized gain of $0.8 million on investments underlying the Company's 2001 Non-Qualified Deferred Compensation Plan at December 31, 2008 and 2007, respectively.

The gross realized gains on sales of available-for-sale securities totaled approximately $2.6 million, $1.1 million and $0.6 million and the gross realized losses totaled $4.6 million, $0.8 million and $0.8 million for the years ended December 31, 2008, 2007 and 2006, respectively.

Contractual maturities of short-term investments at December 31, 2008 were as follows (in thousands):

	Fair Value
Due within 1 year	$430,768
After 1 but within 5 years	111,387
After 5 but within 10 years	6,191
After 10 years	31,229
Total	$579,575

For purposes of these maturity classifications, the final maturity date is used for securities not due at a single maturity date which, for the Company, includes asset-backed and mortgage-backed securities that are included in Obligations of U.S Government-sponsored enterprises in the table above.

The following table shows the gross unrealized losses and fair value of the Company's investments with unrealized losses that are not deemed to be other-than-temporarily impaired, aggregated by

2. Investments (Continued)

investment category and length of time that individual securities have been in a continuous unrealized loss position, at December 31, 2008 (in thousands):

	Less then 12 Months		12 Months or Greater		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
U.S. Treasury securities	$ —	$ —	$ —	$ —	$ —	$ —
Obligations of U.S Government-sponsored enterprises	22,741	(38)	—	—	22,741	(38)
Corporate debt securities	69,235	(756)	72,995	(3,334)	142,230	(4,090)
Asset backed securities	7,628	(76)	19,225	(3,325)	26,853	(3,401)
Mortgage-backed securities	6,513	(560)	23,779	(896)	30,292	(1,456)
	$106,117	$(1,430)	$115,999	$(7,555)	$222,116	$(8,985)

The Company recognized a $5.9 million other-than-temporary impairment loss on an investment in a corporate debt security in the quarter ended September 30, 2008 based upon an assessment of the impact of bankruptcy proceedings of the debt issuer on the recoverability of the Company's investment. The Company determined the fair value of this investment using the quoted market price (Level 1 in the fair value hierarchy) of the security at September 30, 2008. The unrealized losses on the Company's remaining investments is due to the increased volatility in the markets impacting the classes of securities the Company invests in and not a deterioration in credit ratings. The Company's investments have a short effective duration, and since the Company has the ability and intent to hold these investments until a recovery of fair value, which may be maturity, the Company does not consider these investments to be other-than-temporarily impaired at December 31, 2008.

3. Other Financial Information

Inventories consist of the following (in thousands):

	At December 31,	
	2008	2007
Raw materials	$ 74,140	$ 55,706
Work-in process	21,382	24,463
Finished goods	20,301	20,045
	$115,823	$100,214

Other current assets consist of the following (in thousands):

	At December 31,	
	2008	2007
Prepaid expenses	$30,335	$15,787
Interest and other receivables	3,681	5,831
Other current assets	7,022	10,482
	$41,038	$32,100

3. Other Financial Information (Continued)

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

	At December 31, 2008	2007
Land	$ 8,886	$ 7,768
Land improvements	2,990	—
Office equipment and furniture	36,579	30,680
Computer software	46,273	37,988
Laboratory equipment	34,275	29,985
Production equipment	13,610	11,528
Leasehold improvements	71,379	58,977
Building	51,278	1,150
Construction in progress	455,603	260,746
	720,873	438,822
Less accumulated depreciation and amortization	(83,951)	(48,521)
	$636,922	$390,301

Other current liabilities consist of the following (in thousands):

	At December 31, 2008	2007
Contingent share-settled obligation(1)	$ —	$ 30,000
Accrued research and development contract services	9,400	20,107
Accrued rebate discounts	28,575	19,673
Accrued property, plant and equipment additions	6,057	15,559
Other accrued sales allowances	12,011	13,989
Other current liabilities	34,082	23,596
	$90,125	$122,924

(1) Represents a liability for $30 million in milestone payments received from Lilly that were convertible into the Company's common stock at December 31, 2007 (see to note 4).

4. Collaborative Agreements

Collaboration with Eli Lilly and Company

In September 2002, the Company and Lilly entered into a collaboration agreement for the global development and commercialization of exenatide. The agreement was amended in 2006.

This agreement includes BYETTA and any sustained release formulations of exenatide such as once weekly exenatide, the Company's once-weekly formulation of exenatide for the treatment of type 2 diabetes. Under the terms of the agreement, operating profits from products sold in the United States are shared equally between Lilly and us. In 2005, the Company received United States Food and Drug Administration (FDA) approval for the twice-daily formulation of exenatide, which is marketed in

4. Collaborative Agreements (Continued)

the United States under the trade name BYETTA. The agreement provides for tiered royalties payable to us by Lilly based upon the annual gross margin for all exenatide product sales, including any long-acting release formulations, outside of the United States. Royalty payments for exenatide product sales outside of the United States will commence after a one-time cumulative gross margin threshold amount has been met. Lilly is responsible for 100% of the costs related to development of twice-daily BYETTA for sale outside of the United States. Development costs related to all other exenatide products for sale outside of the United States are allocated 80% to Lilly and 20% to us. Lilly is responsible for 100% of the costs related to commercialization of all exenatide products for sale outside of the United States.

At signing, Lilly made initial non-refundable payments to the Company totaling $80 million, of which $50 million was amortized to revenues under collaborative agreements prior to 2004. The remaining $30 million is being amortized to revenues ratably over a seven-year period, which represents the Company's estimate of the period of its performance of significant development activities under the agreement.

In addition to these up-front payments, Lilly agreed to make future milestone payments of up to $85 million upon the achievement of certain development milestones, including milestones relating to both twice daily and sustained release formulations of exenatide such as exenatide once weekly, of which $75 million have been paid through December 31, 2008. No additional development milestones may be earned under the collaboration agreement. In December 2007, the Company received milestone payments of $30 million associated with the results of a thirty week comparator study of exenatide once weekly and BYETTA in patients with type 2 diabetes. Since the New Drug Application filing for exenatide once weekly did not occur by December 31, 2007, Lilly was entitled to and in February 2008 elected to convert the milestones into shares of the Company's common stock. The milestones were converted into 0.8 million shares of the Company's common stock in February 2008 at a conversion price equal to $37.9535, the immediately preceding twenty day average closing market price of the Company's common stock on December 31, 2007.

Lilly also agreed to make additional future milestone payments of up to $130 million contingent upon the commercial launch of exenatide in selected territories throughout the world, including both twice-daily and sustained release formulations, of which $40 million have been paid and recorded as revenue through December 31, 2008.

In May 2008, the Company and Lilly amended their United States co-promotion agreement, resulting in a 40% increase in the total number of sales representatives promoting BYETTA beginning July 1, 2008. To achieve this increase, Lilly's existing third-party sales force for Cialis co-promotes BYETTA in the United States and the Company increased the number of sales representatives in its primary care sales force by approximately 15%. In exchange for Lilly sharing in 50% of the costs related to the Company's additional sales representatives and paying 100% of the third party sales force discussed above, the Company's primary care sales force co-promotes Cialis in the United States. The Company is currently evaluating this element of the co-promotion arrangement with Lilly.

In October 2008, the Company and Lilly entered into an Exenatide Once Weekly Supply Agreement pursuant to which the Company will supply commercial quantities of exenatide once weekly for sale in the United States, if approved by the United States Food and Drug Administration, or FDA. In addition, if Lilly receives approval to market the product in jurisdictions outside the United States,

4. Collaborative Agreements (Continued)

the Company will be required to manufacture the product intended for commercial sale by Lilly in those jurisdictions

Under the terms of the supply agreement, Lilly made a cash payment of $125 million to the Company, which represents an amount to compensate the Company for the cost of carrying Lilly's share of the capital investment made in the Company's manufacturing facility in Ohio. Under the terms of the supply agreement, the Company has agreed not to charge Lilly for Lilly's share of the interest costs capitalized to the facility. Accordingly the Company has determined that a portion of the $125 million payment represents a reimbursement to the Company of Lilly's share of interest costs capitalized to the facility that will be credited to Lilly for its share of the capitalized interest included in the cost of goods sold for exenatide once weekly as incurred. The Company has concluded that any excess amount represents deferred collaborative revenue that will be amortized ratably over the economic useful life of the exenatide once weekly product following its commercial launch. The ultimate allocation of the $125 million payment, which is classified as a long-term deferred credit in the accompanying Consolidated Balance Sheets at December 31, 2008, will be dependent upon the total amount of interest costs capitalized to the facility when it is placed in service. Under certain circumstances, including upon an impairment of the exenatide once weekly manufacturing facility, Lilly may receive a credit for the unearned portion of the $125 million payment which will be applied against Lilly's share of the impairment charge.

In addition to the $125 million cash payment, the Company will recover Lilly's share of the over $500 million capital investment in the facility through an allocation of depreciation to cost of goods sold in accordance with the collaboration agreement. The total amount of the capital investment that will ultimately be recovered from Lilly will be dependent upon the proportion of product supplied for sale in the United States, the cost of which is shared equally by the parties, and the proportion of product supplied for sale outside of the United States, the cost of which is paid for 100% by Lilly.

In October 2008, the Company and Lilly also entered into a loan agreement pursuant to which Lilly will make available to Amylin a $165 million unsecured line of credit that Amylin can draw upon from time to time beginning on December 1, 2009 and ending on June 30, 2011. Any interest due under the credit facility will bear interest at the five-day average three-month LIBOR rate immediately prior to the date of the advance plus 5.25% and shall be due and payable quarterly in arrears on the first business day of each quarter. All outstanding principal, together with all accrued and unpaid interest shall be due and payable the earlier of 36 months following the date on which the loan commitment is fully advanced or June 30, 2014.

4. Collaborative Agreements (Continued)

The following table summarizes the milestones received to date and the manner of recognition in the accompanying consolidated financial statements:

Amount	Year Received	Milestone event	Manner of recognition	Type
$30 million	2003	Completion of Phase 3 clinical trials for BYETTA.	Recognized as revenue under collaborative agreements upon receipt.	Development
$5 million	2003	Completion of Phase 3 clinical trials for BYETTA.	Deferred upon receipt and recognized as revenue under collaborative agreements in 2005 following contents of approved label for BYETTA.	Development
$5 million	2004	Results of clinical study comparing BYETTA to insulin-glargine.	Recognized as revenue under collaborative agreements upon filing of BYETTA New Drug Application in 2004.	Development
$30 million	2005	Regulatory approval and commercial launch of BYETTA.	Recognized as revenue under collaborative agreements upon commercial launch of BYETTA in 2005.	Commercial
$5 million	2007	Results of clinical study comparing BYETTA to insulin-glargine.	Recognized as revenue under collaborative agreements upon receipt.	Development
$10 million	2007	Commercial launch of BYETTA in the EU.	Recognized as revenue under collaborative agreements upon commercial launch of BYETTA in 2007.	Commercial
$30 million	2007	Completion of Phase 3 trial for once weekly exenatide.	Deferred upon receipt until stock conversion rights contingency finalized.(1)	Development

(1) In February 2008, Lilly elected to convert these milestones into shares of the Company's common stock.

The Company recorded revenue under this collaborative agreement of $69.3 million, $78.8 million and $36.8 million in the years ended December 31, 2008, 2007 and 2006, respectively, and incurred reimbursable development expenses of $135.0 million, $100.5 million and $74.7 million in the years ended December 31, 2008, 2007 and 2006, respectively.

4. Collaborative Agreements (Continued)

Reimbursable development expenses consist of direct internal and external expenses for exenatide, including both BYETTA and sustained release formulations.

Collaboration with Alkermes, Inc.

In May 2000, the Company signed an agreement with Alkermes, Inc., a company specializing in the development of products based on proprietary drug delivery technologies, for the development, manufacture and commercialization of an injectable long-acting formulation of exenatide, or exenatide once weekly.

Under the terms of the agreement, Alkermes has granted the Company an exclusive, worldwide license to its Medisorb® technology for the development and commercialization of injectable sustained release formulations of exendins, such as exenatide, and other related compounds that Amylin may develop. In exchange, Alkermes receives funding for research and development and may earn future milestone payments upon achieving specified development and commercialization goals. Alkermes will also receive royalties on any future product sales.

In October 2005, the Company and Alkermes Controlled Therapeutics II, a wholly owned subsidiary of Alkermes, Inc., entered into an Amendment to Development and License Agreement (the "Amendment"), which amends the Development and License Agreement between the parties dated May 15, 2000. Under the terms of the Amendment, the Company will be responsible for manufacturing for commercial sale the once weekly dosing formulation of exenatide once weekly, if approved. The royalty to be paid from the Company to Alkermes for commercial sales of exenatide once weekly was adjusted to reflect the new manufacturing arrangement.

In December 2005, the Company's wholly-owned subsidiary, Amylin Ohio LLC, purchased an existing building and land to house the Company's manufacturing facility in Ohio and the Company is responsible for all costs and expenses associated with the design, construction, validation and utilization of the facility. At December 31, 2008 the Company had capitalized $522.5 million associated with the construction of this facility, which is expected to be completed in 2009.

Other Collaborations

In connection with its strategic equity investments, the Company has entered into collaborative agreements with certain of its equity method investees. Collaborative revenues associated with these agreements were $1.2 million and $0.7 million for the years ended December 31, 2008 and 2007, respectively. There were no collaborative revenues associated with these agreements in 2006.

5. Restructuring

On November 10, 2008, the Company announced a corporate restructuring, ("the Restructuring") that reduced its San Diego work force by approximately 25 percent or 330 employees. The Company has substantially completed all of the activities included in the restructuring plan and all of the costs associated with the restructuring were incurred during the year ended December 31, 2008.

In connection with the Restructuring, the Company recorded restructuring charges of $54.9 million which are reported as a separate line item in the accompanying Consolidated Statement of Operations

5. Restructuring (Continued)

for the year ended December 31, 2008. The following table summarizes the components of the restructuring charges (in thousands):

	Year ended December 31, 2008		
	Accruals	Non-cash items	Total
Facilities related charges	$38,447	$(7,156)	$31,291
Employee separation costs	13,118	786	13,904
Asset impairments	—	8,796	8,796
Other restructuring charges	935	—	935
	$52,500	$ 2,426	$54,926

Facility related charges consist of estimated losses associated with certain facility leases in the Company's San Diego campus that the Company will no longer use in its operations and which the Company ceased using in the quarter ended December 31, 2008. These losses represent the remaining lease payments and other costs due under the lease and costs associated with obtaining sub-leases, net of sub-lease income under executed sub-leases, or to the extent sub-leases have not yet been signed, reasonably expected sub-lease income determined based upon the Company's assessment of market conditions for similar rental properties in its geographic area both of which are discounted at a credit-adjusted risk-free rate of 10%. As of December 31, 2008, the Company had an executed sub-lease for the entire term of its lease obligations for two of the facilities. These two facilities accounted for approximately $15.3 million of the total facility related charges of $31.3 million. The Company expects to incur approximately $12.7 million of accretion expense over the term of the leases, which have expiration dates from 2014 to 2018.

Employee separation costs consist primarily of salaries and benefits earned during the minimum notification period proscribed by law and severance costs associated with the reduction in the Company's San Diego workforce. Asset impairments primarily relate to impaired leasehold improvements associated with the facility leases discussed above. Other restructuring charges consist of incremental direct costs associated with the Restructuring.

The following table sets forth activity in the restructuring liability (in thousands):

	Employee separation costs	Facilities related charges	Other restructuring charges	Total
Balance at December 31, 2007	$ —	$ —	$ —	$ —
Accruals	13,118	38,447	935	52,500
Payments	(4,827)	—	(935)	(5,762)
Balance at December 31, 2008	$ 8,291	$38,447	$ —	$46,738

The Company records restructuring activities in accordance with FASB Statement No. 144, *Accounting for the Impairment and Disposal of Long-Lived Assets* and FASB Statement No. 146, *Accounting for Costs Associated with Exit or Disposal Activities.*

6. Commitments and Contingencies

Lease Commitments

The Company leases its facilities under operating leases, with various terms, the majority of which expire between 2015 and 2019. The minimum annual rent on the Company's facilities is subject to increases based on stated rental adjustment terms of certain leases, taxes, insurance and operating costs. For financial reporting purposes, rent expense is recognized on a straight-line basis over the term of the leases. Accordingly, rent expense recognized in excess of rent paid is reflected as deferred rent. Deferred rent totaled $8.3 million and $9.8 million at December 31, 2008 and 2007, respectively, of which $7.6 million and $8.7 million is included in other long-term obligations, net of current portion in the accompanying Consolidated Balance Sheets at December 31, 2008 and 2007, respectively. Certain of the Company's facility leases contain incentives in the form of reimbursement from the landlord for a portion of the costs of leasehold improvements incurred by the Company. These incentives are recognized as a reduction of rental expense on a straight-line basis over the term of the respective leases. Unamortized leasehold improvement incentives totaled $9.0 million and $14.0 million at December 31, 2008 and 2007, respectively, of which $7.9 million and $12.5 million is included in other long-term obligations, net of current portion in the accompanying consolidated balance sheets at December 31, 2008 and 2007, respectively.

The Company leases vehicles for its field force under operating leases, with lease terms up to four years, of which the first year is non-cancellable. Minimum future payments for the non-cancellable term of these leases are $1.0. million at December 31, 2008.

Minimum future annual obligations for facility and vehicle operating leases for years ending after December 31, 2008 are as follows (in thousands):

2009	$ 23,422
2010	23,138
2011	23,790
2012	24,430
2013	25,055
Thereafter	91,027
Total minimum lease payments	$210,862

Rent expense for the years ended December 31, 2008, 2007 and 2006, was $18.9 million, $16.2 million and $9.8 million, respectively.

Other Commitments

The Company has committed to make potential future milestone payments to third parties as part of in-licensing and development programs primarily related to research and development agreements. Potential future payments generally become due and payable only upon the achievement of certain developmental, regulatory and/or commercial milestones, such as achievement of regulatory approval, successful development and commercialization of products, and subsequent product sales. Because the achievement of these milestones is neither probable nor reasonably estimable, the Company has not recorded a liability on the balance sheet for any such contingencies.

6. Commitments and Contingencies (Continued)

As of December 31, 2008, if all such milestones are successfully achieved, the potential future milestone and other contingency payments due under certain contractual agreements are approximately $303.4 million in aggregate, of which $1.8 million is expected to be paid over the next twelve months.

The Company has committed to make future minimum payments to third parties for certain inventories in the normal course of business. The minimum contractual purchase commitments total $341.9 million as of December 31, 2008, the majority of which relate to exenatide once weekly and BYETTA, including minimum inventory purchases for exenatide once weekly of $311.8 million that are contingent upon FDA approval of exenatide once weekly.

As of December 31, 2008, commitments to complete construction of the Company's exenatide once weekly manufacturing facility in Ohio are $38.9 million.

7. Convertible Senior Notes

In April 2004, the Company issued $200 million aggregate principal amount of 2.5% convertible senior notes due April 15, 2011 in a private placement, referred to as the 2004 Notes. The 2004 Notes have been registered under the Securities Act of 1933, as amended, or the Securities Act, to permit registered resale of the 2004 Notes and of the common stock issuable upon conversion of the 2004 Notes. The 2004 Notes bear interest at 2.5% per year, payable in cash semi-annually and are convertible into a total of up to 5.8 million shares of common stock at a conversion price of $34.35 per share, subject to customary adjustments for stock dividends and other dilutive transactions. The Company incurred debt issuance costs of $6.4 million in connection with the issuance of the 2004 Notes, which are being amortized to interest expense over the term of the 2004 Notes and had a net book value of $2.1 million and $3.0 million at December 31, 2008 and 2007, respectively. Amortization expense associated with these debt issuance costs were approximately $0.9 million for each of the years ended December 31, 2008, 2007 and 2006. The fair value of the 2004 Notes, determined by observed market prices, was $150.0 million and $249.9 million at December 31, 2008 and 2007, respectively.

Upon a change in control, the holders of the 2004 Notes may elect to require the Company to re-purchase the 2004 Notes. The Company may elect to pay the purchase price in common stock instead of cash, or a combination thereof. If paid with common stock the number of shares of common stock a holder will receive will be valued at 95% of the average closing prices of the Company's common stock for the five-day trading period ending on the third trading day before the purchase date.

In June 2007, the Company issued the 2007 Notes in a private placement, which have an aggregate principal amount of $575 million, and are due June 15, 2014. The 2007 Notes are senior unsecured obligations and rank equally with all other existing and future senior unsecured debt. The 2007 Notes bear interest at 3.0% per year, payable in cash semi-annually, and are initially convertible into a total of up to 9.4 million shares of common stock at a conversion price of $61.07 per share, subject to the customary adjustment for stock dividends and other dilutive transactions. In addition, if a "fundamental change" (as defined in the associated indenture agreement) occurs prior to the maturity date, the Company will in some cases increase the conversion rate for a holder of notes that elects to convert its notes in connection with such fundamental change. The maximum conversion rate is 22.9252, which would result in a maximum issuance 13.2 million shares of common stock if all holders converted at the maximum conversion rate.

7. Convertible Senior Notes (Continued)

The 2007 Notes will be convertible into shares of the Company's common stock unless the Company elects net-share settlement. If net-share settlement is elected by the Company, the Company will satisfy the accreted value of the obligation in cash and will satisfy the excess of conversion value over the accreted value in shares of the Company's common stock based on a daily conversion value, determined in accordance with the associated indenture agreement, calculated on a proportionate basis for each day of the relevant 20-day observation period. Holders may convert the 2007 Notes only in the following circumstances and to the following extent: (1) during the five business-day period after any five consecutive trading period (the measurement period) in which the trading price per note for each day of such measurement period was less than 97% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such day; (2) during any calendar quarter after the calendar quarter ending March 31, 2007, if the last reported sale price of the Company's common stock for 20 or more trading days in a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter exceeds 130% of the applicable conversion price in effect on the last trading day of the immediately preceding calendar quarter; (3) upon the occurrence of specified events; and (4) the 2007 Notes will be convertible at any time on or after April 15, 2014 through the scheduled trading day immediately preceding the maturity date.

Subject to certain exceptions, if the Company undergoes a "designated event" (as defined in the associated indenture agreement) including a "fundamental change,", including if a majority of the Company's Board of Directors ceases to be composed of the of the existing directors or other individuals approved by a majority of the existing directors, holders of the 2007 Notes will, for the duration of the notes, have the option to require the Company to repurchase all or any portion of their 2007 Notes. The designated event repurchase price will be 100% of the principal amount of the 2007 Notes to be purchased plus any accrued interest up to but excluding the relevant repurchase date. The Company will pay cash for all notes so repurchased. The Company may not redeem the Notes prior to maturity.

The 2007 Notes have been registered under the Securities Act of 1933, as amended, to permit registered resale of the 2007 Notes and of the common stock issuable upon conversion of the 2007 Notes. Subject to certain limitations, the Company will be required to pay the holders of the 2007 Notes special interest on the 2007 Notes if the Company fails to keep such registration statement effective during specified time periods. The 2007 Notes pay interest in cash, semi-annually in arrears on June 15 and December 15 of each year, which began on December 15, 2007. The Company incurred debt issuance costs of $16.3 million in connection with the issuance of the 2007 Notes, which are being amortized to interest expense over the term of the 2007 Notes and had a net book value of $12.7 million and $15.0 million at December 31, 2008 and 2007, respectively. Amortization expense associated with these debt issuance costs was $2.3 million and $1.3 million in the years ended December 31, 2008 and 2007, respectively. The fair value of the 2007 Notes, determined by observed market prices, was $260.4 and $549.3 million at December 31, 2008 and 2007 respectively.

The Company capitalized $11.7 million, $4.5 million and $0.6 million of interest expense for the years ended December 31, 2008, 2007 and 2006, respectively, associated with construction in progress.

8. Redemption of Convertible Senior Notes

In June and July 2003, the Company issued $175 million of 2.25% convertible senior notes due June 30, 2008 in a private placement referred to as the 2003 Notes. The 2003 Notes were convertible

8. Redemption of Convertible Senior Notes (Continued)

into a total of up to 5.4 million shares of common stock at a conversion price of approximately $32.55 per share. The 2003 notes were provisionally redeemable in whole or in part, at the Company's option at any time on or after June 30, 2006, upon the satisfaction of certain conditions, at specified redemption prices plus accrued interest. The Company called the notes for redemption in July 2006 and issued approximately 5.4 million shares of its common stock to note holders upon the conversion of all of the outstanding 2003 Notes in August 2006. In connection with the conversion, the Company also issued 180,005 shares as a make-whole payment, representing $112.94 per $1,000 principal value of the converted 2003 Notes less interest actually paid. The Company recorded as a one-time, non-cash, non-operating charge of $7.9 million for the make-whole payment in the quarter ended September 30, 2006. Debt issuance costs of $5.3 million were incurred in connection with the issuance of the 2003 Notes and were being amortized to interest expense on a straight-line basis over the contractual term of the 2003 Notes. Amortization expense associated with these debt issuance costs were $0.7 million in the year ended December 31, 2006. Upon conversion, the $2.0 million unamortized balance of these related debt issuance costs were reclassified to additional paid-in capital.

9. Long-Term Note Payable

In December 2007, the Company entered into a $140 million credit agreement with Bank of America, N.A., as administrative agent, collateral agent and letter of credit issuer, Silicon Valley Bank and RBS Asset Finance, Inc., as syndication agents, and Comerica Bank and BMO Capital Markets Financing, Inc., as documentation agents. The credit agreement provides for a $125 million term loan and a $15 million revolving credit facility. The revolving credit facility also provides for the issuance of letters of credit and foreign exchange hedging up to the $15 million borrowing limit. At December 31, 2008 the Company had an outstanding balance of $125.0 million under the term loan and had issued $5.6 million of standby letters of credit under the revolving credit facility, primarily in connection with office leases.

The Company's domestic subsidiaries, Amylin Ohio LLC and Amylin Investments LLC, are co-borrowers under the credit agreement. The loans under the revolving credit facility are collateralized by substantially all of the Company's and the two domestic subsidiaries' assets (other than intellectual property and certain other excluded collateral). The term loan is repayable on a quarterly basis, with no payments due quarters one through four, 6.25% of the outstanding principal due quarters five through eleven, and 56.25% of the outstanding principal due in quarter 12. Interest on the term loan will be paid quarterly on the unpaid principal balance at 1.75% above the London Interbank Offered Rate, or LIBOR, based on the Company's election of either one, two, three, or six months LIBOR term, and payable at the end of the selected interest period but no less frequently than quarterly as of the first business day of the quarter prior to the period in which the quarterly installment is due. The Company has elected to use the three month LIBOR, which was 1.44% at December 31, 2008. Interest periods on the revolving credit facility may be either one, two, three, or six months, and payable at the end of the selected interest period but no less frequently than quarterly, and the interest rate will be either LIBOR plus 1.0% or the Bank of America prime rate, as selected by the Company. Both loans have a final maturity date of December 21, 2010.

The credit agreement contains certain covenants, including a requirement to maintain minimum unrestricted cash and cash equivalents balances, as defined in the agreement, in excess of $400 million, below which certain limitations provided for in the agreement become effective. The credit agreement also contains certain events of default including unrestricted cash and cash equivalents balances, as

9. Long-Term Note Payable (Continued)

defined in the agreement, falling below $280 million, nonpayment of principal, interest, fees or other amounts, violation of covenants, inaccuracy of representations and warranties and default under other indebtedness that would permit the administrative agent to accelerate the Company's outstanding obligations if not cured within applicable grace periods. In addition, the credit agreement provides for automatic acceleration upon the occurrence of bankruptcy, other insolvency events and a change in control as defined in the credit agreement, including if a majority of the Company's Board of Directors ceases to be composed of the of the existing directors or other individuals approved by a majority of the existing directors. There is an annual commitment fee associated with the revolving credit facility of 0.25%.

Maturities of long-term debt for years ending after December 31, 2008 are as follows (in thousands):

2009	$ 31,250
2010	93,750
Thereafter	—
Total minimum long-term debt payments	$125,000

The Company incurred debt issuance costs of $1.7 million in connection with the credit agreement, which are being amortized to interest expense on a straight-line basis over the term of the credit agreement and had a net book value of $1.1 million and $1.5 million at December 31, 2008 and 2007, respectively. Amortization expense associated with these debt issuance costs was $0.6 million and $15.3 thousand in the years ended December 31, 2008 and 2007, respectively.

In connection with the execution of the Term Loan, the Company entered into an interest rate swap with an initial notional amount of $125 million on December 21, 2007 that has resulted in a fixed rate of 5.717% and matures on December 12, 2010. The Company determined that the interest rate swap agreement is defined as Level 2 in the fair value hierarchy. As of December 31, 2008, the fair value of the interest rate swap agreement was a liability of $5.0 million and the recognized loss on the interest rate swap, which is included in interest and other expense, was $4.6 million and $0.4 million for the years ended December 31, 2008 and 2007, respectively.

10. Stockholders' Equity

Stock-based Compensation Plans

Stock Option Plans

The Company has two stock option plans under which it currently grants stock options: the 2001 Equity Incentive Plan, or the 2001 Plan, which replaced the 1991 Stock Option Plan, or the 1991 Plan, upon the 1991 Plan's expiration in October 2001, and the 2003 Non-Employee Directors' Stock Option Plan, or the 2003 Directors' Plan. Under the 2003 Directors' Plan, non-qualified stock options and restricted stock may be granted to non-employee directors of the Company. The 2003 Directors' Plan provides for automatic stock option grants to non-employee directors upon their initial appointment or election to the Company's Board of Directors and are issued from shares authorized under the 2001 Plan. Options granted under the 1991 Plan remain outstanding until exercised or cancelled.

10. Stockholders' Equity (Continued)

To date, stock-based compensation awards under the 1991 Plan, the 2001 Plan and the 2003 Directors' Plan consist primarily of incentive and non-qualified stock options. Stock options granted under the 2001 Plan and the 2003 Directors' Plan must have an exercise price equal to at least 100% of the fair market value of the Company's common stock on the date of grant, have a maximum contractual term of 10 years and generally vest over four years. At December 31, 2008, an aggregate of 24.2 million shares were reserved for future issuance under the Company's stock option plans, of which 5.6 million shares were available for future grants.

A summary of stock option transactions for all stock option plans is presented below:

	Shares (thousands)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (thousands)
Options outstanding at December 31, 2007 .	17,167	$27.67		
Granted	2,924	$25.44		
Exercised	(528)	$13.76		
Cancelled/Forfeited	(958)	$33.97		
Options outstanding at December 31, 2008 .	18,605	$27.39	5.47	$3,033
Options exercisable at December 31, 2008 .	12,496	$25.08	5.01	$3,000
Options vested and expected to vest	17,720	$27.11	5.41	$3,029

The total intrinsic value of stock options exercised was $8.4 million, $72.9 million and $74.8 million during the years ended December 31, 2008, 2007 and 2006, respectively. The Company received cash from the exercise of stock options of $7.3 million, $37.4 million, and $31.6 million during the years ended December 31, 2008, 2007 and 2006, respectively. The Company did not record any tax benefits related to the exercise of employee stock options due to its net loss position. Upon option exercise, the Company issues new shares of its common stock.

At December 31, 2008, total unrecognized estimated non-cash, stock-based compensation expense related to nonvested stock options granted prior to that date was $78.5 million, with a weighted-average amortization period of 2.2 years. The Company records non-cash, stock-based compensation expense for options with pro-rata vesting on a straight-line basis over the awards' vesting period.

Employee Stock Purchase Plan

The Company's 2001 Employee Stock Purchase Plan, or the 2001 Purchase Plan, enables participants to contribute up to 15% of their eligible compensation for the purchase of the Company's common stock at the lower of 85% of the fair market value of the Company's common stock (i) on the employee's enrollment date or (ii) the purchase date. The terms of any offerings under the 2001 Purchase Plan are established by the Compensation and Human Resources Committee of the Board of Directors. In May 2008, the Compensation and Human Resources Committee approved a series of four consecutive six-month offerings commencing on September 1, 2008. At December 31, 2008, 0.9 million shares were reserved for future issuance under the 2001 Purchase Plan.

10. Stockholders' Equity (Continued)

The total intrinsic value of purchase rights exercised was $1.7 million, $1.5 million and $10.4 million during the years ended December 31, 2008, 2007 and 2006, respectively. At December 31, 2008, total unrecognized non-cash, compensation expense for nonvested purchase rights granted prior to that date was $0.7 million, with a weighted-average amortization period of 0.2 years.

Shares Reserved for Future Issuance

The following shares of common stock are reserved for future issuance at December 31, 2008 (in thousands):

Stock Option Plans	24,188
Employee Stock Purchase Plan	950
Directors' Deferred Compensation Plan	4
401(k) Plan	104
Convertible Senior Notes	15,238
	40,484

Issuance of Common Stock

In April 2006, the Company completed a public offering of 11.5 million shares of its common stock at a price of $46.50 per share. This transaction generated net proceeds of approximately $508 million for the Company and was completed pursuant to a shelf registration statement filed with Securities and Exchange Commission in March 2006.

Shareholder Rights Plan

In June 2002, the Company adopted a Preferred Share Purchase Rights Plan (the "Rights Plan"). The Rights Plan provides for a dividend distribution of one preferred stock purchase right (a "Right") for each outstanding share of the Company's common stock, par value $0.001 per share, held of record at the close of business on June 28, 2002. The Rights are not currently exercisable. Under certain conditions involving an acquisition or proposed acquisition by any person or group of 15% or more of the Company's common stock, the Rights permit the holders (other than the 15% holder) to purchase one one-hundredth of a share of Series A Junior Participating Preferred Stock, par value $0.001 per share (the "Preferred Shares") at a price of $100 per one one-hundredth of a Preferred Share, subject to adjustment. Each one one-hundredth of a share of Preferred Shares has designations and powers, preferences and rights and the qualifications, limitations and restrictions which make its value approximately equal to the value of one share of the Company's common stock. Under certain conditions, the Rights are redeemable by the Company's Board of Directors in whole, but not in part, at a price of $0.001 per Right.

11. Benefit Plans

Defined Contribution 401(k) Plan

The Company has a defined contribution 401(k) plan for the benefit of all eligible employees. Discretionary matching contributions are based on a percentage of employee contributions and are funded by newly issued shares of the Company's common stock. The Company recorded expense of

11. Benefit Plans (Continued)

$5.1 million, $4.4 million and $6.0 million for matching contributions in the years ended December 31, 2008, 2007 and 2006, respectively.

Deferred Compensation Plans

In August 1997, the Company adopted a Non-Employee Directors' Deferred Compensation Plan (the "Directors' Deferral Plan") that permits participating non-employee directors to elect, on an annual basis, to defer all or a portion of their cash compensation in a deferred stock account, pursuant to which the deferred fees are credited in the form of phantom shares of the Company's common stock, based on the market price of the stock at the time the fees are earned. Deferred amounts are valued at the fair market value of the Company's common stock at each reporting date and are included in accrued compensation in the accompanying consolidated balance sheets. Upon termination of service the director's account is settled in either cash or stock, at the Company's discretion. The Company recorded a credit associated with this plan of $0.6 million for the year ended December 31, 2008, and recorded an expense associated with this plan of $0.8 million and $0.1 million for the years ended December 31, 2007 and 2006, respectively.

The Company adopted a Deferred Compensation Plan in April 2001, which allows officers and directors to defer up to 100% of their annual compensation. The trust assets, consisting of primarily cash, mutual funds and equity securities are recorded at current market prices. The company-owned assets are placed in a "rabbi trust" and are included in other current assets in the accompanying consolidated balance sheets. The trust assets had a fair value of $6.5 million and $9.3 million at December 31, 2008 and 2007, respectively, including unrealized losses of approximately $3.3 million at December 31, 2008 and unrealized gains of approximately $0.8 million at December 31, 2007. Unrealized gains and losses on the trust assets are included in accumulated other comprehensive loss in the accompanying consolidated balance sheets. The corresponding liability was $6.5 million and $9.3 million at December 31, 2008 and 2007, respectively, of which $6.3 million and $8.6 million are included in other long-term liabilities, net of current portion in the accompanying consolidated balance sheets at December 31, 2008 and 2007, respectively. The current portion of the corresponding liability is included in accrued compensation in the accompanying consolidated balance sheets at December 31, 2008 and 2007. Total contributions to this plan, consisting solely of compensation deferred by participants, were $1.7 million, $3.0 million and $1.0 million for the years ended December 31, 2008, 2007 and 2006, respectively.

Employee Stock Ownership Plan

In December 2007, the Company adopted the ESOP. Active employees who are at least 18 years old and have met minimum service requirements are eligible to participate. Each participant has an account with the ESOP, in which mandatory contributions of 10% of a participant's eligible compensation are made by the Company. The Company may make discretionary contributions for any plan year, and contributions are limited to the lesser of 100% of a participant's plan year compensation and limitations established by the Internal Revenue Service Code (IRS Code). A participant's compensation primarily includes wages and bonus.

Any cash dividends paid with respect to shares of the Company's stock allocated to a participant's account may be used to purchase new shares of the Company's stock, paid by the Company directly in cash to participants on a non-discriminatory basis. Any stock dividends paid with respect to shares of

11. Benefit Plans (Continued)

the Company's stock allocated to a participant's account will be held and distributed in the same manner as the shares of the Company's stock to which such stock dividend applies.

Participants vest in their accounts over four years of service, at 25% for more than one year of service but less than two years, at 50% for more than two years of service but less than three years, at 75% for more than three years of service but less than four years, and 100% for more than four years of service. Any forfeitures of non-vested amounts shall be used to restore any rehired employees who previously forfeited their nonvested balance under certain circumstances, or shall be used to reduce future employer contributions and shall be allocated to the participant accounts. Distributions are made upon termination of employment, when a participant is age 55 and has at least ten years of participation in the ESOP, when the participant is seventy and one-half and is not a five percent owner or the year after a participant is seventy and one-half and is a five percent owner, upon termination of the ESOP, and as necessary by regulatory requirements.

Shares committed to be released or that have been allocated to participant accounts are treated as outstanding shares for calculating earnings per share. The ESOP held 0.7 million shares at December 31, 2008, of which 0.4 million were unvested. The Company recorded ESOP expense of $20.2 million and $17.0 million at December 31, 2008 and 2007, respectively, for the Company's contribution, which is included in other current liabilities in the accompanying consolidated balance sheets.

12. Litigation

From time-to-time the Company becomes involved in various lawsuits, claims and proceedings relating to the conduct of our business, including those pertaining to product liability, patent infringement and employment claims. For example, the Company is currently involved in seven product liability cases, four of which have been stayed pending the U.S. Supreme Court's decision on federal preemption of such cases in *Wyeth v. Levine.* The Company has also been notified of additional claimants who may file product liability complaints. While the Company cannot predict the outcome of any lawsuit, claim or proceeding, the Company believes that the disposition of any current lawsuits is not likely to have a material effect on our financial condition or liquidity.

13. Income Taxes

We have net deferred tax assets relating primarily to net operating loss carry forwards and research and development tax credit carryforwards. Subject to certain limitations, these deferred tax assets may be used to offset taxable income in future periods. Since we have been unprofitable since inception and the likelihood of future profitability is not assured, we have reserved for most of these deferred tax assets in our consolidated balance sheets at December 31, 2008 and 2007, respectively. If we determine that we are able to realize a portion or all of these deferred tax assets in the future, we will record an adjustment to increase their recorded value and a corresponding adjustment to increase income or additional paid in capital, as appropriate, in that same period.

In July 2006, the FASB issued Interpretation No. 48 (FIN 48) *"Accounting for Uncertainty in Income Taxes—An Interpretation of FASB Statement No. 109."* FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an entity's financial statements in accordance with SFAS No. 109 and prescribes a recognition threshold and measurement attributes for financial statement disclosure of tax positions taken or expected to be taken on a tax return. Under FIN 48, the impact of

13. Income Taxes (Continued)

an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. Additionally, FIN 48 provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition.

We adopted the provisions of FASB Interpretation No. 48 and FSP FIN 48-1 effective January 1, 2007. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS No. 109, "Accounting for Income Taxes," and prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. We had no cumulative effect adjustment related to the adoption due to a full valuation allowance against deferred tax assets. We provide estimates for unrecognized tax benefits. These unrecognized tax benefits relate primarily to issues common among corporations in our industry. We apply a variety of methodologies in making these estimates which include advice from industry and subject experts, evaluation of public actions taken by the Internal Revenue Service and other taxing authorities, as well as our own industry experience. If our estimates are not representative of actual outcomes, our results could be materially impacted.

The provision (benefit) for income taxes includes the following (in thousands):

	Years ended December 31,		
	2008	2007	2006
Current (benefit) provision:			
Federal	$(657)	$ —	$—
State	38	38	—
Foreign	18	30	17
Total current (benefit) provision	(601)	68	17
Deferred (benefit) provision:			
Federal	—	—	—
State	26	(1,117)	—
Foreign	—	—	—
Total deferred (benefit) provision	26	(1,117)	—
Total (benefit) provision	$(575)	$(1,049)	$17

These amounts are included in interest and other expense in the accompanying consolidated statements of operations.

The current Federal income tax benefit reflects the refundable research credits net of alternative minimum taxes. The Housing and Economic Recovery Act of 2008 (P.L. 110-289), enacted on July 30, 2008, provides for the acceleration of a portion of unused pre-2006 research credits and alternative minimum tax credits in lieu of claiming the 50% bonus depreciation allowance enacted in the Economic Stimulus Act of 2008. Amylin is electing to refund approximately $1.0 million of research

13. Income Taxes (Continued)

credit carryovers in 2008. The $1.0 million of accelerated research credits have been reflected in the current income tax benefit net of alternative minimum taxes.

The deferred state income tax benefit in 2007 reflects the Texas margin tax (TMT) credit available to offset future margin taxes over the next 19 years. The Company estimates that its future TMT liability will be based on its gross revenues in Texas, rather than its apportioned taxable income. Therefore, it is more likely than not that the Company's TMT credit will be recovered and, accordingly, the Company has not established a valuation allowance against this asset.

Deferred income taxes reflect the temporary differences between the carrying amounts of assets and liabilities for financial statement purposes and the amounts used for income tax purposes and the net tax effects of net operating loss and credit carryforwards. Significant components of the Company's deferred tax assets as of December 31, 2008 and 2007 are shown below (in thousands). A valuation allowance of $694.3 million has been recognized at December 31, 2008 to offset the deferred tax assets, as realization of such assets has not met the more likely than not threshold under SFAS No. 109, *"Accounting for Income Taxes."* Included in the gross deferred tax assets below are pre-January 1, 2006 stock option deductions that, when recognized, are estimated to increase additional paid in capital by $22.4 million.

	2008	2007
Deferred tax assets:		
Net operating loss carryforwards	$ 409,376	$ 412,349
Research tax credits	61,839	58,845
Capitalized research and development expenses	83,564	54,253
Accrued expenses	58,242	36,826
Deferred revenue	49,192	2,919
Stock compensation expense	27,440	18,011
Other, net	5,705	3,060
Total deferred tax assets	695,358	586,263
Valuation allowance for deferred tax assets	(694,267)	(585,146)
Net deferred tax assets	$ 1,091	$ 1,117

The net deferred tax assets are included in other long-term assets in the accompanying consolidated balance sheets.

13. Income Taxes (Continued)

Following is a summary of the Company's Federal net operating loss carryforwards, Federal research tax credit carryforwards and California net operating loss carryforwards at December 31, 2008 (in thousands):

	Federal net operating loss carryforwards	California net operating loss carryforwards	Federal research and development tax credit carryforwards
Expiring within one year	$ —	$ —	$ 1,732
After 1 but within 5 years	717	25,949	3,307
After 5 but within 10 years	29,966	579,506	2,312
After 10 years	1,136,017	—	52,404
	$1,166,700	$605,455	$59,755

Changes in control have occurred that triggered the limitations of Section 382 of the Internal Revenue Code on the Company's net operating loss carryforwards. The Section 382 limitations were immaterial to the Company's total net operating losses and are reflected in the net operating loss of $1.2 billion presented above.

At December 31, 2008, the Company had Federal net operating loss carryforwards of approximately $1.2 billion, which begin to expire at the end of 2011. The Company also has California net operating loss carryforwards of $605.5 million, which begin to expire at the end of 2011, and other state net operating loss carryforwards of approximately $181.8 million, which begin to expire at the end of 2010. The difference between the Federal and California tax loss carryforwards is attributable to the capitalization of research and development expenses for California tax purposes, the prior years' limitation on California loss carryforwards and apportionment of losses to other states. The Company has Federal research tax credit carryforwards of $59.8 million, which begin to expire at the end of 2009, and California research tax credit carryforwards of $29.0 million, which carry forward indefinitely.

The reconciliation between the Company's effective tax rate and the federal statutory rate is as follows:

	Tax rate for the years ended December 31,		
	2008	2007	2006
Federal statutory rate applied to net loss before income tax (benefit) provision	(35.0)%	(35.0)%	(35.0)%
State taxes	(1.6)%	—	(4.0)%
Research and development tax credits	(0.8)%	(3.0)%	(3.2)%
Stock-based compensation	3.1%	4.2%	4.6%
Increase in valuation allowance	34.5%	30.9%	35.1%
Other	(0.4)%	2.4%	2.5%
Effective tax rate	(0.2)%	(0.5)%	—%

The state tax effects during 2007 include the expiration of state net operating loss carryforwards.

13. Income Taxes (Continued)

As a result of the adoption of SFAS No. 123R, the Company recognizes windfall tax benefits associated with the exercise of stock options directly to stockholders' equity only when realized. Accordingly, deferred tax assets are not recognized for net operating loss carryforwards resulting from windfall tax benefits occurring from January 1, 2006 onward. A windfall tax benefit occurs when the actual tax benefit realized upon an employee's disposition of a share-based award exceeds the deferred tax asset, if any, associated with the award. At December 31, 2008, deferred tax assets do not include $44 million of excess tax benefits from stock-based compensation.

Income taxes paid during the years ended December 31, 2008, 2007 and 2006 totaled $63 thousand, $30 thousand and $17 thousand, respectively.

The reconciliation of the total amounts of unrecognized tax benefits at the beginning and end of the years ended December 31, 2008 and 2007 is as follows (in thousands):

	December 31,	
	2008	2007
Reconciliation of unrecognized tax benefits:		
Unrecognized tax benefits related to reductions in tax credits as of the beginning of the year	$ 29,913	$23,645
Decrease in unrecognized tax benefits related to reductions in tax credits as a result of tax positions taken during a prior period	(11,711)	339
Increase in unrecognized tax benefits related to reductions in tax losses and credits as a result of tax positions taken during the current period	4,239	5929
Unrecognized tax benefits related to reductions in tax credits as of the end of the year	$ 22,441	$29,913

The balance of unrecognized tax benefits at December 31, 2008 of $22.4 million are tax benefits that, if recognized, would not affect the Company's effective tax rate as long as they remain subject to a full valuation allowance. The net effect on the deferred tax assets and corresponding decrease in the valuation allowance at December 31, 2008 resulting from unrecognized tax benefits is $15.1 million. The Company has not recognized any accrued interest and penalties related to unrecognized tax benefits during the years ended December 31, 2008, 2007 and 2006. The Company is subject to taxation in the United States and various states and foreign jurisdictions. Effectively, all of the Company's historical tax years are subject to examination by the Internal Revenue Service and various state and foreign jurisdictions due to the generation of net operating loss and credit carryforwards. The Company does not foresee any material changes to unrecognized tax benefits within the next twelve months. The Company will elect a treatment for interest and penalties when they occur.

14. Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods.

14. Quarterly Financial Data (Unaudited) (Continued)

Summarized quarterly data for fiscal 2008 and 2007 are as follows (in thousands, except per share data):

	For the quarters ended			
	March 31	June 30	September 30	December 31
2008:				
Net product sales	$178,721	$200,335	$201,364	$ 184,922
Revenues under collaborative agreements	18,516	21,684	16,998	17,569
Gross profit from product sales	156,697	175,653	177,969	163,427
Restructuring	—	—	—	54,926
Net loss	(68,797)	(64,816)	(77,721)	(104,071)
Basic and diluted net loss per share(1)	$ (0.51)	$ (0.47)	$ (0.57)	$ (0.76)
2007:				
Net product sales	$162,003	$167,337	$177,391	$ 194,719
Revenues under collaborative agreements	9,975	29,616	12,637	27,319
Gross profit from product sales	146,793	152,975	163,641	172,584
Net loss	(49,414)	(45,023)	(39,758)	(76,941)
Basic and diluted net loss per share(1)	$ (0.38)	$ (0.34)	$ (0.30)	$ (0.57)

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per-share calculations will not necessarily equal the annual per share calculation.

AMYLIN PHARMACEUTICALS, INC

Schedule II: Valuation Accounts

(in thousands)

	Balance at beginning of period	Additions	Deductions	Balance at end of period
Year ended December 31, 2008				
Inventory reserve	$ 5,327	7,196	7,422	$ 5,101
Accounts receivable allowances(1)	$12,769	34,996	32,724	$15,041
Year ended December 31, 2007				
Inventory reserve	$ 385	7,637	2,695	$ 5,327
Accounts receivable allowances(1)	$ 6,558	27,787	21,576	$12,769
Year ended December 31, 2006				
Inventory reserve	$ 1,618	3,481	4,714	$ 385
Accounts receivable allowances(1)	$ 1,628	17,203	12,273	$ 6,558

(1) Allowances for prompt payment, product returns, doubtful accounts and wholesaler chargebacks.

BOARD OF DIRECTORS

Joseph C. Cook, Jr.
Chairman of the Board, Amylin Pharmaceuticals, Inc.
Mr. Cook has been a director since 1994 and is a former Chief Executive Officer of Amylin Pharmaceuticals, Inc. He has been Chairman of the Board since March 1998 and serves on the Finance Committee.

Daniel M. Bradbury
President and Chief Executive Officer, Amylin Pharmaceuticals, Inc.
Mr. Bradbury has been a director since June 2006 and serves on the Finance Committee.

Adrian Adams
President and Chief Executive Officer, Sepracor, Inc.
Mr. Adams has been a director since October 2007 and serves as Chair of the Compensation and Human Resources Committee.

Steven R. Altman
President, QUALCOMM, Inc.
Mr. Altman has been a director since March 2006.

Teresa Beck
Former President and Chief Financial Officer, American Stores Company
Ms. Beck has been a director since March 2007 and serves on the Audit Committee.

Karin Eastham
Former Executive Vice President and Chief Operating Officer, Burnham Institute for Medical Research
Ms. Eastham has been a director since September 2005 and serves as Chair of the Audit Committee and on the Compensation and Human Resources Committee.

James R. Gavin III, MD, PhD
Clinical Professor of Medicine at Emory University School of Medicine
Dr. Gavin has been a director since December 2005 and serves as Chair of the Corporate Governance Committee.

Ginger L. Graham
Former Chief Executive Officer, Amylin Pharmaceuticals, Inc.
Ms. Graham has been a director since November 1995 and serves on the Finance Committee.

Jay S. Skyler, MD
Professor of Medicine, Pediatrics and Psychology, University of Miami
Dr. Skyler has been a director since August 1999 and serves on the Corporate Governance Committee.

Joseph P. Sullivan
Chairman of the Board of Advisors, RAND Health & Chairman of the Board of Advisors, UCLA Medical Center
Mr. Sullivan has been a director since September 2003 and serves as Chair of the Finance Committee and on the Audit Committee.

James N. Wilson
Lead Independent Director, Amylin Pharmaceuticals, Inc.
Chairman of the Board, Corcept Therapeutics, Inc.
Mr. Wilson has been a director since March 2002 and serves on the Compensation and Human Resources Committee and on the Corporate Governance Committee.

EXECUTIVE COMMITTEE

Daniel M. Bradbury
President and Chief Executive Officer

Mark G. Foletta
Senior Vice President, Finance and Chief Financial Officer

Mark J. Gergen
Senior Vice President, Corporate Development

Orville G. Kolterman, MD
Senior Vice President, Research and Development

Marcea B. Lloyd
Senior Vice President, Government & Corporate Affairs and General Counsel

Roger Marchetti
Senior Vice President, Human Resources & Information Management

Paul Marshall
Senior Vice President, Operations

Vincent P. Mihalik
Senior Vice President, Sales and Marketing and Chief Commercial Officer

Request for Information

A copy of Amylin Pharmaceuticals Inc.'s annual report to the Securities and Exchange Commission on Form 10-K, including financial statements and financial statement schedules, can be found on the Company's corporate website at www.amylin.com. To have this information mailed to you free of charge, please contact:

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Production Notes

This annual report was printed on paper that is FSC-certified and SFI-certified. The cover and narrative papers are PEFC-certified and made with 10% post-consumer waste recycled fibers. The financial paper is made with Elemental Chlorine Free (ECF) virgin fiber content.

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