



AMYLIN PHARMACEUTICALS, INC.  
ANNUAL REPORT 2004





Challenging Science.  
Changing Lives.

# MESSAGE TO SHAREHOLDERS



GINGER L. GRAHAM  
PRESIDENT AND CHIEF EXECUTIVE OFFICER



JOSEPH C. COOK, JR.  
CHAIRMAN OF THE BOARD

**FOR AMYLIN PHARMACEUTICALS, 2004 WAS A YEAR OF MAJOR ACCOMPLISHMENT** We achieved all of our development milestones as planned, including the submission of a New Drug Application to the U.S. Food and Drug Administration (FDA) for regulatory approval of exenatide, a new treatment in development for type 2 diabetes. We also submitted a complete response to the FDA's second approvable letter for SYMLIN®, an adjunctive therapy to insulin for the treatment of type 1 and insulin-using type 2 diabetes. **WE ARE VERY PLEASED TO REPORT THAT SYMLIN** was approved by the FDA in March 2005 as a first-in-class therapy, and our second first-in-class drug candidate, exenatide, is under FDA review, with an action date in April. We prepared for product launches throughout 2004 and continued to expand our commercial capabilities to support the supply of two new diabetes medicines. We believe the launch of SYMLIN and our anticipated launch of exenatide will not only provide exceptional opportunity for our company and our shareholders, but also redefine traditional thinking about the progression of diabetes, the treatment continuum, and patient care. **DIABETES IS A COMPLEX METABOLIC DISEASE** and a global epidemic affecting more than 18 million people in the United States alone. Because more than 60 percent of patients are not meeting their glucose control targets, they risk severe long-term complications such as kidney failure, nerve damage, blindness, amputation, and cardiovascular disease. By discovering, developing and delivering innovative, life-changing therapies that improve glucose

control, we can help physicians change outcomes for these patients, and ultimately enhance the lives of millions of people worldwide. **SYMLIN® (PRAMLINTIDE ACETATE) INJECTION** Approved by the FDA on March 16, 2005, SYMLIN is a synthetic version of the naturally occurring hormone amylin, which is produced in the pancreas and co-secreted with insulin. Both hormones are deficient in people with advanced diabetes, and we believe that for many people who require insulin, SYMLIN can be an important addition in managing their diabetes. **ABOUT 4.5 MILLION PEOPLE IN THE UNITED STATES** are currently using insulin, and approximately 20,000 doctors write 50% of the prescriptions. Our medical education and marketing efforts will focus on these physicians, explaining the potential benefits of SYMLIN therapy for insulin-using patients, and the appropriate management techniques to aid patients as they add SYMLIN to their existing therapy regimens. At this writing, we estimate product launch by July 1, 2005, and we look forward with great enthusiasm to bringing this new therapy to the patients who might benefit. **EXENATIDE** The New Drug Application for exenatide was submitted on June 29, 2004, and accepted for FDA review. We were notified that the FDA does not expect to hold an advisory committee meeting for exenatide, and we expect a response to our application by April 30, 2005. Exenatide is a synthetically produced compound that, in humans, stimulates the body's own production of insulin, but only in the presence of elevated blood sugar. As blood sugar drops below normal, exenatide's effects

essentially shut down, and there is no drug currently available to patients that does this. **THE CLINICAL COMPONENT OF OUR NDA** was based on 30-week data from three blinded pivotal trials involving more than 1,400 patients with type 2 diabetes who were unable to control their blood sugar on common oral therapies, including metformin, sulfonylurea, or a combination of the two. We also included data from open-label studies, including 52-week data from our pivotal trial extensions. **AS A ROUTINE FOLLOW-UP**, we subsequently submitted a 120-day safety update, demonstrating a consistent safety profile at one year with what we had observed at 30 weeks. We believe that the clinical data from more than 29 studies, completed or in progress, demonstrate a robust and durable response to this new therapy. **WE BEGAN OUR CLINICAL STUDIES OF EXENATIDE** in 1998 and initiated our Phase 3 clinical trials more than three years ago. We now have about 900 patients who have received exenatide for over one year and almost 400 who have been on the therapy for 18 months or longer. The total number of patients receiving exenatide has increased to more than 2,000, and patient years of exposure have reached approximately 1,800. **POSITIONED FOR LAUNCH** In preparing to launch two new diabetes compounds into one of the world's largest healthcare markets, we built an operations organization designed to ensure high quality manufacturing, reliable delivery, and consistent product availability. The new organization includes supply chain management, manufacturing, quality control, distribution,

customer service and technical support. **WE HAVE FINALIZED OUR MARKETING AND SALES PLANS**, including the recruiting process, and expect to add 300–350 experienced field personnel to our existing staff. In April 2004, we signed an agreement with Reliant Pharmaceuticals, Inc. to co-promote Reliant's cardiovascular products to a target group of endocrinologists, which has allowed us to retain our specialty sales force and maintain established physician relationships as we waited for the potential launch of our diabetes compounds. Full commercialization of SYMLIN will include the deployment of our own field organization. To support the launch of exenatide, Eli Lilly and Company, our partner in its development and commercialization, will provide additional field resources. **WE STRENGTHENED OUR FINANCIAL POSITION** with a \$200 million convertible debt placement completed in April 2004, and also received a development milestone payment of \$5 million from Lilly, based on the completion and analysis of a six-month study comparing exenatide with insulin glargine, a human insulin analog. We finished the year with \$293.8 million in cash and, through an equity offering in the first quarter of 2005, netted an additional \$190.5 million. **MOVING FORWARD** The launch of one new first-in-class compound in 2005—and the anticipated launch of another—is a major milestone for Amylin in the development of innovative therapies for both type 1 and type 2 diabetes. We believe this will be a solid platform for continuing growth, as we leverage our science not only to advance diabetes care, but also to develop

new treatments for obesity and cardiovascular disease. In 2004, we completed two clinical studies of potential therapies for obesity, and submitted an Investigational New Drug Application for heart failure. (See details on pages 26–29.) Three Phase 2 clinical studies are now in progress, including a multi-dose study of exenatide LAR (long-acting release) in patients with type 2 diabetes; a study to evaluate AC137 (pramlintide) for obesity; and the AC2592 (GLP-1) study for congestive heart failure. **IN MOVING FORWARD**, our priorities are clear: build a commercial capability that will ensure strong and successful product launches and continuously increasing product acceptance among healthcare professionals

and patients; advance our Phase 2 programs as quickly as possible with good science; and continue expanding our leadership team and talent pool to keep pace with the future growth of our business. **IN THE FINAL ANALYSIS**, our business is healthcare. That's a privilege shared by all of us at Amylin, and a privilege that we treasure. Our science is driving the development of new and emerging therapies with the potential to improve the quality of life and extend the lives of millions of people around the globe. That's what we're all about at Amylin: **CHALLENGING SCIENCE. CHANGING LIVES.** Thank you for your continued support.



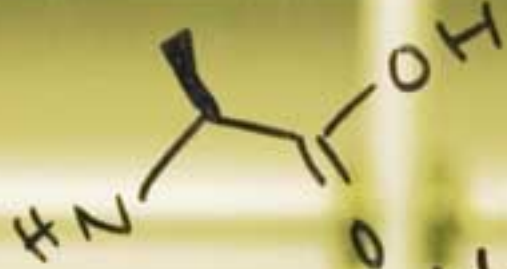
JOSEPH C. COOK, JR.  
CHAIRMAN OF THE BOARD



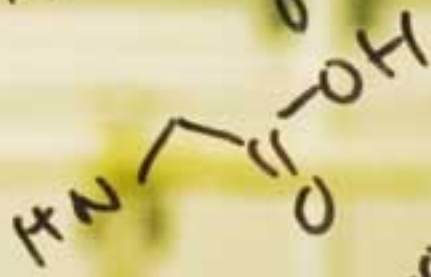
GINGER L. GRAHAM  
PRESIDENT AND CHIEF EXECUTIVE OFFICER

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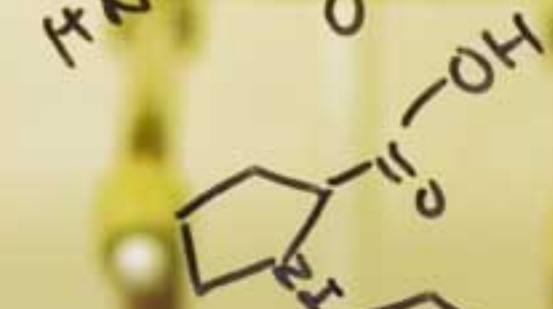
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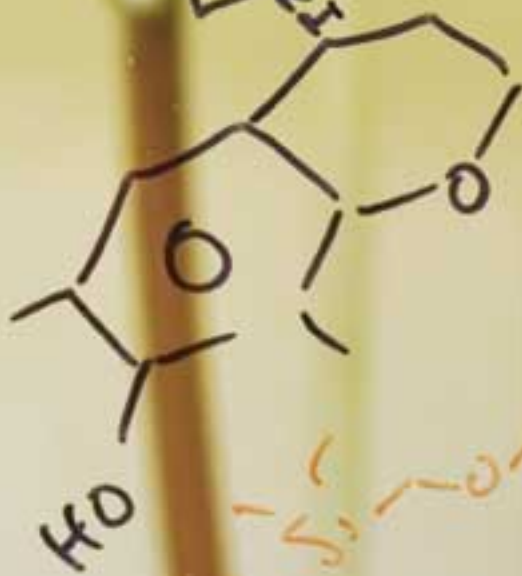
Gly



Pro



CHALLENGING SCIENCE



The discovery and development of peptide hormones with life-changing therapeutic potential is a difficult and demanding process. It depends on an open-minded approach with no preconceptions, unwavering perseverance, and a willingness to challenge scientific dogma and conventional wisdom. Perhaps most importantly, it requires a different way of thinking about what could be a drug, and how that drug could be developed.

**STANDARD DRUG DEVELOPMENT** Sequencing of the human genome and the gene accumulation that followed have enabled the pharmaceutical industry to accelerate its pace of drug development by focusing on specific molecular “targets” that have already been described. Compounds or molecules are screened against these targets in the search for potential drug candidates, but despite a high-throughput process, only one out of 10,000 actually hit the target. Some of these are eliminated because of toxicity shown in animal testing, and of those nominated, approximately 90% fail when they’re put into man. Even after regulatory approval, some of these are beleaguered by unforeseen risk factors and withdrawn from the market.

**TAKING A DIFFERENT APPROACH** Amylin has taken an integrated biological rather than target-driven approach. Research is centered on peptide hormones that play an important metabolic role, and are considered more likely to have an acceptable safety profile because they’ve existed in the human body for millions of years. The development path begins with identifying a particular peptide structurally defined as a molecular chain of amino acids – and determining that it is a circulating hormone, a substance that travels through the bloodstream to affect bodily functions. Understanding

its functionality and its potential impact on disease becomes the next challenge, and it’s formidable. As opposed to starting with a known biology and targeting it with molecules to modify, enhance, or block it, Amylin scientists are discovering biology – the biology of peptides previously unknown – and, within that biology, uncovering the utility, and translating that into a potential new therapy that could change patient lives.

**MOVING QUICKLY TO MAN** While the conventional development process emphasizes isolated cells or molecular targets in drug discovery, Amylin scientists quickly move to *in vivo* testing. From their highly predictive animal models, they design information-rich clinical trials, which they believe are the only way to truly determine the potential pharmaceutical benefit in humans.

**THE FIRST-IN-CLASS CHALLENGE** Because Amylin is developing innovative new compounds without precedents, long-established regulatory guidelines may not apply. Regulatory science is challenged to develop a new set of rules for molecules and mechanisms of action that hadn’t been seen before, and to establish a new roadmap to approval. The developmental path is typically smoother for drugs that are second or third or fourth in their class, but in pharmaceutical development, the reward is usually commensurate with the challenge. And challenge is the business of Amylin – the challenging science of changing lives.





**ALAIN D. BARON, M.D.**  
SENIOR VICE PRESIDENT, RESEARCH

Dr. Baron's numerous honors for research in diabetes and vascular disease include a National Institutes of Health MERIT award and the Outstanding Clinical Investigator Award from the American Federation for Medical Research. He earned his M.D. from the Medical College of Georgia and completed postdoctoral studies at the University of California, San Diego, where he is currently an adjunct professor of medicine. He is co-editor of a diabetes textbook, and had been professor of medicine and director, Division of Endocrinology and Metabolism, at the Indiana University School of Medicine. He formerly held academic positions in the Division of Endocrinology and Metabolism at the University of California, San Diego.





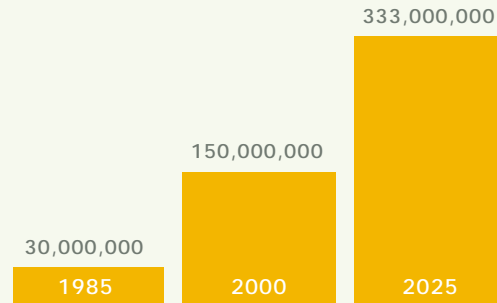
CHANGING LIVES

MORE THAN  
**18 MILLION**  
AMERICANS  
HAVE  
**DIABETES**

# MORE THAN 5 MILLION DON'T KNOW IT YET

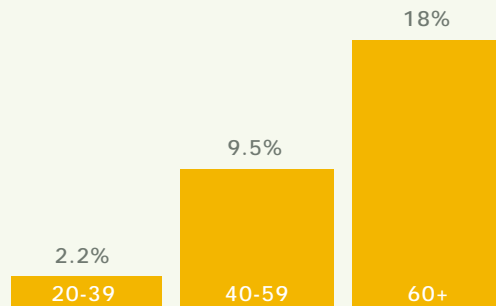
## A GROWING EPIDEMIC

In just 15 years, the number of people estimated to have diabetes climbed from 30 million to 150 million worldwide, and an increase to approximately 333 million is projected by 2025.



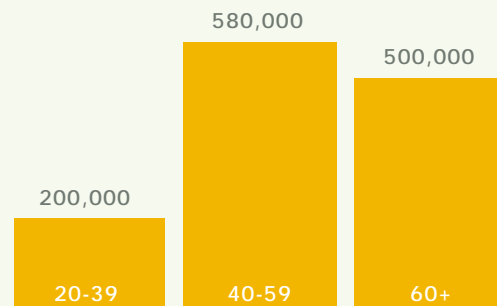
International Diabetes Federation

## TOTAL PREVALENCE OF DIABETES IN PEOPLE AGED 20 YEARS OR OLDER, BY AGE GROUP UNITED STATES, 2002



Centers for Disease Control and Prevention

## NUMBER OF NEW CASES OF DIAGNOSED DIABETES IN PEOPLE AGED 20 YEARS OR OLDER, BY AGE GROUP UNITED STATES, 2002



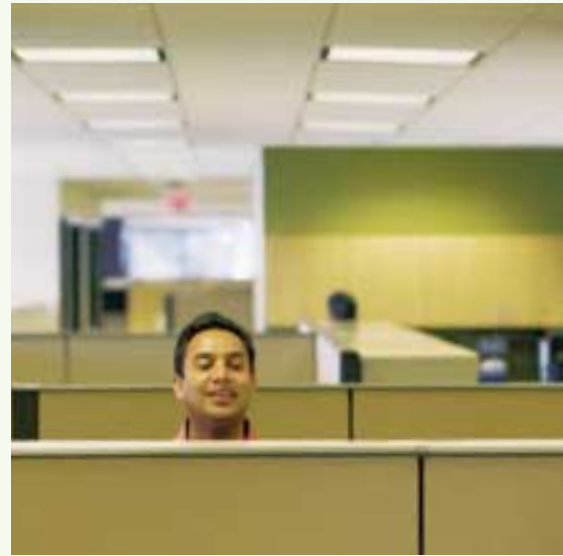
Centers for Disease Control and Prevention

**THERE ARE CURRENTLY ALMOST 200 MILLION PEOPLE WITH DIABETES WORLDWIDE**—more than the entire populations of Argentina, Australia, Saudi Arabia, South Africa and Spain combined. This is a global epidemic of major proportion and, if nothing is done to slow its growth, the number of people suffering from diabetes is expected to exceed 330 million by 2025. **THE UNITED STATES HAS THE WORLD'S THIRD LARGEST POPULATION WITH DIABETES**, following India and China. It is estimated that 6.3% of the U.S. population—18.2 million people—have diabetes, and 5.2 million, or nearly one-third, are unaware of it. On average, 1.3 million new cases are diagnosed annually, and the total annual economic cost to the nation is estimated at \$132 billion, or one out of every 10 health-care dollars. **A METABOLIC DISEASE** Diabetes is a complex disorder of carbohydrate, fat and protein metabolism. In type 1 diabetes, accounting for 5-10% of all Americans who have the disease, the body is unable to produce insulin, a hormone secreted by the beta cells of the pancreas, needed to convert sugar, starches and other foods into energy. Type 2 diabetes, the most common form of the disease, reflects a combination of relative insulin deficiency, due to beta cell failure, and insulin resistance, an inability to use the hormone properly. **LACK OF GLUCOSE CONTROL** In people with diabetes, not enough glucose can enter and fuel the body's cells. Consequently, glucose increases in the blood stream, causing hyperglycemia (high blood sugar), which can lead to serious complications. At the other end of the spectrum is hypoglycemia (low blood sugar), usually caused by an excess of insulin in the bloodstream. People managing their

diabetes with insulin injections are especially vulnerable to the swings of high to low, and the risk of very low blood sugar, which can cause life-threatening situations. **MEDICAL COMPLICATIONS** The risk of stroke and heart disease is 2–4 times higher among people with diabetes, and about 65% die because of these illnesses. Diabetes is the leading cause of blindness among adults, and the leading cause of treated end-stage kidney disease, accounting for 43% of new cases. From 60% to 70% of people with diabetes suffer some level of nervous system damage, and severe forms are a major contributing cause of lower-extremity amputations. Diabetes, in fact, is the most common cause of amputation not resulting from accidents. **UNKNOWN CAUSE** Although the cause of diabetes remains unknown, both genetic and environmental factors such as obesity and lack of exercise seem to play a role in this chronic and pervasive illness, which has become America's sixth leading cause of death. **LIFE-CHANGING THERAPIES** Unfortunately, there is no known cure for diabetes, but Amylin scientists are discovering and developing innovative new treatments that are designed to improve the lives, and possibly extend the lives, of millions of people worldwide living with diabetes and other metabolic disorders. These potential advancements in the treatment of diabetes, obesity and congestive heart failure are highlighted on the pages that follow.

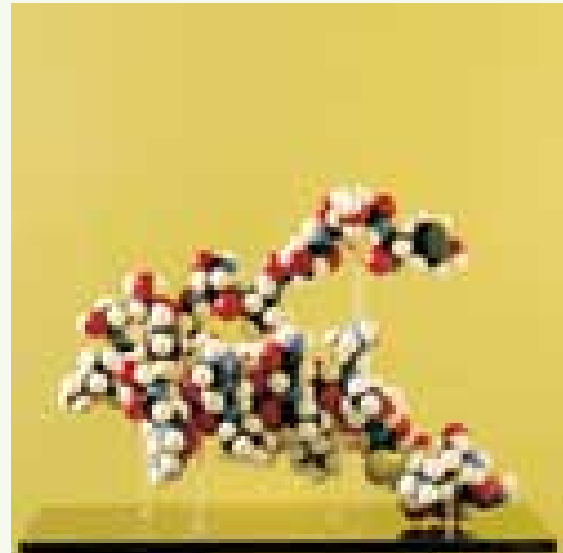
Sources: American Diabetes Association and International Diabetes Federation





**ORVILLE G. KOLTERMAN, M.D.**  
SENIOR VICE PRESIDENT, CLINICAL AFFAIRS

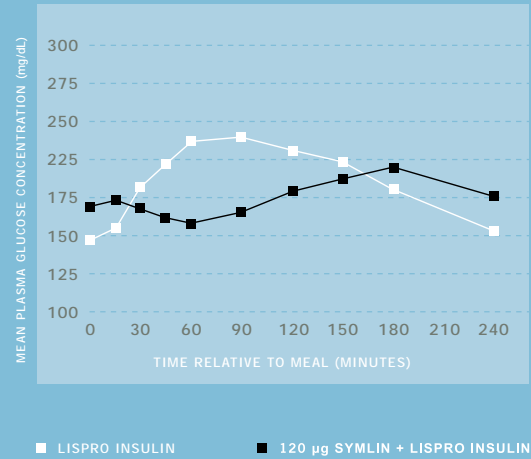
In addition to his current position with Amylin, Dr. Kolterman is adjunct professor of medicine at the University of California, San Diego. For nearly a decade he had been program director, General Clinical Research Center, and medical director, Diabetes Center, at the University of California, San Diego Medical Center. He was a principal investigator for the Diabetes Control and Complications Trial Study Group, and is a current member of the Epidemiology of Diabetes Intervention and Complications Study. He is past president of the California Affiliate of the American Diabetes Association, and earned his M.D. from the Stanford University School of Medicine.



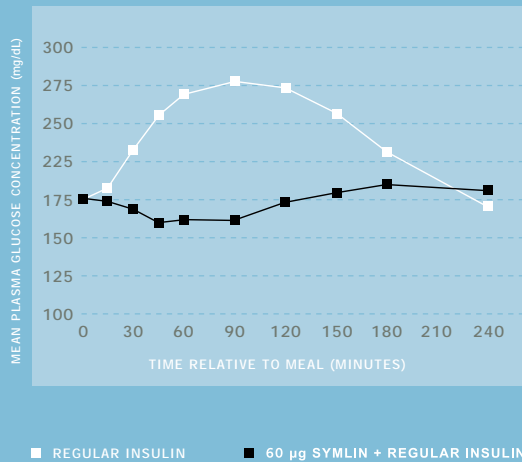
APPROVED BY THE FDA IN  
MARCH 2005 AS AN ADJUNCTIVE  
THERAPY TO INSULIN IN TREATING  
DIABETES, **SYMLIN<sup>®</sup>** HELPS  
**PATIENTS REDUCE FLUCTUATIONS  
OF BLOOD GLUCOSE LEVELS  
AND ACHIEVE BETTER LONG-TERM  
GLUCOSE CONTROL THAN WHEN  
USING INSULIN ALONE.**

# POSTPRANDIAL PLASMA GLUCOSE REDUCTIONS IN PATIENTS WITH TYPE 2 AND TYPE 1 DIABETES ON SYMLIN WITH INSULIN COMPARED TO INSULIN ALONE

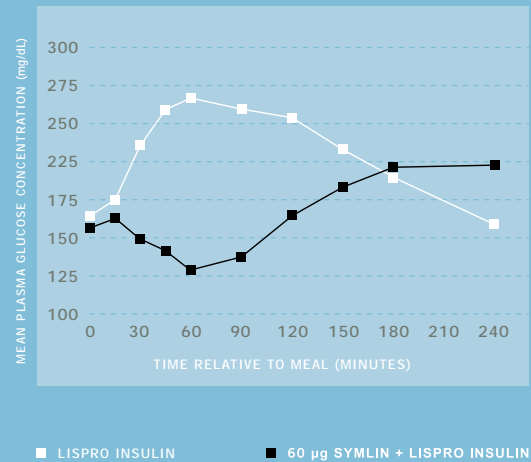
## LISPRO INSULIN: TYPE 2 PATIENTS



## REGULAR INSULIN: TYPE 1 PATIENTS



## LISPRO INSULIN: TYPE 1 PATIENTS



**SYMLIN® (PRAMLINTIDE ACETATE) INJECTION** is a synthetic version of the naturally occurring human peptide hormone amylin, which is co-secreted with insulin by the beta cells of the pancreas. In people with diabetes, both of these hormones are deficient, but, while insulin was extracted from a human pancreas and administered to a patient as early as 1922, amylin remained completely unknown until the mid-1980s. Because it was produced and released by pancreatic beta cells, it appeared to have some connection with metabolism and diabetes, but its function and utility were mysteries waiting to be solved. **AMYLIN PHARMACEUTICALS HAS BEEN HAS FOCUSED ON THIS COMPOUND FOR THE PAST 18 YEARS**, and with continuous research and uncommon tenacity, the company's scientists have discovered its functionality as a partner to insulin and the critical role it plays in glucose control. By changing its molecular structure, they improved its properties and transformed it into a new pharmaceutical called SYMLIN, a first-in-class adjunctive therapy to insulin, approved by the FDA on March 16, 2005. In the clinical program leading to its approval, SYMLIN demonstrated its safety and efficacy in treating more than 5,300 individuals, including patients with type 1 diabetes and patients with type 2 diabetes who use insulin. Patient years of exposure now exceed 3,000. **IMPROVED GLUCOSE CONTROL** Insulin controls blood glucose by accelerating the rate at which glucose leaves the bloodstream to enter muscle cells and other tissues. The natural hormone amylin—and its synthetic version, SYMLIN—slows the rate at which glucose enters the blood following meals. Both actions work together to better

manage the swings in blood sugar. Perhaps this analogy explains it best: the water level in a swimming pool is controlled by two different valves. One controls the amount and speed of water entering the pool (amylin/SYMLIN); the other controls how much is allowed to drain away (insulin). **MAJOR LANDMARK STUDIES OF DIABETES** have shown that maintaining good glucose control reduces the risk of long-term complications. But research has also shown that approximately 75% of people with diabetes who are using insulin—4.5 million in the United States alone—are not achieving adequate control. **MOMENT-TO-MOMENT FLUCTUATIONS** Average glucose levels in the bloodstream are measured by HbA1c (A1C), an integrated biochemical value that reflects average blood glucose over the previous three months. People without diabetes typically have A1C measurements of 4-6%, and the American Diabetes Association recommends that people with diabetes work to keep their A1C measurements below 7% to reduce the risks of complications. A1C is a measure of averages over time; however, it provides no indication of moment-to-moment glucose levels in the bloodstream. Even in well-managed patients, these can fluctuate dramatically, causing a continuing series of micro-episodes of both hyperglycemia and hypoglycemia, which patients feel impairs their sense of well-being. But when amylin—the second “missing hormone” in diabetes patients—is replaced by SYMLIN, the fluctuations in blood sugar are reduced significantly. A self-administered injection of SYMLIN prior to meals helps patients achieve lower blood glucose levels after meals, leading to less fluctuation during the day and better long-term glucose control.

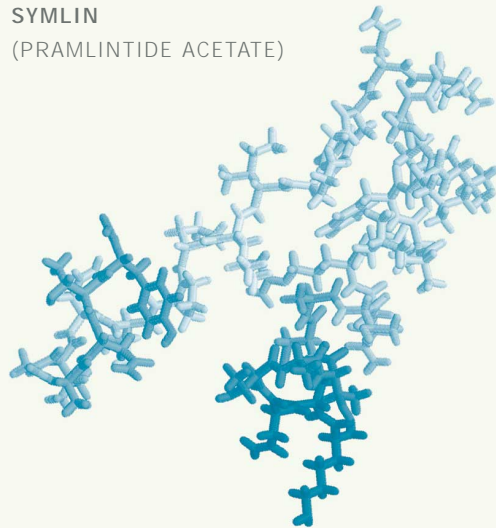
**A NEW PARADIGM FOR DIABETES TREATMENT** According to reports from patients using insulin, improving the stability and predictability of blood glucose levels leading to more consistent glycemic control can lift a psychological burden, allowing greater peace of mind, sounder sleep, and an increased sense of well-being. When SYMLIN is part of the treatment regimen, less insulin is required. And because SYMLIN also sends a satiety signal to the brain, patients experience a decrease in appetite, which can lead to weight loss rather than the weight gain typically associated with insulin therapy. SYMLIN is used with insulin and has been associated with an increased risk of insulin-induced severe hypoglycemia, but 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. **THE COMPANY'S HIGHLY TARGETED** marketing efforts, with a strong educational component, are focused on endocrinologists, diabetologists, and other healthcare professionals who understand insulin therapy and can assist patients in adding SYMLIN to their existing insulin regimens. Acceptance of this first-in-class therapy, 100% owned by Amylin Pharmaceuticals, is expected to build over time as patients understand its benefit in providing better glucose control without weight gain, and physicians adopt this new paradigm in the treatment and management of diabetes.

#### **MOLECULAR REDESIGN**

Changing the molecular structure of native amylin eliminated the formation of amyloid fibrils, highly aggregated protein that, when accumulated, can be extremely disruptive to some human tissues. This was part of the process of transforming a natural substance into a first-in-class pharmaceutical.

**SYMLIN**  
(PRAMLINTIDE ACETATE)







**CRAIG A. EBERHARD**  
VICE PRESIDENT, SALES

With 23 years of experience in pharmaceutical sales and sales management, Craig Eberhard has recruited, trained and supervised sales directors and managers; developed and implemented market-specific sales and promotional initiatives for new and established products; and directed numerous national product launches and market expansions. Prior to joining Amylin, he had been a vice president of sales for Pharmacia Corporation, where he led the sales launch of Detrol LA, which achieved market leadership in just three months and drove market growth from \$60 million to \$1 billion in three years. Mr. Eberhard holds a B.S. in biology from California Lutheran University.



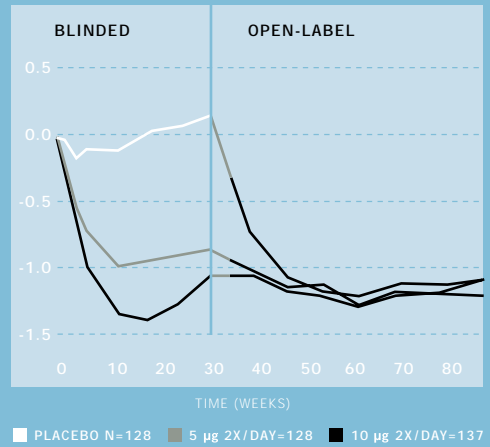
**EXENATIDE** IS A POTENTIAL FIRST-IN-CLASS THERAPY THAT INCREASES INSULIN SECRETION ONLY WHEN BLOOD GLUCOSE IS HIGH, ESSENTIALLY PROVIDING SELF-REGULATING CONTROL FOR TYPE 2 DIABETES. **THERE IS NO DRUG AVAILABLE TO PATIENTS THAT DOES THIS.**

## EXENATIDE SHOWED DURABLE EFFECT ON A1C

SUBJECTS COMPLETING 82 WEEKS

COMBINED BASELINE A1C = 8.3%  
COMPLETER POPULATION (N=393) AT 82 WEEKS

## CHANGE IN A1C FROM BASELINE (%)

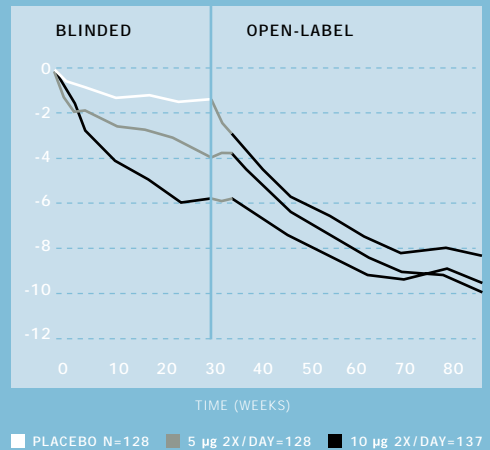


## EXENATIDE SHOWED DURABLE EFFECT ON WEIGHT

SUBJECTS COMPLETING 82 WEEKS

COMBINED BASELINE BODY WEIGHT = 218.3 LBS;  
COMPLETER POPULATION (N=393) AT 82 WEEKS

## CHANGE IN BODY WEIGHT FROM BASELINE (LBS)



**ABOUT 15 YEARS AGO**, scientists began to recognize the potential value of a naturally occurring human hormone, glucagon-like peptide 1 (GLP-1), in treating people with type 2 diabetes. These patients have a deficiency of GLP-1, which is normally secreted in the intestinal tract and plays an important role in the body's regulation of blood glucose. Most importantly, GLP-1's action on insulin secretion is glucose dependent: it increases the body's ability to secrete its own insulin, but only when blood sugar (glucose) levels are normal or high. When blood glucose is low, its effects essentially shut down, minimizing the possibility of hypoglycemia (low blood sugar), a common problem with a number of diabetes therapies, including insulin. **THE PROBLEM WITH GLP-1** is that the hormone degrades within a few minutes of entering the bloodstream and, if used as a therapy, would require continuous infusion. The challenge was to discover a longer-lasting, degradation-resistant version, and many major pharmaceutical companies entered the search. Despite their best efforts, the development of a man-made compound to mimic the effect of GLP-1 remained elusive. **A NATURAL SOLUTION** The animal kingdom is rich in evolutionary biology: genes that seem to have originated from a common ancestor; and structures that correspond in origin and function to structures of other species, like the flippers of a seal and human hands. Substances are found in the lower classes of vertebrates that are related to the hormones of mammals, and some of those may make better pharmaceuticals than their mammalian counterparts. Exenatide is a case in point. **EXENATIDE IS A SYNTHETIC**

**VERSION OF A NATURALLY OCCURRING PEPTIDE** that was originally isolated from the saliva of the Gila monster, a three-to-five pound lizard found throughout the southwestern United States and northern Mexico. It mimics certain actions of GLP-1, but its effects last much longer. **NINE YEARS IN DEVELOPMENT** From molecular exploration to clinical studies, Amylin scientists have worked for nine years in developing exenatide, a potential new therapy for type 2 diabetes. Exenatide is expected to be the first in a new class of compounds known as incretin mimetics that exhibit many of the same effects as GLP-1. With other therapies, improved blood sugar control is often accompanied by weight gain, but studies have shown that in patients unable to achieve acceptable control using common oral medications, exenatide significantly lowered average blood sugar levels and also resulted in reduced body weight. **PHASE 3 CLINICAL TRIALS**, begun late in 2001, included approximately 1,400 patients with type 2 diabetes, who were failing to control their blood glucose levels with either one of the two most frequently prescribed oral agents, metformin and sulfonylurea, or a combination of both. Among these patients, the average A1C—the standard measurement of blood glucose—was about 8.4% at the beginning of the trial. When exenatide was added to the treatment regimen, A1C was reduced by approximately 1%, a statistically significant improvement. During the 30-week studies, approximately 40% of these patients reached the treatment goal of 7%. In addition, with no diet or exercise counseling, patients also experienced an average weight loss of approximately four pounds.

**THE MOST COMMON ADVERSE EFFECTS** were mild to moderate nausea, which tended to dissipate with time. Dropouts due to nausea were 3% in the exenatide groups, compared to less than 1% for placebo. Mild to moderate hypoglycemia was also observed, primarily in conjunction with sulfonylurea therapy, known to induce that condition.

**ADDITIONAL STUDIES** A six-month study was completed comparing exenatide and insulin glargine, a long-acting insulin used in type 2 diabetes patients failing to achieve glycemic control with multiple oral agents. Exenatide demonstrated equivalent effects in lowering A1C, and did so in a context of weight loss, while patients on insulin experienced weight gain. **SINCE THE FIRST PHASE 1 CLINICAL STUDY IN 1998**, the total number of people receiving exenatide has exceeded 2,000, and patient years of exposure have climbed to approximately 1,800. Additional clinical trials to further increase understanding of exenatide's potential patient benefits are currently being pursued, as are studies directed toward international approvals. **GOING TO MARKET** The company will go to market with an expanded sales force, and a national recruitment effort is expected to add 300-350 new personnel to its field organization. Together with the sales representatives of Eli Lilly and Company, Amylin's collaborator on the development and commercialization of exenatide, they will provide coast-to-coast coverage of the highly concentrated market for oral therapies, where about 70% of all prescriptions are written by approximately 65,000 physicians. In addition, a specialized staff will call on managed care organizations, pharmacy benefit

management organizations and government agencies. A medical education program has been developed, manufacturing capacity has been secured, and a 24/7 customer service call center is already in place. **EXENATIDE LAR** Because of exenatide's potency, relatively long half-life and glucose-dependent action, it is well suited for a long-acting release formulation, which could increase the opportunity for more type 2 diabetes patients to benefit from this new therapy. Amylin and Lilly are currently working with Alkermes, Inc. on exenatide LAR, a formulation that would allow patients to shift from twice-daily injections to a single injection once a week. A Phase 2 single-dose study has demonstrated sustained exenatide release with no dose-limiting side effects, and the injection was well tolerated. A Phase 2 multi-dose study was initiated in the first quarter of 2005.

AMYLIN IS LEVERAGING  
ITS STRENGTH IN METABOLIC  
MEDICINE AND DEEP  
UNDERSTANDING OF PEPTIDE  
HORMONES TO LEAD THE WAY  
IN CONTROLLING **OBESITY**  
THROUGH AN **INNOVATIVE AND  
UNIQUE NEW APPROACH.**

**OBESITY IS A GLOBAL EPIDEMIC** increasing at an alarming rate worldwide. In the United States, the number of obese adults has continued to increase since 1960, and this complex and chronic disease now affects nearly one-third of the adult population, about 60 million people. Associated with more than 30 medical conditions, obesity is known to increase the risk of high blood pressure, type 2 diabetes, heart disease, stroke, and cancer of the breast, prostate, and colon. According to the American Obesity Association, healthcare costs of American adults with obesity amount to over \$100 billion annually. The human cost is incalculable—obesity is the second leading cause of preventable deaths in the United States.

**LEVERAGING SCIENCE** Amylin scientists are leveraging their deep understanding of peptide hormones—their function and utility at normal levels (physiology) and at various concentrations (pharmacology)—to develop innovative new therapies designed to control obesity. The company's obesity programs are a direct outgrowth of the experience gained in developing potential first-in-class medicines for diabetes and, in particular, the consistent observation of weight loss among clinical study subjects with type 1 or type 2 diabetes who were overweight.

**METABOLIC REMODELING** Hormones play a critical role in adjusting the processes that help the body achieve homeostatic balance, an internal equilibrium that promotes healthy survival. Controlled functions not only include heartbeat, blood pressure and respiration, but also body weight. The regulatory network establishes a set point for normal weight, like the temperature selection on a thermostat, and the body fights to maintain it. In

individuals with obesity, the metabolic balance is set at the wrong level, leading to significant weight gain. Amylin scientists believe that hormone intervention at highly concentrated levels can reset the “thermostat,” a process termed “metabolic remodeling.” Amylin is leading the way in pursuing this unique approach to obesity control.

**CLINICAL STUDIES** The company has two obesity programs currently in development. A Phase 1 dose-rising safety study for a naturally occurring human peptide called PYY 3-36 was completed in 2004, as well as a Phase 2 dose-escalation study of pramlintide (the same compound contained in SYMLIN). The pramlintide study was designed to evaluate the safety and tolerability of progressively higher doses in 200 obese subjects with and without diabetes. At 16 weeks, 31% of patients on pramlintide had achieved a 5% or greater weight loss. Approximately 90% of those receiving pramlintide were able to progress to the highest dose of 240 micrograms three times daily; the most common side effect was mild transient nausea. A Phase 2 dose-ranging study will be conducted in 2005.

FOCUSED ON METABOLIC SOLUTIONS RATHER THAN MECHANICAL, AMYLIN IS DEVELOPING A PROMISING NEW TREATMENT FOR **HEART FAILURE**, WHICH COULD BECOME ANOTHER **FIRST-IN-CLASS DRUG THERAPY** IN ITS PRODUCT PORTFOLIO.

**ACCORDING TO THE AMERICAN HEART ASSOCIATION**, there are about 5 million heart failure patients in the United States, and 550,000 new cases are diagnosed every year. For people aged 65 or older, heart failure is the leading cause of hospitalization, affecting approximately 10 out of every 1,000 people in this age group. **ALSO KNOWN AS CONGESTIVE HEART FAILURE**, this is a serious condition in which the heart muscle gradually weakens and becomes increasingly unable to pump enough blood to meet the body's need for oxygen. Inefficient pumping often results in congestion of the lungs, and the heart responds by trying to work harder, which only exacerbates the problem. **PROGRESSIVE AND LIFE THREATENING** Heart failure steadily worsens over time and symptoms become increasingly severe. These include shortness of breath and difficulty breathing, swelling in the legs and ankles, and a pervasive feeling of weakness so that everyday activities like climbing a flight of stairs become exhausting. Based on symptom severity, the New York Heart Association has classified heart failure into four categories. In class 3, patients have difficulty participating in mildly strenuous activities and are comfortable only when resting. In class 4, they are unable to do any physical activity without discomfort and experience symptoms even at rest. The ability of the heart muscle to pump continues to deteriorate, and no cure has been discovered. **IMPROVING HEART EFFICIENCY** To improve the quality of life and, hopefully, extend the lives of millions of heart failure patients, Amylin scientists are building on their experience with incretin hormones to discover a new solution for improved heart efficiency.

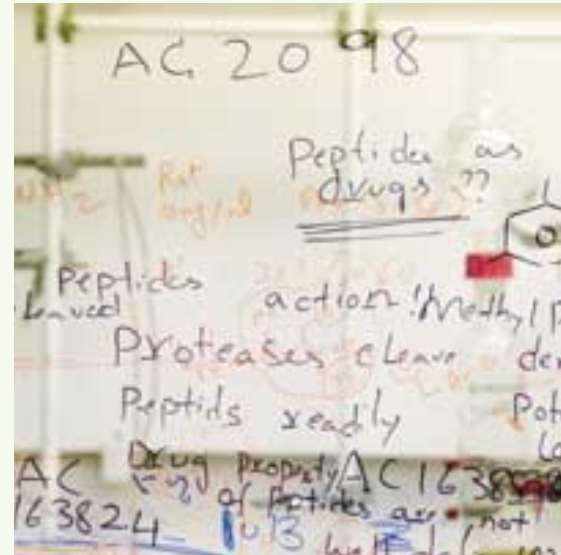
They believe that high levels of a naturally occurring human hormone, glucagon-like peptide 1 (GLP-1), can switch the energy fuel the heart uses from fat to glucose, leading to an improved heartbeat and pumping function—not because the heart is working any harder, but because it's working more efficiently. By taking a metabolic rather than mechanical approach, they are developing a promising new treatment and a potentially first-in-class therapy for heart failure. **ADVANCING THE PROGRAM** In 2004, Amylin submitted an Investigational New Drug Application to the FDA for AC2592 (synthetic GLP-1), as a potential therapy for congestive heart failure, delivered as continuous infusion. In the fourth quarter, the company initiated a Phase 2 clinical study of this new drug candidate, which will enroll approximately 180 subjects with advanced heart failure (New York Heart Association classes 3 and 4) on two different doses of GLP-1 versus placebo. The primary endpoint is peak oxygen consumption; secondary endpoints include various measures of quality of life and cardiac function. Results are expected in late 2005 or early in 2006.

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**AMYLIN PHARMACEUTICALS** is built on a process of continuous discovery: uncovering the therapeutic potential of novel peptide hormones; improving the performance of peptides as therapeutics; and developing new indications designed to change the lives of millions of patients. Identifying previously unknown peptide hormones, discovering their biologic utility and ultimately their therapeutic potential is a challenging approach to biopharmaceutical development, but Amylin is prepared to meet that challenge. **A UNIVERSE TO DISCOVER** Based on a premise that every peptide hormone has a utility—and a potential therapeutic benefit—Amylin has developed a proprietary and continually growing peptide hormone library (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. **THE SNOWBALL EFFECT** The expanding knowledge base at Amylin is a powerful engine for growth. Proprietary knowledge gained through one discovery can be transferred to the next. And the development of one single platform—a patented peptide hormone—brings an opportunity for multiple indications, products forms, and delivery systems. All of the company's current Phase 2 studies are leveraging previous discoveries, so that the risk of a major safety failure or other roadblock to these downstream development programs is significantly less than what might typically be expected because the molecules under investigation have already been clinically

studied. Pramlintide, the same compound contained in SYMLIN (approved for diabetes), is now being studied at different doses and in a different patient population as an anti-obesity drug. Exenatide is being developed in a long-acting release form, and the experience gained from its development for the treatment of diabetes is being leveraged into the GLP-1 program for heart failure. **THE OPPORTUNITY PIPELINE** Because type 2 diabetes, obesity, and congestive heart failure each have multiple causes, there are many potential therapeutic paths that could have significant impact. There are three classifications of obesity, for instance, and a different product form or therapy could be considered for each subtype. There are also variations in patient responses that could drive product modifications, and therapies involving energy expenditure and absorption that have yet to be explored. Advancements in delivery technologies are also providing opportunity and, in addition to the long-acting release form of exenatide now under study, the company is also investigating the feasibility of other means of delivery, such as nasal, transdermal, inhalation and oral delivery systems. **CONTINUOUS LEARNING** Amylin scientists are convinced that peptide hormones are naturally good therapeutics that could be targeted to any number of diseases. What they see at any given moment is the disease space they're working in, but the exploration and mastery of that space brings them to the next level. And based on the learning that has gone before, they can see a whole new horizon.





**MICHAEL R. HANLEY, PH.D.**  
**VICE PRESIDENT, DISCOVERY RESEARCH**

Dr. Hanley served on Amylin's Scientific Advisory Board for more than a decade prior to joining the company full time. He previously held senior tenured faculty positions at Imperial College (London), the Medical Research Council Laboratories (Cambridge), and the University of California at Davis Medical School, where he was professor of biological chemistry. He has served on advisory or review panels for the National Institutes of Health, the National Science Foundation, the UK Medical Research Council, World Health Organization and the governments of Australia, Denmark, Hong Kong, Japan, New Zealand, and Singapore. His A.B. in biochemistry and Ph.D. in molecular biology are from the University of California, Berkeley.



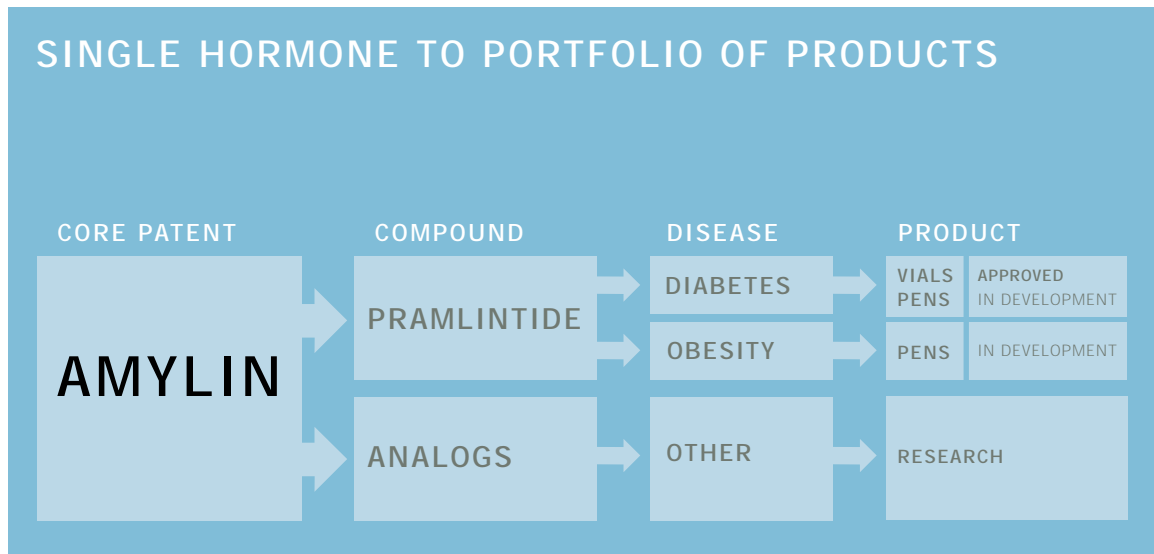
**SCALING THE PROCESS** Amylin has scaled the process of biologic discovery, and the company's scientists are doing the kind of work that is done at a much slower pace in academic settings. They are discovering the physiology and functionality of peptide hormones and at the same time optimizing molecules to improve their physical and chemical properties and suitability as pharmaceuticals. A wide range of practical commercial considerations—like shelf life, stability in transport, or suitability for drug delivery—must be addressed early in the development process. Through intelligent molecular design and proprietary methods, Amylin scientists are altering the structures of these naturally occurring substances and transforming them into potential drug candidates for commercialization.

**RAMPING UP FOR HIGH PRODUCTION** In preparing for two potential first-in-class product launches in 2005, the company aligned all functional areas involved in delivering its new therapies to physicians, healthcare professionals, and patients. The newly formed operations organization includes supply chain management, manufacturing, quality control, distribution, customer service and technical support. Manufacturers have been selected, contracted and audited, and their processes have been validated in accordance with cGMP (current Good Manufacturing Practices) and Amylin specifications. The company's commercial manufacturing team has been deployed to all manufacturing sites to ensure that each operation meets Amylin objectives for repeatable, reliable and consistent production that will maintain product quality, integrity and efficacy. **BUILDING THE COMMERCIAL ORGANIZATION** Amylin currently has more than 50 specialty sales representatives in the field,

calling on the nation's leading diabetes experts and covering clinics and practices that treat large numbers of patients with diabetes. The company expects to add another 300-350 highly qualified, clinically educated professionals to its national field organization, and its human resource and sales management professionals are currently working with a major recruitment firm in identifying and contacting those individuals. In addition, Eli Lilly and Company, Amylin's partner in exenatide's development and commercialization, will deploy a sales force and co-promote the compound. The Lilly sales force will expand the reach to several thousand additional healthcare professionals. Sales calls will target endocrinologists, diabetologists, and primary care physicians. Managed care organizations, pharmacy benefit management organizations, state Medicaid organizations and federal government offices (Veterans Administration hospitals, military installations and penal institutions) will be covered by Amylin's managed care directors. At the same time, the company's medical science liaisons will focus on clinical investigators, academicians and other thought leaders, while diabetes clinical liaisons, who are certified diabetes educators, will work with their clinical counterparts in diabetes specialty centers. **MARKETING SUPPORT** Medical education will be a major priority, and initiatives will include a series of satellite symposia, featuring some of the nation's leading physicians; locally based speakers programs in major population centers; product literature for healthcare professionals; web-based programs for physicians and patients; and a 24/7 customer call center that is already in place.

**MULTIPLICITY** Hormones, by definition, have multiple actions, a strong indicator of multiple potential utilities. That's why just one of these compounds can often be used in the treatment of several diseases to benefit a variety of patient populations. New product forms and alternative delivery systems can lead to a multiplicity of product life cycles, all beginning with the patent estate of one discovery.

EVERY NEW  
DISCOVERY  
IS ANOTHER  
PLATFORM  
FOR GROWTH



## 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. He has been Chairman of the Board since March 1998 and serves as chair of the Finance Committee.



**GINGER L. GRAHAM** PRESIDENT AND CHIEF EXECUTIVE OFFICER, AMYLIN PHARMACEUTICALS, INC. Ms. Graham has been a director since November 1995 and serves on the Finance Committee. She is a former Group Chairman, Office of the President for Guidant Corporation.



**VAUGHN D. BRYSON** CHIEF EXECUTIVE OFFICER, ELI LILLY AND COMPANY (RETIRED). Mr. Bryson has been a director since July 1999 and serves as chair of the Nominating and Governance Committee and on the Compensation and Human Resources Committee.



**HOWARD E. (TED) GREENE, JR.** COFOUNDER, AMYLIN PHARMACEUTICALS, INC. Mr. Greene is former Chief Executive Officer of Amylin Pharmaceuticals, Inc. and has been a director since September 1987. He serves on the Audit Committee and the Finance Committee.



**TERRANCE H. GREGG** PRESIDENT, MEDTRONIC MINIMED (RETIRED) Mr. Gregg has been a director since October 2001 and serves on the Compensation and Human Resources Committee and the Nominating and Governance Committee.



**JAY S. SKYLER, M.D.** PROFESSOR OF MEDICINE, PEDIATRICS AND PSYCHOLOGY, UNIVERSITY OF MIAMI Dr. Skyler has been a director since August 1999.



**JOSEPH P. SULLIVAN** CHAIRMAN OF THE BOARD OF ADVISORS, RAND HEALTH Mr. Sullivan has been a director since September 2003 and serves on the Audit Committee and the Finance Committee.



**THOMAS R. TESTMAN** MANAGING PARTNER, ERNST & YOUNG LLP (RETIRED) Mr. Testman has been a director since December 2002 and serves as chair of the Audit Committee.



**JAMES N. WILSON** CHAIRMAN OF THE BOARD, CORCEPT THERAPEUTICS INCORPORATED Mr. Wilson has been a director since March 2002 and serves as chair of the Compensation and Human Resources Committee and on the Nominating and Governance Committee.

# EXECUTIVE MANAGEMENT



**GINGER L. GRAHAM**  
PRESIDENT AND CHIEF EXECUTIVE  
OFFICER



**DANIEL M. BRADBURY**  
CHIEF OPERATING OFFICER



**ALAIN D. BARON, M.D.**  
SENIOR VICE PRESIDENT,  
RESEARCH



**MARTIN R. BROWN**  
SENIOR VICE PRESIDENT,  
HUMAN RESOURCES AND  
CORPORATE SERVICES



**JOANN L. DATA, M.D., PH.D.**  
SENIOR VICE PRESIDENT,  
REGULATORY AFFAIRS AND  
QUALITY ASSURANCE



**DWAYNE M. ELWOOD**  
SENIOR VICE PRESIDENT,  
MARKETING



**ORVILLE G. KOLTERMAN, M.D.**  
SENIOR VICE PRESIDENT,  
CLINICAL AFFAIRS



**CRAIG A. EBERHARD**  
VICE PRESIDENT, SALES



**MARK G. FOLETTA, CPA**  
VICE PRESIDENT, FINANCE AND  
CHIEF FINANCIAL OFFICER



**MICHAEL R. HANLEY, PH.D.**  
VICE PRESIDENT,  
DISCOVERY RESEARCH



**JONI HARVEY**  
VICE PRESIDENT, TECHNICAL  
OPERATIONS



**RICHARD A. HILES, PH.D.**  
VICE PRESIDENT, NONCLINICAL  
DRUG SAFETY/BIOANALYTICAL



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VICE PRESIDENT, MEDICAL AFFAIRS



**LISA E. PORTER, M.D.**  
VICE PRESIDENT,  
CLINICAL DEVELOPMENT



**LLOYD A. ROWLAND**  
VICE PRESIDENT, LEGAL, SECRETARY  
AND GENERAL COUNSEL



**GREGG STETSKO, PH.D.**  
VICE PRESIDENT, OPERATIONS



**ANDREW A. YOUNG, M.D., PH.D.**  
VICE PRESIDENT AND SENIOR  
RESEARCH FELLOW



## MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is traded on The Nasdaq National 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 National Market:

	HIGH	LOW
<b>YEAR ENDED DECEMBER 31, 2004</b>		
Fourth Quarter	\$ 24.01	\$ 18.80
Third Quarter	23.25	16.48
Second Quarter	26.80	19.69
First Quarter	25.63	18.49
<b>YEAR ENDED DECEMBER 31, 2003</b>		
Fourth Quarter	\$ 30.40	\$ 21.30
Third Quarter	30.75	20.95
Second Quarter	26.86	15.47
First Quarter	17.95	13.73

The last reported sale price of our common stock on The Nasdaq National Market on March 1, 2005 was \$20.71. As of March 1, 2005, there were approximately 850 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.

## 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.

(IN THOUSANDS, EXCEPT FOR PER SHARE AMOUNTS)	YEARS ENDED DECEMBER 31,				
	2004	2003	2002	2001	2000
<b>CONSOLIDATED STATEMENTS OF OPERATIONS DATA:</b>					
Revenue under collaborative agreements	\$ 34,268	\$ 85,652	\$ 13,395	\$ —	\$ —
Expenses:					
Research and development	119,558	149,431	94,456	49,601	33,807
Selling, general and administrative	66,958	56,761	25,334	20,469	10,716
Acquired in-process research and development	—	3,300	—	—	—
	186,516	209,492	119,790	70,070	44,523
Net interest and other income (expense)	(4,909)	1,032	(3,392)	(1,902)	480
Net loss	(157,157)	(122,808)	(109,787)	(71,972)	(44,043)
Net loss per share — basic and diluted	\$ (1.67)	\$ (1.33)	\$ (1.39)	\$ (1.09)	\$ (0.71)
Shares used in calculating net loss per share — basic and diluted	94,054	92,396	79,106	65,927	61,644
<b>CONSOLIDATED BALANCE SHEETS DATA:</b>					
Cash, cash equivalents and short-term investments	\$ 293,756	\$ 269,776	\$ 147,358	\$ 46,574	\$ 82,899
Working capital	282,421	243,144	92,368	47,188	78,380
Total assets	357,800	311,045	168,545	63,527	90,635
Long-term obligations	403,233	202,425	88,234	58,073	52,103
Accumulated deficit	(797,496)	(640,339)	(517,531)	(407,744)	(335,772)
Total stockholders’ equity (deficit)	(87,370)	63,216	12,298	(3,483)	31,286

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

**OVERVIEW** Amylin Pharmaceuticals, Inc. is a biopharmaceutical company engaged in the discovery, development and commercialization of drug candidates for the treatment of diabetes, obesity and cardiovascular disease. We have one approved product, SYMLIN® (pramlintide acetate) Injection, and one late-stage drug candidate, exenatide, under regulatory review in the United States.

SYMLIN is the first in a new class of compounds called amylinomimetics and is a synthetic version of human amylin, a hormone co-secreted with insulin in normal physiology. On March 16, 2005, the United States Food and Drug Administration, or FDA, approved SYMLIN to be used in conjunction with insulin to treat diabetes. SYMLIN is to be used at mealtime in patients with type 2 or type 1 diabetes who have failed to achieve desired glucose control despite optimal insulin therapy. We expect that SYMLIN will be commercially available by July 1, 2005.

Exenatide is the first in a new class of compounds known as incretin mimetics. We are developing exenatide, including both twice-daily and sustained-release formulations, with Lilly to improve glucose control in patients with type 2 diabetes who are not achieving target glucose levels with metformin and/or sulfonylureas, two of the most commonly used oral therapies to treat type 2 diabetes, pursuant to a global development and commercialization agreement entered into in 2002. Our agreement with Lilly provides for equal sharing of exenatide operating profits in the United States. Operating profits outside of the United States are split 80% to Lilly and 20% to us. We submitted a New Drug Application, or NDA, to the FDA for the twice-daily formulation of exenatide

in June 2004 and we expect the FDA to respond to this filing by April 30, 2005.

Our pipeline includes a Phase 2 program for each of the therapeutic areas of diabetes, obesity and cardiovascular disease. Additionally, we have two Phase 1 programs and maintain a discovery research program focused on peptide therapeutics. We are actively seeking to in-license additional drug candidates.

In 2005 we are preparing to expand our organization to support the commercial launch of SYMLIN, and the planned launch of exenatide, pending regulatory approval. This planned expansion will require a significant investment in our commercial capabilities, including the addition of approximately 300-350 field personnel, including our sales force, and medical affairs and managed care personnel, and increased medical education activities. The majority of this planned growth in our commercial capabilities will be required to support the commercial launch of exenatide, if approved. In addition, we anticipate expanding our business infrastructure in 2005 to support these activities. We also intend to continue our investment in our research and development programs, as more fully described below under the heading "Research and Development Programs."

Since our inception in September 1987, we have devoted substantially all of our resources to our research and development programs. All of our revenues to date have been derived from fees and expense reimbursements under our exenatide collaboration agreement with Lilly, previous SYMLIN collaborative agreements and co-promotion agreements with each of Lilly and Reliant Pharmaceuticals, Inc. We

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

have not received any revenues from the sale of any of our drug candidates. We have been unprofitable since inception and expect to incur additional operating losses for at least the next few years. As of December 31, 2004, our accumulated deficit was approximately \$797.5 million.

At December 31, 2004, we had approximately \$294 million in cash, cash equivalents and short-term investments. In February 2005 we completed a public offering of our common stock, generating net proceeds to us of approximately \$190.5 million. We do not expect to generate positive

operating cash flows for at least the next few years and accordingly, we will need to raise additional funds from outside sources. Refer to the discussion under the heading "Liquidity and Capital Resources" for further discussion regarding our anticipated future capital requirements.

**RESEARCH AND DEVELOPMENT PROGRAMS** Currently, our research and development efforts are focused on programs for the treatment of diabetes, obesity and cardiovascular disease in various stages of development as summarized in the following table:

PHASE OF DEVELOPMENT	COMPOUND	PROPOSED INDICATION
COMMERCIALIZATION	SYMLIN® (pramlintide acetate) INJECTION	Insulin-using type 2 and type 1 diabetes*
REGULATORY REVIEW	EXENATIDE	Type 2 diabetes
PHASE 2	EXENATIDE LAR AC137 (pramlintide acetate) AC2592 (GLP-1)	Type 2 diabetes Obesity Late-stage congestive heart failure
PHASE 1	AC162352 (PYY 3-36) AC3056	Obesity Atherosclerosis

\*approved March 16, 2005

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 exenatide and exenatide LAR. As we continue to expand our pipeline, our investment in our other programs will continue to increase.

The drug development process, from discovery through regulatory approval, takes an average of 12 years according to recent industry reports. The process includes several steps defined by the FDA. The process begins with discovery and preclinical evaluation leading up to the submission of an investigational new drug application, or IND, to the FDA, which allows for the initiation of the clinical evaluation in

humans of a drug candidate. 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, as these trials are typically the longest and largest trials 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 labels 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 expenses are comprised of salaries and benefits; costs paid to third-party contractors to perform research, conduct clinical trials, develop and manufacture drug materials and delivery devices; and a portion of our 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 overall 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 provides information regarding our research and development expenses for our major projects (in millions):

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
SYMLIN	\$ 15.8	\$ 27.3	\$ 17.3
Exenatide	40.0	80.1	47.7
Phase 2 programs	22.1	7.8	—
Early stage programs and research	12.2	12.2	15.7
Unallocated	29.5	22.0	13.8
	<b>\$ 119.6</b>	<b>\$ 149.4</b>	<b>\$ 94.5</b>

**SYMLIN** On March 16, 2005, the FDA approved SYMLIN to be used in conjunction with mealtime insulin to treat diabetes. Following commercial availability of SYMLIN, our planned 2005 development efforts will include the commencement of a controlled, open label study to evaluate SYMLIN use in clinical practice in up to 2,000 patients over two years.

The timing of material net cash inflows from SYMLIN is dependent upon market acceptance following its planned commercial launch by July 1, 2005.

**EXENATIDE** Our 2004 development activities for exenatide included the continuation of ongoing open-label studies, additional clinical studies to both support regulatory filings outside of the United States and increase our understanding of exenatide's market potential in the United States and elsewhere, preparation of our NDA filing with the FDA and the continuation of manufacturing scale-up. In July 2004, we

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

announced the results from a six-month clinical study that compared exenatide and insulin glargine in patients failing to achieve acceptable glycemic control with common oral therapies. In connection with the results of this study we received a \$5 million milestone payment from Lilly.

Our 2005 development activities for exenatide are planned to include the continuation of ongoing studies to support regulatory filings outside of the United States and the continuation of an ongoing study in patients who are currently not achieving target blood glucose concentrations using thiazolidinediones, or TZDs, another common oral therapy used to treat type 2 diabetes. In addition, we have additional clinical research that we intend to pursue for label expansion following regulatory approval, if received.

The timing of material net cash inflows from our exenatide development program is dependent upon regulatory approvals and subsequent market acceptance.

**PHASE 2 PROGRAMS** We currently have a Phase 2 program in each of the therapeutic areas of diabetes, obesity and cardiovascular disease. In diabetes, we are studying exenatide LAR, a sustained-release formulation of exenatide. We recently initiated a Phase 2 multi-dose study of exenatide LAR, utilizing a once-a-week dosing regimen. This study was initiated following the review of data from a Phase 2 single-dose study completed in early 2005. We are developing exenatide LAR in collaboration with Lilly and Alkermes.

In obesity, we are studying AC137 (pramlintide acetate), the same compound contained in SYMLIN. Following the review of data from a 16-week Phase 2 study completed in 2004, we are preparing to commence a Phase 2b dose-ranging study of AC137 in 2005. In cardiovascular disease, we have a Phase 2 program for AC2592 (GLP-1) for the treatment of congestive heart failure. We submitted an IND for AC2592 in the second half of 2004 and initiated a Phase 2 study in the fourth quarter of 2004.

**EARLY-STAGE PROGRAMS AND RESEARCH** In addition to our late stage development programs in diabetes and our Phase 2 programs in diabetes, obesity and cardiovascular disease, we also have two Phase 1 programs. We are studying AC162352 (PYY 3-36) for potential utility as a treatment for obesity. We are studying AC3056 for the treatment of atherosclerosis-related cardiovascular disease. We also maintain a discovery research program focused on peptide therapeutics and we are actively seeking to in-license additional drug candidates.

### RESULTS OF OPERATIONS

**REVENUE UNDER COLLABORATIVE AGREEMENTS** Revenue under collaborative agreements was \$34.3 million in 2004, compared to \$85.7 million in 2003 and \$13.4 million in 2002. Substantially all of the revenue recorded in these periods consists of amounts earned pursuant to our collaboration agreement with Lilly for exenatide.

The following table summarizes the components of revenues under collaborative agreements for the years ended December 31, 2004, 2003 and 2002 (in millions):

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
Amortization of up-front payment	\$ 4.4	\$ 42.1	\$ 13.4
Recognition of milestone payments	5.0	30.0	—
Cost-sharing and co-promotion payments	24.9	13.6	—
	<b>\$ 34.3</b>	<b>\$ 85.7</b>	<b>\$ 13.4</b>

The \$51.4 million decrease in revenue under collaborative agreements in 2004, as compared to 2003, reflects a shift in the relative proportion of total development expenses related to exenatide recorded by us and by Lilly and a reduction in milestone revenue. Milestone revenue in 2004 consists of a \$5 million payment from Lilly in connection with the results of a clinical study comparing exenatide to insulin glargine in the third quarter of 2004. Milestone revenue in 2003 consisted of a \$30 million payment from Lilly following the completion of the three pivotal Phase 3 trials for exenatide in the fourth quarter of 2003. The increase in 2003, as compared to 2002, reflects a partial year of activity following the signing of the collaboration agreement in September 2002.

In September 2002, Lilly made an \$80 million non-refundable payment to us, and we agreed to incur the first \$101.2 million of development costs following the date of the agreement. Accordingly, we recorded 100% of the first \$101.2 million of U.S. development costs for exenatide, whether incurred by

us or by Lilly, and we recorded as revenue approximately 50% of these development costs through an amortization of \$50 million of the up-front payment, which amortization was completed during the third quarter of 2003. The remaining \$30 million is being amortized to revenues ratably over a 7-year period.

During the third quarter of 2003, we reached the \$101.2 million level of cumulative exenatide development costs. Subsequently, Lilly became responsible to fund, on an ongoing basis, 50% of development costs in the United States and 80% of development costs outside of the United States. While we continue to lead exenatide development efforts in the United States, Lilly is also directly incurring exenatide development expenses and makes cost-sharing payments to us to equalize development costs, which are recorded as revenues under collaborative agreements in the period in which the related development expenses are incurred.

In future periods, revenue under collaborative agreements will consist of ongoing cost-sharing payments from Lilly to equalize United States development costs, possible future milestone payments, the continued amortization of the \$30 million portion of the up-front payment, amounts earned pursuant to our co-promotion agreement with Reliant and also may include revenues under collaborative agreements entered into in the future. The amount of cost-sharing revenue recorded will be dependent on the timing, extent and relative proportion of total development costs for the exenatide development program incurred by us and by Lilly. The receipt and recognition as revenue of future milestone payments is subject to the achievement of performance

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

requirements underlying such milestone payments and, for certain development milestones, the expiration of stock conversion rights associated with such payments.

**RESEARCH AND DEVELOPMENT EXPENSES** Research and development expenses were \$119.6 million, \$149.4 million and \$94.5 million in the years ended December 31, 2004, 2003 and 2002, respectively.

The \$29.8 million decrease in 2004 compared to 2003 reflects reduced expenses of \$40.1 million and \$11.5 million for our exenatide and SYMLIN development programs, respectively, partially offset by increased expenses of \$14.3 million for our Phase 2 programs and a \$7.5 million increase in unallocated research and development expenses.

The \$40.1 million decrease in exenatide expenses in 2004 as compared to 2003 primarily reflects reduced clinical development costs due primarily to the completion of the pivotal Phase 3 program for exenatide in the fourth quarter of 2003 and the fact that we recorded 100% of exenatide development expenses, including those incurred by Lilly through the third quarter of 2003.

The \$11.5 million decrease in SYMLIN expenses in 2004 as compared to 2003 primarily reflects reduced clinical development costs in 2004 due primarily to the completion in 2003 of a dose-titration trial, and several smaller trials that formed the basis of an NDA amendment for SYMLIN submitted to the FDA in June 2003.

The \$14.3 million increase in expenses for our Phase 2 programs in 2004 as compared to 2003 primarily reflects

increased clinical development costs for our AC137 development program for obesity associated with the 16-week Phase 2 study completed in 2004. It also includes to a lesser extent increased development expenses for exenatide LAR associated with a single-dose Phase 2 study in 2004 and increased costs for manufacturing scale-up for exenatide LAR.

The \$7.5 million increase in unallocated research and development expenses in 2004 as compared to 2003 primarily reflects increased facilities costs, a portion of which are allocated to research and development expense.

We expect that our research and development expenses in 2005 will increase slightly compared to 2004. Our 2005 planned development activities include the continuation of development work to expand our knowledge of the clinical utility of SYMLIN and exenatide to support regulatory submissions outside of the United States. We also plan to continue to advance our Phase 2 development programs.

The \$54.9 million increase in research and development expenses in 2003 compared to 2002 reflects growth across all aspects of our research and development programs. Exenatide development expenses increased by \$32.4 million in 2003 as compared to 2002 due primarily to costs associated with the three pivotal Phase 3 trials, including open label extensions of those trials, and the fact that we recorded 100% of exenatide development expenses for the majority of 2003, whether incurred by us or by Lilly. SYMLIN development expenses increased by \$10.0 million in 2003 as compared to 2002, which reflects increased costs associated with the completion of the dose-titration trial completed in 2003 and

increased costs associated with manufacturing scale-up. Unallocated research and development expenses increased by \$8.2 million in 2003 as compared to 2002, principally due to increased facilities costs. The \$7.8 million increase in costs for our Phase 2 programs in 2003 as compared to 2002 primarily reflects costs associated with formulation development for exenatide LAR.

#### **SELLING, GENERAL AND ADMINISTRATIVE EXPENSES**

Selling, general and administrative expenses were \$67.0 million, \$56.8 million and \$25.3 million in the years ended December 31, 2004, 2003 and 2002 respectively.

The \$10.2 million increase in 2004 as compared to 2003 reflects increased business support and facilities costs to support future product launches and to a lesser extent increased pre-launch expenses, consisting primarily of medical education activities for exenatide. The \$31.5 million increase in 2003 compared to 2002 is due primarily to costs associated with the continued investment in our commercial and business support organizations to support future product launches, as well as increased facilities costs required to support our growth. The expansion of our commercial organization in 2003 included the addition of a 50-person sales force, increased medical education activities for SYMLIN, and growth in our managed care and other sales support functions.

Selling, general and administrative expenses are expected to increase in 2005 to support the commercial launch of SYMLIN, and the planned commercial launch of exenatide, if approved. This expected increase reflects continuing investments to prepare us for commercialization of SYMLIN in the early part of

2005. More significant increases are planned around the potential approval of exenatide, including the addition of 300 to 350 field personnel, expanded medical education activities to support a full market launch and further increases in our business infrastructure. A significant portion of this business infrastructure will also support our launch plans for SYMLIN.

**OTHER INCOME AND EXPENSE** Interest and other income consist primarily of interest income from investment of cash and investments. Interest and other income was \$4.7 million in 2004, \$7.1 million in 2003, and \$2.6 million in 2002. The decrease in 2004 reflects the fact that in 2003 interest and other income included a one-time \$3.6 million gain on early retirement of debt at a discount. The increase in 2003 as compared to 2002 reflects primarily the aforementioned \$3.6 million gain and higher average cash reserves available for investment.

Interest and other expense consist primarily of interest expense resulting from long-term debt obligations and include interest payments and the amortization of debt issuance costs. Interest and other expense was \$9.6 million in 2004, \$6.0 million in 2003 and \$6.0 million in 2002. The increase in 2004 reflects additional interest expense associated with the issuance of \$200 million of 2.5% convertible senior notes in April 2004.

**NET LOSS** Our net loss for the year ended December 31, 2004 was \$157.2 million compared to \$122.8 million in 2003 and \$109.8 million in 2002. The increase in the net loss in 2004 compared to 2003 primarily reflects the decrease in revenue under collaborative agreements, partially

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

offset by the decrease in operating expenses discussed above. The increase in the net loss in 2003 compared to 2002 reflects the increased operating expenses, partially offset by the increases in revenues from collaborative agreements and interest and other income, discussed above.

We expect to incur substantial operating losses for at least the next few years due to ongoing expenses associated with the continuation and potential expansion of our research and development programs, exenatide and our Phase 2 and earlier stage development programs, the commercialization of SYMLIN, the planned commercialization of exenatide and related general and administrative support. Operating losses 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 and private placements of common stock and preferred stock, debt financings, payments received pursuant to our exenatide collaboration with Lilly and reimbursement of SYMLIN development expenses through earlier collaboration agreements.

At December 31, 2004, we had \$293.8 million in cash, cash equivalents and short-term investments compared to \$269.8 million at December 31, 2003. The increase in our cash, cash equivalents and short-term investments in 2004 primarily reflects approximately \$200.6 million provided by our financing activities, partially offset by \$162.9 million used to fund operating activities during 2004. Financing activities in 2004 include \$193.6 million in net proceeds from a private placement of 2.5% convertible senior notes

in April 2004. In February 2005 we completed a public offering of our common stock, generating net proceeds to us of approximately \$190.5 million.

We expect our use of cash to fund our operating activities to increase during 2005, as compared to 2004. This expected increase primarily reflects continuing investments in the early part of 2005 to prepare us for the commercial launch of SYMLIN. More significant increases are planned around the potential approval of exenatide, including the addition of 300 to 350 field personnel, expanded medical education activities to support a full market launch and further increases in our business infrastructure. A significant portion of this business infrastructure will also support our launch plans for SYMLIN.

In December 2003, we filed a shelf registration statement with the Securities and Exchange Commission, which currently allows us to sell up to \$98 million of various securities in one or more offerings in the future. The terms of any offering will be established at the time of sale. The SEC declared this registration statement effective in February 2004. In February 2005 we completed a public offering of 9.2 million shares of our common stock pursuant to this shelf registration, generating net proceeds to us of approximately \$190.5 million.

We also have a loan facility available from Lilly that, subject to certain defined development and regulatory events, over time could provide us up to \$110 million to fund a portion of our development and commercialization costs for exenatide. At December 31, 2004, \$40 million of this facility was available to us and there were no amounts outstanding. We expect

approximately \$70 million to be available following FDA approval, if any, of exenatide. Any loans under this facility would be secured by some of our patents and other tangible assets and, at Lilly's option, are convertible into our common stock if amounts remain outstanding for more than two years.

We used cash of \$162.9 million, \$143.4 million and \$20.4 million for our operating activities in the years ended December 31, 2004, 2003 and 2002, respectively. Our operating activities in 2003 and 2002 reflect payments received from Lilly of a \$35 million milestone payment and an \$80 million up-front payment, respectively. Our investing activities used \$53.8 million, \$128.3 million and \$57.2 million in the years ended December 31, 2004, 2003, and 2002, respectively. Investing activities in all three years consisted primarily of purchases and sales of short-term investments, but also included purchases of laboratory and office equipment and patent additions. Financing activities provided \$200.6 million, \$278.9 million and \$124.6 million in the years ended December 31, 2004, 2003 and 2002, respectively. These amounts consisted

primarily of proceeds from sales of common stock and the issuance of convertible senior notes, partially offset by principal payments on notes payable and capital lease obligations.

At December 31, 2004, we had outstanding long-term debt of \$375 million. This amount includes \$175 million aggregate principal amount of the 2.25% senior convertible notes due 2008, or the 2003 Notes. The 2003 Notes are currently convertible into a total of up to 5.4 million shares of our common stock at approximately \$32.55 per share. Under certain circumstances, the 2003 Notes are redeemable in whole or in part, at our option, on or after June 30, 2006, at specified redemption prices plus accrued and unpaid interest. The remainder of our long-term debt balance at December 31, 2004 consists of \$200 million aggregate principal amount of the 2.5% convertible senior notes due 2011, or the 2004 Notes. 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. The 2004 Notes are not redeemable at our option.

The following table summarizes our contractual obligations and maturity dates as of December 31, 2004 (in thousands).

CONTRACTUAL OBLIGATIONS	PAYMENTS DUE BY PERIOD				
	TOTAL	LESS THAN 1 YEAR	2-3 YEARS	4-5 YEARS	AFTER 5 YEARS
Long-term debt	\$ 375,000	\$ —	\$ —	\$ 175,000	\$ 200,000
Interest on long-term debt	46,282	8,938	17,875	11,969	7,500
Capital lease obligations	28	13	15	—	—
Operating leases	65,302	4,834	17,429	16,600	26,439
Total <sup>1</sup>	\$ 486,612	\$ 13,785	\$ 35,319	\$ 203,569	\$ 233,939

(1) Excludes long-term obligation of \$3.1 million related to deferred compensation, the payment of which is subject to elections made by participants that are subject to change.

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

In addition, under certain license and collaboration agreements with other companies we are required to pay royalties and/or milestone payments upon the successful development and commercialization of related products. We do not expect to make any significant milestone payments under these agreements within 12 months from the date of this report.

At December 31, 2004, we had outstanding commitments to purchase approximately \$13.7 million of SYMLIN and exenatide inventory. If FDA approval for exenatide is received, our commitments to purchase inventories will increase substantially. Some of our commercial supply agreements for exenatide and SYMLIN have minimum annual purchase requirements subsequent to FDA approval. Additionally, as a result of FDA approval of SYMLIN, we are committed to purchase approximately \$10.1 million of SYMLIN bulk drug material from a former collaborative partner. We expect to purchase this material during the second quarter of 2005.

Our future capital requirements will depend on many factors, including: the timing and costs involved in obtaining regulatory approval for exenatide; whether regulatory approval for the marketing of exenatide is received; if regulatory approval is received, costs associated with the commercialization of exenatide and our ability to effectively market SYMLIN and exenatide; costs associated with the commercialization of SYMLIN; our ability to receive milestone payments or access to loan amounts pursuant to our collaboration with Lilly; our ability and the extent to which we establish commercialization arrangements, if any, for SYMLIN; our ability to progress with other ongoing and new clinical and preclinical trials and the extent of these trials; progress in our other research and

development programs and the magnitude of these programs; the costs involved in preparing, filing, prosecuting, maintaining, enforcing or defending our patents; competing technological and market developments; changes in or new collaborative relationships; costs of manufacturing, including scale-up costs of our drug candidates; the costs of potential licenses or acquisitions; and the need to repay existing indebtedness.

**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 and expenses, and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates, including those related to inventory costs. 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 63).

**REVENUE RECOGNITION** We recognize revenue when all four of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products and/or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectibility is reasonably assured. In addition, we follow the provisions of the Securities and Exchange Commission's Staff Accounting Bulletin, No. 104, "Revenue Recognition," which sets forth guidelines on the timing of revenue recognition based upon factors such as passage of title, installation, payments and customer acceptance. 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. Amounts received for 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.

**INVENTORY AND RELATED RESERVES** We capitalize inventory costs associated with our drug candidates prior to receipt of regulatory approval, based on management's judgment of probable future commercialization. We would be required to expense these capitalized costs upon a change in such judgment, due to, among other factors, a decision denying approval of the drug candidate by regulatory agencies.

At December 31, 2004, gross capitalized inventory, the majority of which relates to SYMLIN, totaled \$18.8 million. On March 16, 2005, the FDA approved SYMLIN for marketing in the United States.

Additionally, approximately \$4.7 million of the \$18.8 million of total inventory of SYMLIN is in finished dosage form, the majority of which was manufactured in late 2003. Finished SYMLIN inventory has a thirty-six month expiration period. We evaluate the recoverability of our finished inventory in consideration of our expected potential launch dates and estimated sales volumes. In consideration of the age of the inventory and planned launch date for SYMLIN, we have provided for a valuation reserve of \$3.1 million at December 31, 2004 related to our finished SYMLIN inventory.

**RESEARCH AND DEVELOPMENT EXPENSES** Research and development costs are expensed as incurred and include salaries and benefits; costs paid to third-party contractors to perform research, conduct clinical trials, develop and manufacture 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 not been material and are adjusted for in the period in which they become known.

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS (CONTINUED)

**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 fully reserved for these deferred tax assets in our consolidated balance sheets at December 31, 2004 and 2003, 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.

**RECENTLY ISSUED ACCOUNTING PRONOUNCEMENTS** In December 2004, the Financial Accounting Standards Board ("FASB") issued SFAS 123 (R) "Share-Based Payment," which requires stock-based compensation for an award of equity instruments, including stock options and employee stock purchase rights, issued to employees to be recognized as a cost in the financial statements. The cost of these awards are measured according to the grant date fair value of the stock options and is recognized over the period during which an employee is required to provide service in exchange for the award, which is usually the vesting period. In the absence of an observable market price for the stock awards, the grant-date fair value of the stock options would be based upon a valuation methodology that takes into consideration various factors, including the exercise price of the option, the expected term of the option, the current price of the underlying shares, the expected volatility of the underlying share price, the expected

dividends on the underlying shares and the risk-free interest rate. The requirements of SFAS 123 (R) are effective for us in the first interim period beginning after June 15, 2005. The adoption of this standard is expected to increase operating expenses and we are currently evaluating the extent of this impact on our financial statements.

**QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK** We invest our excess cash primarily in U.S. Government securities, asset-backed securities and debt instruments of financial institutions and corporations with strong 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. At December 31, 2004, the fair value of our 2003 Notes and 2004 Notes were \$181.3 million and \$202.8 million, respectively. 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.

## 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, 2004.

Our management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is set forth on the next page.

# REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM ON INTERNAL CONTROL OVER FINANCIAL REPORTING

TO THE BOARD OF DIRECTORS AND STOCKHOLDERS OF  
AMYLIN PHARMACEUTICALS, INC.

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that Amylin Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, 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. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of 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, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, 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, management's assessment that Amylin Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Amylin Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets as of December 31, 2004 and 2003, and the related consolidated statements of operations, shareholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2004 of Amylin Pharmaceuticals, Inc. and our report dated March 7, 2005 expressed an unqualified opinion thereon.

*Ernst + Young LLP*

San Diego, California  
March 7, 2005

# REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

## TO THE BOARD OF DIRECTORS AND STOCKHOLDERS OF AMYLIN PHARMACEUTICALS, INC.

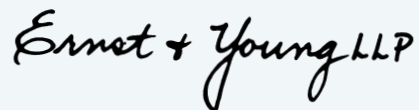
We have audited the accompanying consolidated balance sheets of Amylin Pharmaceuticals, Inc. as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. 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, 2004 and 2003, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Amylin Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2004, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 7, 2005 expressed an unqualified opinion thereon.

The logo for Ernst & Young LLP is written in a black, cursive script font. The words "Ernst & Young" are connected together, and "LLP" is written in a slightly smaller, more upright font to the right.

San Diego, California  
March 7, 2005

# CONSOLIDATED BALANCE SHEETS

(IN THOUSANDS, EXCEPT FOR PER SHARE AMOUNTS)

	DECEMBER 31,	
	2004	2003
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 60,583	\$ 76,615
Short-term investments	233,173	193,161
Receivables from collaborative partners	5,770	791
Inventories, net	15,676	11,841
Other current assets	9,156	6,140
Total current assets	324,358	288,548
Property and equipment, net	20,739	13,691
Patents and other assets, net	3,258	4,044
Debt issuance costs, net	9,445	4,762
	<b>\$ 357,800</b>	<b>\$ 311,045</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)</b>		
Current liabilities:		
Accounts payable, accrued expenses and other current liabilities	\$ 24,145	\$ 31,636
Accrued compensation	13,506	9,482
Current portion of deferred revenue	4,286	4,286
Total current liabilities	41,937	45,404
Deferred revenue, net of current portion	20,943	25,229
Other long-term obligations, net of current portion	7,290	2,196
Convertible senior notes	375,000	175,000
Commitments and contingencies		
Stockholders' equity (deficit):		
Preferred stock, \$.001 par value, 7,500 shares authorized, none issued and outstanding at December 31, 2004 and 2003	—	—
Common stock, \$.001 par value, 200,000 shares authorized, 94,489 and 93,625 issued and outstanding at December 31, 2004 and 2003, respectively	94	94
Additional paid-in capital	710,457	703,479
Accumulated deficit	(797,496)	(640,339)
Deferred compensation	(162)	(310)
Accumulated other comprehensive income	(263)	292
Total stockholders' equity (deficit)	(87,370)	63,216
	<b>\$ 357,800</b>	<b>\$ 311,045</b>

See accompanying notes to consolidated financial statements.

# CONSOLIDATED STATEMENTS OF OPERATIONS

(IN THOUSANDS, EXCEPT FOR PER SHARE AMOUNTS)

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
Revenues under collaborative agreements	\$ 34,268	\$ 85,652	\$ 13,395
Operating expenses:			
Research and development	119,558	149,431	94,456
Selling, general and administrative	66,958	56,761	25,334
Acquired in-process research and development	—	3,300	—
	<b>186,516</b>	209,492	119,790
Loss from operations	<b>(152,248)</b>	(123,840)	(106,395)
Interest and other income	4,696	7,079	2,619
Interest and other expense	(9,605)	(6,047)	(6,011)
Net loss	<b>\$ (157,157)</b>	\$ (122,808)	\$ (109,787)
Net loss per share — basic and diluted	<b>\$ (1.67)</b>	\$ (1.33)	\$ (1.39)
Weighted average shares — basic and diluted	<b>94,054</b>	92,396	79,106

See accompanying notes to consolidated financial statements.

# CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

(IN THOUSANDS)

FOR THE YEARS ENDED DECEMBER 31, 2004, 2003 AND 2002	SHARES	AMOUNT	ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	DEFERRED COMPEN- SATION	ACCUMULATED OTHER COMPRE- HENSIVE INCOME (LOSS)	TOTAL STOCK- HOLDERS' EQUITY (DEFECIT)
<b>BALANCE AT DECEMBER 31, 2001</b>	67,554	\$ 68	\$ 404,114	\$ (407,744)	\$ (309)	\$ 388	\$ (3,483)
Comprehensive loss:							
Net loss	—	—	—	(109,787)	—	—	(109,787)
Unrealized loss on available-for-sale securities	—	—	—	—	—	(221)	(221)
Comprehensive loss	—	—	—	—	—	—	(110,008)
Issuance of common stock upon exercise of options and warrants	601	—	3,474	—	—	—	3,474
Issuance of common stock for other employee benefit plans	144	—	1,377	—	—	—	1,377
Stock-based compensation	—	—	103	—	—	—	103
Issuance of common stock in public offering	12,075	12	90,742	—	—	—	90,754
Issuance of common stock in connection with collaboration agreement	1,605	2	29,998	—	—	—	30,000
Deferred compensation related to stock options	—	—	215	—	(215)	—	—
Amortization of deferred compensation	—	—	—	—	81	—	81
<b>BALANCE AT DECEMBER 31, 2002</b>	81,979	82	530,023	(517,531)	(443)	167	12,298
Comprehensive loss:							
Net loss	—	—	—	(122,808)	—	—	(122,808)
Unrealized gain on available-for-sale securities	—	—	—	—	—	125	125
Comprehensive loss	—	—	—	—	—	—	(122,683)
Issuance of common stock upon exercise of options and warrants	898	1	6,376	—	—	—	6,377
Issuance of common stock for other employee benefit plans	206	—	2,257	—	—	—	2,257
Stock-based compensation	—	—	84	—	—	—	84
Issuance of common stock in public offering	10,542	11	164,674	—	—	—	164,685
Deferred compensation related to stock options	—	—	65	—	(65)	—	—
Amortization of deferred compensation	—	—	—	—	198	—	198
<b>BALANCE AT DECEMBER 31, 2003</b>	93,625	94	703,479	(640,339)	(310)	292	63,216
Comprehensive loss:							
Net loss	—	—	—	(157,157)	—	—	(157,157)
Unrealized loss on available-for-sale securities	—	—	—	—	—	(555)	(555)
Comprehensive loss	—	—	—	—	—	—	(157,712)
Issuance of common stock upon exercise of options	667	—	4,554	—	—	—	4,554
Issuance of common stock for other employee benefit plans	197	—	2,462	—	—	—	2,462
Deferred compensation related to stock options	—	—	(38)	—	38	—	—
Amortization of deferred compensation	—	—	—	—	110	—	110
<b>BALANCE AT DECEMBER 31, 2004</b>	94,489	\$ 94	\$ 710,457	\$ (797,496)	\$ (162)	\$ (263)	\$ (87,370)

See accompanying notes to consolidated financial statements.

# CONSOLIDATED STATEMENTS OF CASH FLOWS

(IN THOUSANDS)

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
<b>OPERATING ACTIVITIES:</b>			
Net loss	\$ (157,157)	\$ (122,808)	\$ (109,787)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	7,307	4,481	2,105
Amortization of debt discount	—	655	1,198
Inventory reserve	(237)	2,186	1,015
Accrued interest added to note payable	—	2,701	4,725
Gain on early retirement of note payable	—	(3,567)	—
Other non-cash expenses	1,320	1,303	1,000
Changes in operating assets:			
Inventories	(3,598)	(4,207)	(2,834)
Receivables from collaborative partners	(4,979)	(791)	—
Other current assets	(2,904)	(3,137)	(1,702)
Accounts payable and accrued liabilities	(3,467)	15,820	16,984
Deferred revenue	(4,286)	(37,090)	66,605
Other assets and liabilities, net	5,148	1,049	297
Net cash used in operating activities	(162,853)	(143,405)	(20,394)
<b>INVESTING ACTIVITIES:</b>			
Purchases of short-term investments	(237,735)	(335,756)	(152,136)
Sales and maturities of short-term investments	197,056	220,329	98,200
Purchases of equipment, net	(12,904)	(12,314)	(2,535)
Increase in patents	(211)	(546)	(701)
Net cash used in investing activities	(53,794)	(128,287)	(57,172)
<b>FINANCING ACTIVITIES:</b>			
Proceeds from issuance of common stock, net	7,016	172,446	125,133
Proceeds from issuance of convertible debt, net	193,613	169,696	—
Principal payments on notes payable and capital leases	(14)	(63,250)	(547)
Net cash provided by financing activities	200,615	278,892	124,586
Increase (decrease) in cash and cash equivalents	(16,032)	7,200	47,020
Cash and cash equivalents at beginning of year	76,615	69,415	22,395
Cash and cash equivalents at end of year	\$ 60,583	\$ 76,615	\$ 69,415
<b>SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:</b>			
Interest paid	\$ 6,563	\$ 2,065	\$ 47

See accompanying notes to consolidated financial statements.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

## 1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

**ORGANIZATION** Amylin Pharmaceuticals, Inc. (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 cardiovascular disease.

**PRINCIPLES OF CONSOLIDATION** The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Amylin Europe Limited. All significant intercompany transactions and balances have been eliminated in consolidation.

**USE OF ESTIMATES** The preparation of financial statements in conformity with accounting principles generally accepted in the United States 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** Revenue is recognized when all four of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products and/or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectibility is reasonably assured. In addition, the Company follows the provisions of the Securities and Exchange Commission’s (SEC) Staff Accounting Bulletin (SAB) No. 104, “Revenue Recognition,” which sets forth

guidelines on the timing of revenue recognition based upon factors such as passage of title, installation, payments and customer acceptance. 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. Amounts received for 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 these revenue recognition criteria will be recorded as deferred revenue in the accompanying consolidated balance sheets.

**RESEARCH AND DEVELOPMENT EXPENSES** Research and development costs are expensed as incurred and include salaries and benefits, costs paid to third-party contractors to perform research, conduct clinical trials, develop and manufacture drug materials and delivery devices, and a portion of 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. The Company accrues the costs of services rendered in connection with third-party contractor activities based on its estimate of management fees, site management and monitoring costs and data management costs. Actual clinical trial costs may differ from estimated clinical trial costs and are adjusted for in the period in which they become known.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

**CONCENTRATIONS OF RISK** The Company invests its excess cash in U.S. Government securities and debt instruments of financial institutions and corporations with strong credit ratings. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. These guidelines are periodically reviewed. Financial instruments that potentially subject the Company to significant credit risk consist principally of cash equivalents and short-term investments.

Eli Lilly and Company, or Lilly, provides funding for 50% of the development and commercialization expenses for exenatide in the United States pursuant to a global development and commercialization agreement between the parties. Following approval of exenatide in the United States, if received, Lilly will co-promote the product with the Company in the United States and will manufacture pen devices for the administration of exenatide. 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.

**CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS** Cash, cash equivalents and short-term investments consist principally of U.S. Government securities and other highly liquid debt instruments. 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 includes certificates of deposits underlying letters of credit of \$1.6 million and \$215,000 at December 31, 2004 and 2003, respectively.

**INVESTMENTS** The Company has classified its debt securities as available-for-sale and are stated at fair value, and unrealized holding gains or losses on these securities are carried as a separate component of stockholders' equity (deficit). The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary (of which there have been none to date) on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method.

**INVENTORIES** Inventories are stated at the lower of cost (FIFO) or market. Raw materials consists of SYMLIN® (pramlintide acetate) and exenatide bulk drug material and finished goods consists of finished SYMLIN drug product in vials for syringe administration.

**PROPERTY AND EQUIPMENT** Property and equipment, consisting primarily of leasehold improvements, office and laboratory equipment, are recorded at cost. Depreciation of equipment is computed using the straight-line method, over three to five 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. Amortization of equipment under capital leases is reported with depreciation of property and equipment. The Company recorded depreciation expense of \$5.3 million, \$3.1 million and \$1.7 million in the years ended December 31, 2004, 2003 and 2002, respectively.

The Company records impairment losses on property 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. To date, the Company has not experienced any impairment losses on its long-lived assets used in operations. 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 as of December 31, 2004.

**PATENTS** The Company has filed a number of patent applications with the United States Patent and Trademark Office and in foreign countries. 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 \$4.0 million and \$4.7 million at December 31, 2004 and 2003, respectively. Accumulated amortization was approximately \$1.9 million and \$1.9 million at December 31, 2004 and 2003, respectively. The Company recorded patent amortization expense of \$0.3 million, \$0.8 million and \$0.4 million in the years ended December 31, 2004, 2003 and 2002, respectively. Capitalized costs related to patent applications are charged to operations 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, 2004, 2003 and 2002, respectively.

**DEBT ISSUANCE COSTS** Debt issuance costs relate to the \$175 million aggregate principal amount of 2.25% convertible senior notes, due June 30, 2008, which were issued in June and July of 2003, referred to as the 2003 Notes; and the \$200 million aggregate principal amount of 2.5% convertible senior notes, due April 15, 2011, which were issued in April 2004, referred to as the 2004 Notes. Debt issuance costs are being amortized to interest expense on a straight-line basis over the contractual term of the respective notes. The Company incurred total debt issuance costs of \$5.3 million in connection with the 2003 Notes and \$6.4 million in connection with the 2004 Notes and recorded \$1.7 million and \$0.5 million of amortization of such costs in the years ended December 31, 2004 and 2003, 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 4.1 million, 4.3 million and 1.9 million were excluded from the calculation of net loss per share for the years ended December 31, 2004, 2003 and 2002, respectively, because the effect would be antidilutive. In addition, common stock equivalents from shares underlying our convertible senior notes of 11.2 million, 5.8 million and none were excluded from the net loss per share for the years ended December 31, 2004, 2003 and 2002, respectively,

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

because the effect would be antidilutive. In future periods, if the Company reports net income and the common share equivalents for our 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.

**FOREIGN CURRENCY TRANSLATION** Assets and liabilities of foreign operations where the functional currency is other than the U.S. dollar are translated at fiscal year-end rates of exchange, and the related revenue and expense amounts are translated at the average rates of exchange during the fiscal year. Gains and losses resulting from translating foreign currency financial statements resulted in an immaterial impact to the Company's financial statements for the years ended December 31, 2004, 2003 and 2002.

**COMPREHENSIVE INCOME (LOSS)** Statement of Financial Accounting Standards ("SFAS") No. 130, "Reporting Comprehensive Income" requires that all components of comprehensive income (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 income (loss) and other comprehensive income (loss), including unrealized gains and losses on investments, shall be reported, net of their related tax effect, to arrive at comprehensive income (loss).

**STOCK-BASED COMPENSATION** The Company records compensation expense for employee stock options based upon the intrinsic value on the date of grant pursuant to Accounting Principles Board (APB) Opinion No. 25, "Accounting for Stock Issued to Employees." Because the Company establishes the exercise price based on the fair market value of the Company's stock at the date of grant, the options have no intrinsic value upon grant, and therefore no expense is recorded.

As required under SFAS No. 123, "Accounting for Stock-Based Compensation," and SFAS No. 148, "Accounting for Stock Based Compensation Transition and Disclosure," the pro forma effects of stock-based compensation on net income and net earnings per common share have been estimated at the date of grant using the Black-Scholes option pricing model based on the following assumptions:

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
Risk-free interest rate	3.68%	3.25%	3.75%
Dividend yield	– %	– %	– %
Volatility factor	88%	121%	131%
Weighted-average expected life	5.75	5.87	5.89

For purposes of pro forma disclosures, the estimated fair value of the options is assumed to be amortized to expense over the options' vesting periods. These pro forma amounts may not be representative of the effects on reported net income (loss) for future years due to the uncertainty of stock

option grant volume and potential changes in assumptions driven by market factors. The pro forma effects of recognizing compensation expense under the fair value method on net income (loss) and net earnings per common share were as follows (in thousands, except for net loss per share):

	YEARS ENDED DECEMBER 31,		
	2004	2003	2002
Net loss as reported	<b>\$(157,157)</b>	\$(122,808)	\$(109,787)
Deduct:			
Stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	<b>33,343</b>	23,159	11,549
Pro forma net loss	<b>\$(190,500)</b>	\$(145,967)	\$(121,336)
Net loss per share:			
Basic and diluted — as reported	<b>\$(1.67)</b>	\$(1.33)	\$(1.39)
Basic and diluted — pro forma	<b>\$(2.03)</b>	\$(1.58)	\$(1.53)

**RECLASSIFICATIONS** Certain reclassifications have been made to the consolidated financial statements to provide consistent presentation for all periods presented.

**RECENTLY ISSUED ACCOUNTING STANDARDS** In December 2004, The Financial Accounting Standards Board (“FASB”) issued SFAS 123 (R) “Share-Based Payment,” which requires stock-based compensation for an award of equity instruments, including stock options and employee stock purchase rights, issued to employees to be recognized as a cost in the financial statements. The cost of these awards are measured according to the grant date fair value of the stock options and is recognized over the period during which an employee is required to provide service in exchange for the award, which is usually the vesting period. In the absence of an observable market price for the stock awards, the grant-date fair value of the stock options would be based upon a valuation methodology that takes into consideration various factors, including the exercise price of the option, the expected term of the option, the current price of the underlying shares, the expected volatility of the underlying share price, the expected dividends on the underlying shares and the risk-free interest rate. The requirements of SFAS 123 (R) are effective for the Company in the first interim period beginning after June 15, 2005. The adoption of this standard is expected to increase operating expenses and the Company is currently evaluating the extent of this impact on its financial statements.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

### 2. INVESTMENTS

The following is a summary of short-term investments as of December 31, 2004 and 2003 (in thousands).

	AVAILABLE-FOR-SALE SECURITIES			
	AMORTIZED COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	ESTIMATED FAIR VALUE
<b>DECEMBER 31, 2004</b>				
U.S. Treasury securities and obligations of U.S. Government agencies	\$ 53,321	\$ —	\$ (200)	\$ 53,121
Corporate debt securities	76,004	3	(63)	75,944
Asset-backed securities	70,991	—	(353)	70,638
Mortgage-backed securities	13,735	1	(64)	13,672
Debt securities issued by states of the United States and political subdivisions of the states	19,814	—	(16)	19,798
Total	\$ 233,865	\$ 4	\$ (696)	\$ 233,173
<b>DECEMBER 31, 2003</b>				
U.S. Treasury securities and obligations of U.S. Government agencies	\$ 64,188	\$ 31	\$ (42)	\$ 64,177
Corporate debt securities	61,902	37	(14)	61,925
Asset-backed securities	48,467	31	(2)	48,496
Mortgage-backed securities	15,580	—	(67)	15,513
Debt securities issued by states of the United States and political subdivisions of the states	3,050	—	—	3,050
Total	\$ 193,187	\$ 99	\$ (125)	\$ 193,161

The gross realized gains on sales of available-for-sale securities totaled approximately \$45,000, \$0.2 million and \$0.5 million and the gross realized losses totaled \$0.6 million, \$1.6 million,

and \$0.6 million for the years ended December 31, 2004, 2003 and 2002, respectively.

Contractual maturities of short-term investments at December 31, 2004 were as follows (in thousands):

FAIR VALUE	
Due within 1 year	\$ 94,140
After 1 but within 5 years	94,888
After 5 but within 10 years	8,161
After 10 years	35,984
Total	\$ 233,173

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.

### 3. OTHER FINANCIAL INFORMATION

Inventories consist of the following (in thousands):

	DECEMBER 31,	
	2004	2003
Raw materials	\$ 14,052	\$ 6,108
Finished goods	4,724	9,070
Valuation reserve	(3,100)	(3,337)
	\$ 15,676	\$ 11,841

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

	DECEMBER 31,	
	2004	2003
Interest and other receivables	\$ 1,311	\$ 1,380
Prepaid expenses	7,845	4,760
	\$ 9,156	\$ 6,140

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

	DECEMBER 31,	
	2004	2003
Office equipment and furniture	\$ 10,673	\$ 7,262
Laboratory equipment	10,602	6,653
Production equipment	1,166	608
Leasehold improvements	9,059	6,673
	31,500	21,196
Less accumulated depreciation and amortization	(10,761)	(7,505)
	\$ 20,739	\$ 13,691

Accounts payable, accrued expenses and other current liabilities consist of the following (in thousands):

	DECEMBER 31,	
	2004	2003
Accounts payable	\$ 20,135	\$ 28,713
Accrued expenses	3,997	2,911
Current portion of capital leases	13	12
	\$ 24,145	\$ 31,636

### 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, including both twice-daily and sustained release formulations. Under the terms of the agreement Amylin and Lilly will share U.S. development and commercialization costs equally. Development costs outside of the United States will be shared 80% by Lilly and

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

20% by the Company and Lilly will be responsible for all commercialization costs outside of the United States.

The Company and Lilly will share equally in operating profits from the sale of collaboration products in the United States. Operating profits from the sale of product outside of the United States will be shared at approximately 80% to Lilly and 20% to Amylin. Amylin will record all U.S. product revenues and Lilly will record all other product revenues.

At signing, Lilly made initial non-refundable payments to the Company totaling \$80 million and Amylin agreed to incur the first \$101.2 million of development expenses for exenatide following the date of the agreement. This cumulative level of development expenses was reached during the year ended December 31, 2003. Subsequent to this \$101.2 million of cumulative development expenses, Lilly has funded, on an ongoing basis, 50% of development costs in the U.S and 80% of development costs outside of the United States.

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. The Company received a \$5 million development milestone in August 2004 in connection with the results of a clinical study comparing exenatide to insulin-glargine. This milestone was recorded as revenues under collaborative agreements in the third quarter of 2004. In 2003, the Company received development milestones of \$35 million following the successful completion of the Phase 3 clinical program for exenatide. Of this amount, \$30 million was recognized as revenues under collaborative agreements

in the accompanying consolidated statements of operations and \$5 million was deferred as long-term deferred revenue in the accompanying consolidated balance sheets as it is potentially creditable against future milestone payments. Certain of the future development milestone payments may be converted into Amylin common stock, at Lilly's option, if the filing of a New Drug Application with the United States Food and Drug Administration ("FDA") for exenatide LAR is delayed beyond December 31, 2007. Lilly has 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.

The Company recorded revenue under this collaborative agreement of \$32.6 million, \$85.7 million and \$13.4 million in the years ended December 31, 2004, 2003 and 2002, respectively, and incurred reimbursable development expenses of \$53.0, \$88.3 million and \$22.7 million in the years ended December 31, 2004, 2003 and 2002, respectively. Reimbursable development expenses consist of direct internal and external expenses for exenatide, including both twice-daily and sustained release formulations.

The Company has a loan facility with Lilly that, subject to certain defined development and regulatory events, over time could provide the Company up to \$110 million to fund a portion of its development and commercialization costs for exenatide. At December 31, 2004, \$40 million was available to the Company under this loan facility and there were no amounts outstanding. Debt incurred under this agreement will be secured debt and becomes due upon the earlier of

June 30, 2007, or the first anniversary of the date when a product developed under the collaboration agreement with Lilly is first launched.

**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 LAR, with the goal of developing a product that would allow up to a once-a-month administration of exenatide.

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 a combination of royalty payments and manufacturing fees based on any future product sales.

## 5. LEASE COMMITMENTS

The Company leases its facilities under operating leases. 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 of approximately \$3.3 million at December 31, 2004 is included in other long-term obligations, net of current portion in the accompanying consolidated balance sheets and deferred rent of approximately \$229,000 at December 31, 2003 is included in accounts payable and accrued expenses in the accompanying consolidated balance sheets.

Minimum future annual obligations for operating leases for years ending after December 31, 2004 are as follows (in thousands):

2005	\$ 4,834
2006	8,404
2007	9,025
2008	9,114
2009	7,486
Thereafter	26,439
Total minimum lease payments	\$ 65,302

Rent expense for the years ended December 31 2004, 2003, and 2002, was \$8.2 million, \$4.5 million, and \$2.0 million, respectively.

## 6. NOTE PAYABLE AND RELATED COMMITMENTS

In July 2003, the Company repaid all its outstanding indebtedness to a former collaborative partner for \$62.7 million, representing a discount of 7 percent from face value on the date of payment. This transaction resulted in a gain of \$3.6 million, which is included in interest and other income in the

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

accompanying consolidated statements of operations for the year ended December 31, 2003.

In September 1998, the Company entered into an agreement with an affiliate of the same former collaborative partner, which provided for the possible future purchase by the Company of commercial grade SYMLIN bulk drug material purchased by the former collaborative partner during the collaboration agreement. The Company must purchase the drug material in full on the first to occur of certain events, including the execution of an agreement with a major pharmaceutical company relating to the development, commercialization and/or sale of SYMLIN, receipt of regulatory approval for the sale of SYMLIN, or a change in control of the Company. The purchase price to the Company will be the original purchase price plus a carrying cost equivalent to the current five-year U.S. Treasury note rate plus 3%, equaling \$10.1 million at December 31, 2004. If none of the aforementioned events occurs, the Company has no obligation related to this agreement.

### 7. CONVERTIBLE SENIOR NOTES

In June and July 2003, the Company issued the 2003 Notes, which have an aggregate principal amount of \$175 million, in a private placement. The 2003 Notes have been registered under the Securities Act of 1933, as amended, or the Securities Act, to permit registered resale of the 2003 Notes and of the common stock issuable upon conversion of the 2003 Notes. The 2003 Notes bear interest at a rate of 2.25% per year, payable in cash semi-annually, and are convertible into a total of up to 5.4 million shares

of common stock at a conversion price of approximately \$32.55 per share, subject to customary adjustments such as stock dividends and other dilutive transactions.

The 2003 Notes are redeemable at the Company's option in whole or in part on or after June 30, 2006, at a redemption price equal to 100% of the principal amount of the notes to be redeemed plus accrued and unpaid interest to the redemption date, at the Company's option, if the closing price of the Company's common stock has exceeded 140% of the conversion price for at least 20 trading days in any consecutive 30-day trading period. At the time of any such redemption, the Company will also make an additional payment on the redeemed 2003 Notes equal to \$112.94 per \$1,000 principal amount of the 2003 Notes, less interest actually paid or accrued but unpaid on the 2003 Notes. At December 31, 2004 and 2003, the fair value of the 2003 notes, based on observed market prices, was \$181.3 and \$176.5 million, respectively.

In April 2004, the Company issued the 2004 Notes, which have an aggregate principal amount of \$200 million, in a private placement. The 2004 Notes have been registered under 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 may not redeem the 2004 Notes prior to maturity. The fair value of the 2004 Notes, based on an

observed market price, was \$202.8 million at December 31, 2004.

Upon a change in control, the holders of the 2003 and 2004 Notes may elect to require the Company to re-purchase the 2003 or 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 closing prices of our common stock for the five-day trading period ending on the third day before the purchase date.

#### 8. STOCKHOLDERS' EQUITY (DEFICIT)

**STOCK PURCHASE PLANS** In March 2001, the Company adopted the 2001 Employee Stock Purchase Plan (the "2001 Stock Purchase Plan"), under which 400,000 shares of common stock may be issued to eligible employees, including officers. Contributions to this plan may not exceed 15% of the participant's eligible compensation. The Company's stockholders approved this plan at its 2001 annual meeting. At its 2004 annual meeting, the Company's stockholders approved an increase in the aggregate number of shares authorized for issuance under the 2001 Stock Purchase Plan of 750,000 shares. The price of common stock issued under the 2001 Stock Purchase Plan is equal to the lesser of 85% of the market price on the effective date of an employee's participation in the plan or 85% of the fair market value of the common stock at the purchase date. At December 31, 2004, approximately 411,000 shares of common stock had been issued under the 2001 Stock Purchase Plan.

**STOCK OPTION PLANS** Under the Company's 1991 Stock Option Plan (the "1991 Plan"), 7.8 million shares of common stock were reserved for issuance upon exercise of options granted to employees and consultants of the Company. The 1991 Plan provides for the grant of incentive and nonstatutory stock options. The exercise price of incentive stock options must equal at least the fair market value on the date of grant, and the exercise price of nonstatutory stock options may be no less than 85% of the fair market value on the date of grant. Generally, options are granted at prices equal to at least 100% of the fair market value of the stock subject to the option at the date of grant, expire not later than ten years from the date of grant and vest over a four-year period, with one-quarter becoming exercisable one year following the date of grant and the remainder becoming exercisable in monthly increments over a three-year period. From time to time, as approved by the Company's Board of Directors, options with differing terms have also been granted.

In December 2000, the Company adopted the 2001 Equity Incentive Plan (the "2001 Plan"), which provides for an additional 11.5 million shares of common stock reserved for issuance upon exercise of options granted to employees and consultants of the Company. The 2001 Plan provides for up to an additional 5.3 million shares to be reserved for issuance upon exercise of options to the extent that options issued under the 1991 Plan expire or are cancelled subsequent to the adoption of the 2001 Plan. The 2001 Plan was approved at a meeting of stockholders in January 2001. The 2001 Plan was amended to increase the number of shares authorized for issuance of common stock to 11.5 million in April 2003. The Company's stockholders approved the 2001 Plan, as

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

amended, at its 2003 annual meeting. The exercise price of incentive stock options may not be less than 100% of the fair market value of the stock subject to the option on the date of the grant and, in some cases, may not be less than 110% of such fair market value. The exercise price of nonstatutory options may not be less than 85% of the fair market value of the stock on the date of the grant and, in some cases, may not be less than 100% of such fair market value. Options issued under the 2001 Plan are generally issued, vest and expire on the same terms as the 1991 Plan.

Under the Company's Non-Employee Directors' Stock Option Plan (the "Directors' Plan"), 450,000 shares of common stock are reserved for issuance upon exercise of nonqualified stock options granted to non-employee directors of the Company. The Company's stockholders approved the Directors' Plan at its 2001 annual meeting. Options granted under the Directors' Plan must have an exercise price of at least 100% of the fair market value of the stock subject to the option on the date of grant, vest ratably over periods ranging from twelve to thirty-six months and expire not later than ten years from the date of grant. Options ceased being granted under the Directors' Plan upon the approval of the 2003 Non-Employee Directors' Stock Option Plan described below.

In April 2003, the Company adopted the 2003 Non-Employee Directors Stock Option Plan (the "2003 Directors' Plan"). The 2003 Directors' Plan provides for automatic grants to non-employee directors upon their initial appointment or election to the Company's Board of Directors. Options granted under the 2003 Directors' Plan are issued under the 2001 Plan described above. Options are granted at prices

that may not be less than 100% of the fair market value of the stock subject to the option at the date of grant, expire not later than ten years from the date of grant and vest over a four-year period, with one-quarter becoming exercisable one year following the date of grant and the remainder becoming exercisable in monthly increments over a three-year period.

The following table summarizes option activity for all of the option plans (in thousands, except per share data):

	SHARES UNDER OPTION	WEIGHTED AVERAGE EXERCISE PRICE
Outstanding at December 31, 2001	7,064	\$ 7.80
Granted	1,685	\$ 12.93
Exercised	(593)	\$ 5.86
Cancelled	(192)	\$ 10.80
Outstanding at December 31, 2002	7,964	\$ 8.96
Granted	3,665	\$ 20.40
Exercised	(898)	\$ 7.68
Cancelled	(161)	\$ 11.74
Outstanding at December 31, 2003	10,570	\$ 13.01
Granted	3,133	\$ 22.30
Exercised	(702)	\$ 7.56
Cancelled	(379)	\$ 19.20
Outstanding at December 31, 2004	12,622	\$ 15.43

At December 31, 2004, approximately 1.8 million shares remained available for grant under the Company's stock option plans. The weighted average grant-date fair value of options granted by the Company was \$16.36, \$17.69 and \$11.74 in the years ended December 31, 2004, 2003 and 2002 respectively.

Following is a further breakdown of the options outstanding as of December 31, 2004 (in thousands, except life and per share data):

RANGE OF EXERCISE PRICE	NUMBER OUTSTANDING	WEIGHTED AVERAGE REMAINING CONTRACTUAL LIFE	WEIGHTED AVERAGE EXERCISE PRICE	NUMBER EXERCISABLE	WEIGHTED AVERAGE EXERCISE PRICE
\$ 0.313 - \$ 1.065	372	4.02	\$ 0.633	372	\$ 0.633
\$ 1.125 - \$ 1.605	37	4.38	\$ 1.320	37	\$ 1.320
\$ 2.500 - \$ 3.630	634	3.47	\$ 2.678	634	\$ 2.678
\$ 4.375 - \$ 5.460	118	2.31	\$ 4.827	118	\$ 4.827
\$ 5.590 - \$ 8.205	1,132	5.42	\$ 6.153	936	\$ 6.223
\$ 8.260 - \$ 12.315	2,322	6.44	\$ 10.607	1,885	\$ 10.469
\$ 12.320 - \$ 18.480	2,047	6.41	\$ 15.194	1,551	\$ 14.743
\$ 18.510 - \$ 27.735	5,781	8.92	\$ 21.521	1,179	\$ 20.583
\$ 27.770 - \$ 29.980	179	8.73	\$ 28.619	55	\$ 28.621
	12,622			6,767	

**STOCK WARRANTS** The Company has warrants outstanding, which were granted in 1997 and 2000, to purchase a total of 1.6 million shares of its common stock. The warrants are exercisable at prices from \$10.01 to \$12.00 and expire through March 2008.

**SHARES RESERVED FOR FUTURE ISSUANCE** The following shares of common stock are reserved for future issuance at December 31, 2004 (in thousands):

Stock Option Plans	14,392
Stock Purchase Plan	739
401(k) Plan	500
Directors' Deferred Compensation Plan	24
Warrants	1,626
Convertible Senior Notes	11,199
	28,480

**ISSUANCE OF COMMON STOCK** In February 2002, the Company completed a public offering of 12.075 million shares of its common stock at a price of \$8.00 per share. This offering was completed pursuant to a 13.3 million share universal shelf registration statement initially filed with the Securities and Exchange Commission in December 2001. This transaction generated net proceeds of approximately \$90.7 million for the Company.

In September 2002, in connection with the Lilly collaboration, Lilly purchased approximately 1.6 million shares of the Company's common stock at a purchase price of \$30 million, or \$18.69 per share. These shares are not registered under the Securities Act of 1933 ("the Act"), as amended and will be subject to restrictions on the transfer or resale pursuant to the Act. Lilly has certain registration rights with respect to these

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

shares that became exercisable upon the completion of all three of the ongoing Phase 3 clinical trials for exenatide in the fourth quarter of 2003.

In January 2003, the Company completed a public offering of approximately 10.5 million shares of its common stock at a price of \$16.60 per share. This offering was completed pursuant to a \$175 million universal shelf registration statement initially filed with the Securities and Exchange Commission in November 2002. This transaction generated net proceeds of approximately \$165 million for the Company.

**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 (the "Common Shares"), 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 a Common Share. Under certain conditions, the Rights may be redeemed by the Company's Board of Directors in whole, but not in part, at a price of \$0.001 per Right.

### 9. BENEFIT PLANS

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 fair market value of matching contributions made by the Company for the benefit of its employees in 2004, 2003 and 2002 was \$1.0 million, \$873,000 and \$475,000, respectively.

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 expense associated with this plan of \$323,000, \$521,000 and \$499,000 for the years ended December 31, 2004, 2003 and 2002, 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 corresponding liability was \$3.3 million and \$2.3 million at December 31, 2004 and 2003, respectively, of which \$3.1 million and \$2.2 million is included in other long-term liabilities, net of current portion in the accompanying consolidated balance sheets at December 31, 2004 and 2003, respectively. The current portion of the corresponding liability is included in accrued compensation in the accompanying consolidated balance sheets at December 31, 2004 and 2003. Total contributions to this plan, consisting solely of compensation deferred by participants, were \$1.0 million, \$1.2 million, and \$318,000 for the years ended December 31, 2004, 2003 and 2002, respectively.

## 10. INCOME TAXES

Significant components of the Company's deferred tax assets as of December 31, 2004 and 2003 are shown below (in thousands). A valuation allowance of approximately \$358 million has been recognized at December 31, 2004 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." The deferred tax asset at December 31, 2004 includes a future tax benefit of approximately \$13.2 million related to stock option deductions, which, if recognized, will be allocated to additional paid-in capital.

	2004	2003
Deferred tax assets:		
Net operating loss carryforwards	<b>\$ 197,955</b>	\$ 190,433
Research tax credits	<b>43,437</b>	37,311
Deferred revenue	<b>10,280</b>	12,026
Capitalized research and development expenses	<b>102,961</b>	47,304
Other	<b>5,478</b>	4,356
Total deferred tax assets	<b>360,111</b>	291,430
Deferred tax liabilities:		
Intangibles	<b>(1,631)</b>	(1,926)
Valuation allowance for deferred tax assets	<b>(358,480)</b>	(289,504)
Net deferred tax assets	<b>\$ —</b>	\$ —

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, 2004 (in thousands):

	FEDERAL NET OPERATING LOSS CARRYFORWARDS	CALIFORNIA NET OPERATING LOSS CARRYFORWARDS	FEDERAL RESEARCH AND DEVELOPMENT TAX CREDIT CARRYFORWARDS
Expiring within one year	\$ —	\$ 15,118	\$ 293
After 1 but within 5 years	58,961	33,745	4,252
After 5 but within 10 years	194,707	90,970	6,357
After 10 years	282,245	—	23,432
	<b>\$ 535,913</b>	<b>\$ 139,833</b>	<b>\$ 34,334</b>

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

At December 31, 2004, the Company had Federal net operating loss carryforwards of approximately \$536 million, which begin to expire in 2007. During the year, the Company elected to capitalize prior years' research and development expenses for tax purposes, which resulted in a corresponding reduction in its net operating losses. The Company also has California net operating loss carryforwards of approximately \$140 million, which being to expire in 2005, and UK net operating loss carryforwards of approximately \$8 million, which carry forward indefinitely. The difference between the Federal and California tax loss carryforwards is attributable to the capitalization of research and development expenses for California tax purposes and the prior years' limitation on California loss carryforwards. The Company has Federal research tax credit carryforwards of \$34 million, which continue to expire in 2005, and California research tax credit carryforwards of \$14 million, which carry forward indefinitely.

Pursuant to Internal Revenue Code Sections 382 and 383, the use of the Company's net operating loss and credit carryforwards may be limited if a cumulative change in ownership of more than 50% occurs within a three-year period. Although the Company has not completed a formal Section 382 and 383 analysis, the Company believes any resulting limitation would not have a material impact on its financial statements.

### 11. LEGAL PROCEEDINGS

Since August 2001, the Company was subject to an ongoing class action lawsuit filed by certain shareholders in the United States District Court for the Southern District of

California against the Company, its Chairman and former Chief Executive Officer and one director, alleging violations of the federal securities laws related to declines in the Company's stock price. The complaint alleged securities fraud in connection with various statements and alleged omissions to the public and to the securities markets. The Company believes that the lawsuit is without merit. In July 2004, the Company executed a memorandum of understanding with plaintiffs to settle the lawsuit, subject to approval by the court. The terms of the memorandum of understanding include payment by the Company of \$2.1 million, all of which will be paid by the Company's insurance. Any of the \$2.1 million amount remaining after full reimbursement to class members and payment of plaintiff legal fees will be donated to the American Diabetes Association. On December 30, 2004, the court gave final approval to the settlement, dismissing the lawsuits with prejudice.

In October 2002, Roman Glowacki filed a shareholder derivative lawsuit purportedly on behalf of the Company against the Chairman and former Chief Executive Officer and several other present and former members of the Board of Directors of the Company in the California State Superior Court in San Diego County. The derivative complaint alleged that the named defendants breached their fiduciary duty, abused corporate control, engaged in mismanagement, wasted corporate assets and committed "constructive" fraud as a result of the same activities alleged in the Federal class action lawsuit discussed above. The derivative complaint sought attorney fees and the payment of damages to the Company. On November 2, 2004, the court approved a negotiated settlement dismissing the lawsuit with prejudice. The settle-

ment includes the payment of \$250,000 to the plaintiffs' attorneys to be funded by the Company's insurance carrier, along with an agreement to retain some of the existing corporate governance policies and practices at the Company.

## 12. SUBSEQUENT EVENTS

On February 1, 2005, the Company completed a public offering of 9.2 million shares of its common stock at a price of \$22.00 per share. This transaction generated net proceeds of approximately \$190.5 million for the Company and was completed pursuant to a \$300 million universal shelf registration

statement initially filed with Securities and Exchange Commission in December 2003. On March 16, 2005 the U.S. Food and Drug Administration, or FDA, approved SYMLIN® (pramlintide acetate) Injection to be used in conjunction with insulin to treat diabetes.

## 13. 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.

Summarized quarterly data for fiscal 2004 and 2003 are as follows (in thousands, except per share data):

	FOR THE QUARTERS ENDED			
	MARCH 31	JUNE 30	SEPTEMBER 30	DECEMBER 31
<b>2004:</b>				
Revenue under collaborative agreements	\$ 6,689	\$ 7,559	\$ 13,423	\$ 6,597
Loss from operations	\$ (36,856)	(38,064)	(32,417)	(44,911)
Net loss	(37,273)	(39,427)	(34,056)	(46,401)
Basic and diluted net loss per share <sup>(1)</sup>	\$ (0.40)	\$ (0.42)	\$ (0.36)	\$ (0.49)
<b>2003:</b>				
Revenue under collaborative agreements	\$ 11,885	\$ 17,384	\$ 15,361	\$ 41,022
Loss from operations	\$ (30,052)	(36,421)	(40,424)	(16,943)
Net loss	(30,810)	(37,156)	(37,504)	(17,338)
Basic and diluted net loss per share <sup>(1)</sup>	\$ (0.34)	\$ (0.40)	\$ (0.40)	\$ (0.19)

(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.

**REQUEST FOR INFORMATION**

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

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**ANNUAL MEETING**

The next annual meeting of stockholders will be held on May 25, 2005 at 10:00 a.m. at:  
Amylin Pharmaceuticals, Inc.  
9360 Towne Centre Drive  
San Diego, California 92121  
(858) 552-2200



**AMYLIN PHARMACEUTICALS, INC.**

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