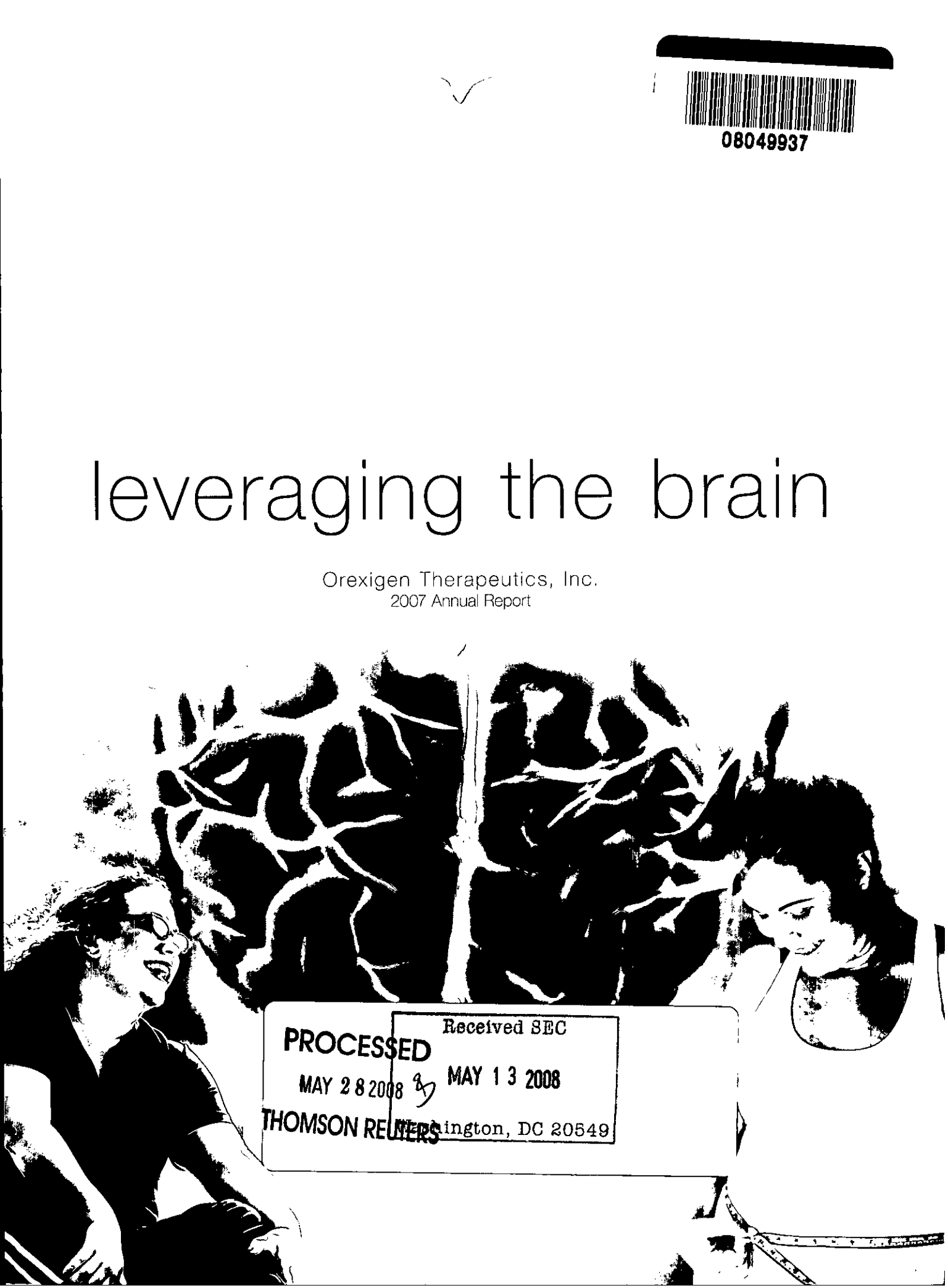


leveraging the brain

Orexigen Therapeutics, Inc.
2007 Annual Report

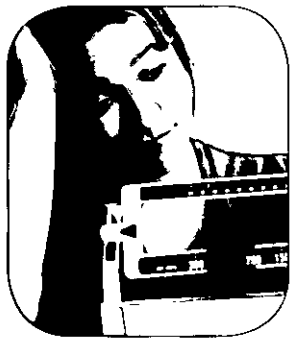
OREXIGEN

OREXIGEN® THERAPEUTICS, INC. is a biopharmaceutical company focused on the development of pharmaceutical product candidates for the treatment of central nervous system (CNS) disorders, including obesity. We combine approved generic drugs with established safety records to create new therapeutics. Our lead product candidates reflect our understanding of how the brain appears to regulate appetite and energy expenditure, as well as the mechanisms that come into play to limit weight loss over time. These include Contrave®, which is in Phase III clinical trials, and Empatic™, which is in the later stages of Phase II development. In addition, we have begun developing two other CNS product candidates: OREX-003 for the mitigation of weight gain associated with antipsychotic therapy and OREX-004 for the treatment of obsessive-compulsive disorder (OCD). We believe there is a substantial unmet medical need in both of these areas, and we expect that a combination approach may improve the therapeutic options that are available for both patient groups.

Obesity is a disorder involving the human brain.

The brain operates as the "master regulator" of our body weight. Signals received by the brain from various parts of the body help determine both a person's appetite and expenditure of energy. The balance between these two factors determines whether we gain or lose weight. In obese individuals, a key region in the brain fails to recognize these signals. Based on our understanding of these relationships, we have chosen drug candidates that we believe help restore our brain's ability to control the balance of appetite and energy expenditure and, thus, body weight.

Losing weight over time is difficult.



Most treatment strategies for obesity are characterized by a "plateau" or loss of effect after three to six months. The reason behind this phenomenon is that the human body, through actions in the brain, exerts a number of compensatory mechanisms designed to limit weight loss. Our lead product candidates to treat obesity are a combination of two drugs: one to initiate weight loss and a second to target one of these key compensatory pathways and minimize its impact. We believe that a combination approach can mitigate the body's efforts to resist long-term, sustained weight loss.

Why do we eat when we're really not that hungry?

We have a "reward circuit" in the brain that reinforces important behaviors. One of those behaviors is eating. However, medical science has shown that reward signals can reinforce unhealthy patterns of eating, leading to obesity. The loss of control over what, when, and how much we eat results from certain behaviors: food cravings, eating in response to our mood or stress level, or compulsive eating patterns in select situations or places. Some of us choose to eat certain types of food because they bring us a degree of pleasure or relaxation.

The benefits of regaining control:

We believe that many obese people, using a strategy of medication, diet and exercise, can successfully lose meaningful amounts of weight. Besides feeling and looking better, even modest weight reduction can have substantial health benefits. Studies have shown that weight loss can reduce the risk of many serious conditions including Type II diabetes, hypertension, heart disease, stroke and sleep apnea.

Gary D. Tollefson, M.D., Ph.D.
President and Chief Executive Officer

Dear Orexigen Stockholder,

On behalf of the Orexigen management team, I would like to extend our sincere appreciation for your support of the Company over this past year. Two thousand and seven has proven to be a year of tremendous progress, full of important milestones. It is with a sense of great accomplishment that I share some of these events with you.

At the beginning of 2007, we set a number of key objectives for the Company including:

- successful completion of our Phase IIb trial of Contrave© and, based on those results, agreement with FDA on the essential elements necessary for our first New Drug Application;
- initiation of a series of concurrent one-year Phase III trials for Contrave (incorporating our proprietary sustained release formulation of naltrexone), in accordance with FDA guidelines and input;
- successful completion of our Phase IIb trial for Empatic™ using the Company's proprietary oral, sustained release formulation of zonisamide;
- conducting preclinical concept work on two pipeline candidates;
- continued "de-virtualization" of the Company by establishing a long-term corporate headquarters and filling numerous key positions with top talent;
- enhancing the Company's recognition and reputation in the investment, analyst and physician communities; and
- execution of a successful initial public offering on the Nasdaq Global Market.

I am pleased to report that we succeeded in meeting each and every one of these objectives. In fact, not only did we achieve them, but we exceeded our own expectations in a number of ways.

With regard to Contrave, our Phase IIb trial demonstrated weight loss at one year, in the absence of a significant diet or exercise regimen, ranging from 8.0% to 10.7% for patients who completed the trial. No serious adverse events were attributed to Contrave by our investigators. The most common adverse event leading to early study discontinuation was nausea, a well-known side effect of naltrexone. We were very pleased with these results because of the favorable risk/benefit profile shown by Contrave. The tolerability profile was especially reassuring because this trial was conducted using an older, immediate release formulation of naltrexone. In Phase I testing, our proprietary sustained release naltrexone has shown a tolerability advantage over its immediate release counterpart. We expect that using our sustained release naltrexone in Phase III trials will result in lowered rates of nausea and other side effects.

We were also enthusiastic about the results of our Phase IIb trial of Empatic. Empatic demonstrated weight loss after one year ranging up to 15% for patients who completed the trial. As with Contrave, no serious adverse events were attributed to the combination by the investigators. We were particularly pleased with the tolerability profile: across all of the six Empatic dosages the rate of discontinuation due to adverse events was not significantly different from that seen with placebo. Notably, in the highest dose tested, the rate of discontinuation due to an adverse event was not significantly different from placebo. In light of these results, we believe that Empatic holds great promise, particularly for the more severely obese patients whose only current therapeutic alternative is an invasive surgical procedure.

During the last year we have also made great progress as a corporation. We completed our initial public offering in April, which was one of the strongest recent U.S. biotech offerings in terms of pricing and demand. We have attracted a number of extremely experienced, highly respected health care investors. In addition, having begun operations using a "virtual" model, we continued to bring operations in-house and expand our necessary infrastructure. We have recently

moved into new corporate offices in the Torrey Pines area of San Diego, which will provide space necessary for our growth over the foreseeable future. As the scope of our business has grown, we have expanded our internal headcount. However, we have done so with a philosophy mandating continued improvement in efficiency and control, as well as a clear cost-based justification. We continue to put a premium on experience and integrity.

Finally, we received notification that the U.S. Patent and Trademark Office issued a Notice of Allowance for our Weber/Cowley patent, which is the basis on which the Company was founded. The application covers sustained release compositions of bupropion and naltrexone combined in a single dosage form. This patent, if issued, will extend patent protection in the United States for Contrave by 11 years, into the year 2024. We also received a similar notice from the European Patent Office covering the composition and use of Contrave, a key milestone toward eventual approval in various European countries. These were major wins for the Company, as they significantly improve the net present value of the Contrave program.

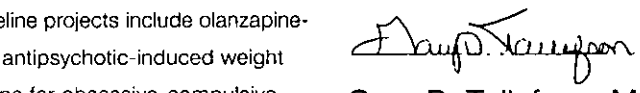
With these major achievements in the past year, we believe Orexigen is on a steady course for continued success. We expect to see initial results in late 2008 or early 2009 with the Contrave Phase III program. Our NDA team is already being assembled in advance of the extensive document preparation that will be necessary in 2009. We continue to anticipate our NDA submission for Contrave in late 2009. For Empatic, we expect to initiate a Phase IIb trial comparing the combination to its individual components and placebo in mid-2008. Results should be available from this trial in mid-2009. This is our last anticipated trial before starting the Phase III development program for Empatic.

Our recently announced pipeline projects include olanzapine-zonisamide for mitigation of antipsychotic-induced weight gain and naltrexone-fluoxetine for obsessive-compulsive disorder. We are now poised to begin Phase II proof-of-concept studies this summer. Based on the results of our preclinical work, we are enthusiastic about the prospects for both of these product combinations to address serious unmet needs within these CNS therapeutic arenas.

With all of our focus on corporate performance, we should acknowledge the reason we are here in the first place: the patient. The obesity epidemic continues unabated. Fully one-third of the American adult population now meets the CDC criteria for obesity, and another one-third is overweight. Moreover, every week there seems to be new research detailing the consequences of obesity ranging from diabetes to cancer to depression. The morbidity, mortality and cost associated with obesity make this one of the most significant public health challenges we face. However, the magnitude of this challenge also represents a major opportunity for pharmaceutical product development. We consistently hear from patients and physicians that they are anxious for a solution. With one promising product candidate in Phase III and another in Phase II, we believe we are very well-positioned to address this area of critical, unmet need.

At Orexigen, we emphasize effective implementation and timely deliverables. Looking back on the past year, in short, we have exceeded our own clinical and corporate objectives. We have established a trajectory of success that suggests a bright future for Orexigen. In closing, I would take this opportunity to thank our employees, investors, clinical investigators and especially our trial participants for their continued support. We have great confidence in the progress and opportunity of our clinical development programs. We expect to provide meaningful therapeutic solutions for patients and, in turn, economic rewards to our investors.

Sincerely,



Gary D. Tollefson, M.D., Ph.D.
President and Chief Executive Officer

OREX PIPELINE

| Preclinical | Phase 1 | Phase 2 | Phase 3 | NDA | Market |

Obesity

- Contrave®
- Empatic™

Mitigation of Antipsychotic-Induced Weight Gain

- OREX-003

Obsessive-Compulsive Disorder

- OREX-004

Contrave©

Contrave© is in Phase III trials for obesity. It combines bupropion SR, a well-known anti-depressant, with our proprietary sustained release formulation of naltrexone, a drug for alcohol and opioid addiction. While bupropion triggers an appetite suppression pathway in the brain, naltrexone keeps endorphins from slowing down appetite suppression and weight loss. In addition, through its mechanism of action, it is believed that Contrave is the first obesity drug to address the "reward" system in the brain that causes food cravings. In a Phase II trial, patients who completed the trial lost between 8.0% and 10.7% in body weight over one year.

Empatic™

Empatic™ is in the later stages of Phase II clinical development for obesity. It combines bupropion SR with our proprietary sustained release formulation of zonisamide, an anticonvulsant. We believe that zonisamide inhibits a pathway that would otherwise counter the appetite suppression and energy expenditure induced by bupropion. In a Phase IIb trial, patients who completed the trial on double blind therapy lost between 11.0% and 15.1% in body weight over one year.

OREX-003

OREX-003 is our olanzapine/zonisamide SR combination product candidate for the mitigation of weight gain associated with antipsychotic therapy. Olanzapine (marketed as Zyprexa©), while effective in the treatment of psychosis, has been shown to cause weight gain and metabolic side effects. Based on preclinical work that we have conducted, we believe the addition of zonisamide could attenuate the increase in appetite that olanzapine often induces.

OREX-004

OREX-004 is our fluoxetine/naltrexone SR combination product candidate for the treatment of obsessive-compulsive disorder. Based on preclinical work that we have conducted, we believe there may be synergy between these agents in treating the symptoms of OCD in humans.

OREXIGEN

Form 10-K

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

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2007

Or

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

For the transition period from to

Commission file number 001-33415

OREXIGEN THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**65-1178822**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*
12481 High Bluff Drive, Suite 160, San Diego, California	**92130**
(Address of Principal Executive Offices)	*(Zip Code)*

(858) 436-8600

(Registrant's Telephone Number, Including Area Code)

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

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

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

None

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

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

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

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

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

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☑ Smaller reporting company ☐

(Do not check if a smaller reporting company)

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

As of June 29, 2007, the aggregate market value of voting stock held by nonaffiliates of the registrant was approximately $158.3 million based on the closing stock price as reported by the NASDAQ Global Market for such date. Shares of common stock held by each officer and director and by each person or group who owns 5% or more of the outstanding common stock have been excluded in that such persons or groups may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 14, 2008, the Registrant had 34,309,036 shares of its $0.001 par value common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2008 Annual Meeting of Stockholders are incorporated by reference into Part III of this Report. Such proxy statement will be filed with the Securities and Exchange Commission subsequent to the date hereof but not later than 120 days after registrant's fiscal year ended December 31, 2007.

OREXIGEN THERAPEUTICS, INC.

FORM 10-K FOR THE FISCAL YEAR ENDED DECEMBER 31, 2007

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PART 1

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K and the information incorporated herein by reference contain certain forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and is subject to the Safe Harbor provisions created by that statute. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. All statements other than statements of historical facts are "forward-looking statements" for purposes of these provisions. Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "hopes," "may," "will," "plans," "intends," "indicates," "suggests," "assuming," "designed," "estimates," "could," "should," "would," "continue," "seeks," "aims," "projects," "predicts," "pro forma," "anticipates," "potential" or other similar expressions that are intended to qualify forward-looking statements. These statements include but are not limited to statements regarding the progress and timing of clinical trials, the safety and efficacy of our product candidates, the goals of our development activities, the scope of our intellectual property protection, estimates of the potential markets for our product candidates, estimates of the capacity of manufacturing and other facilities to support our products, our operating and growth strategies, our industry, our projected cash needs, liquidity and capital resources and our expected future revenues, operations and expenditures. For example, we make forward-looking statements regarding the enrollment, timing and completion of clinical trials of Contrave and Empatic, the potential to obtain regulatory approval for, and effectively treat obesity with, Contrave and Empatic and the issuance of patents extending intellectual property protection for Contrave and Empatic. These statements involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading "Item 1A — Risk Factors."

Given these risks and uncertainties, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify our forward-looking statements by these cautionary statements. We undertake no obligation to update publicly any forward-looking statements or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, whether as a result of new information, future events, or for any other reason.

Item 1. *Business.*

Overview

Orexigen™ Therapeutics, Inc. ("Orexigen", "we", "our" and "us") is a biopharmaceutical company focused on the development of pharmaceutical product candidates for the treatment of central nervous system, or CNS, disorders, including obesity. Our lead product candidates targeted for obesity are Contrave™, which is in Phase III clinical trials, and Empatic™, which is in the later stages of Phase II clinical development. Each of these product candidates is a combination of generic drugs, which we have systematically screened for synergistic CNS activity. We seek to combine chemical entities that, individually, have already received regulatory approval and have been commercialized previously, into new product candidates that we believe address unmet medical needs and are patentable. We are testing these combinations in an effort to demonstrate adequate efficacy and safety for potential regulatory approval. We have not yet received regulatory approval for any product candidate. In addition, we plan to continue to screen drugs for synergistic CNS activity and, based on the results, we may advance other potential combination product candidates into clinical trials.

We have selected our product candidates for obesity based on our research regarding CNS regulation of appetite and energy expenditure, as well as the reward-based mechanisms in the brain that reinforce unhealthy eating behaviors. These product candidates suggested a synergy within our screening model, which enabled us to prioritize them over others considered. In particular, we have focused our clinical development programs on drug combinations that we expect will generate weight loss and attenuate, or limit the effect of, the pathways in the brain

that prevent extended weight loss. Our combination approach contrasts with most currently-approved weight loss drug therapies, which utilize a single active ingredient and have typically shown early weight loss followed by a plateau after several months of treatment. We believe that our approach to obesity drug development will permit a sustained, clinically-relevant pattern of weight reduction. Results from our clinical trials to date for both Contrave and Empatic have supported this hypothesis. We believe that our strategy will increase our probability of technical success while reducing both the time and cost associated with development.

In addition, we are seeking to improve the profiles of our product candidates by developing proprietary sustained release, or SR, drug delivery formulations for their constituent drugs. In the clinical trial data collected to date, compositions of Contrave and Empatic using these proprietary SR formulations for the constituents naltrexone and zonisamide, respectively, have demonstrated improved patient tolerability compared to those using previously approved immediate release, or IR, formulations of naltrexone and zonisamide. Because of differences in pharmacokinetics between the generically available formulations and our proprietary SR formulations, we believe we can enhance patient outcomes and our competitive position.

We have begun developing two additional product candidates: OREX-003 for the mitigation of weight gain associated with antipsychotic therapy and OREX-004 for the treatment of obsessive-compulsive disorder. We believe there is a substantial unmet medical need in both of these areas, and we expect that a combination approach may improve the therapeutic options available for both patient groups. Preclinical data on both programs appear to have substantiated the validity of our initial hypotheses. We expect to initiate Phase II clinical trials for each product candidate in the third quarter of 2008.

We maintain an aggressive intellectual property strategy, which includes patent and trademark filings in multiple jurisdictions including the United States and other commercially significant markets. We hold exclusive licenses to two issued U.S. patents covering the Contrave composition and an exclusive license to an issued U.S. patent covering the Empatic composition and methods of use in obesity. In addition, we own or have exclusive rights to numerous patent applications currently pending in the United States and in jurisdictions outside of the United States with respect to various compositions, methods of use and formulations relating to Contrave and/or Empatic.

In April 2006, we met with the U.S. Food and Drug Administration, or FDA, to discuss the clinical trial requirements for submission of new drug application, or NDA, filings for both Contrave and Empatic. Based on feedback from the FDA, we are conducting clinical trials for Contrave, and intend to conduct clinical trials for Empatic, to provide substantial evidence of their safety and effectiveness in treating obesity. Our understanding of the NDA filing requirements for Contrave was confirmed in our end-of-Phase-II meeting with the FDA in October 2007. Accordingly, our clinical development plan for Contrave is designed to obtain data on 1,500 patients exposed to drug for one year, under double-blind, placebo-controlled conditions. We expect the Phase III clinical development plan for Empatic will follow a similar design. Our clinical trials may not corroborate our earlier results. In addition, undesirable side effects of Contrave and Empatic may delay or prevent their regulatory approval. We expect to file an NDA with the FDA in late 2009 for Contrave and in early 2012 for Empatic, assuming that our clinical trials proceed as planned and are successful.

We currently retain worldwide marketing rights for both Contrave and Empatic. If approved, we may consider marketing these product candidates to select specialists; however, we expect that Contrave and Empatic have the potential to be prescribed to a significant extent by primary care physicians. In order to target this large group of potential prescribers, we may consider entering into a collaboration with a pharmaceutical company with the sales force and marketing resources to adequately address this physician audience. We expect to position Contrave for mild to moderate weight loss, particularly in women who report food craving. Empatic, in contrast, may be better suited for moderate to severe obesity in men and post-menopausal women.

The Obesity Epidemic

Obesity is a serious condition that is growing in prevalence and afflicts populations worldwide. In 1980, approximately 15% of the adult population in the United States was obese, according to the National Health and Nutrition Examination Survey. By 2002, the obesity rate had doubled to approximately 30% of the U.S. adult population, according to a later installment of the same survey. In addition, the survey estimated that another 34% of

the U.S. adult population was overweight in 2002. We expect that given current trends, many members of this group will become obese in coming years. These estimates are based on thresholds of Body Mass Index, or BMI, which measures weight on a height-adjusted basis. A BMI level exceeding 30, or a BMI over 27 with other risk factors, is typically classified as obese, while a BMI between 25 and 30 is typically categorized as overweight. As an example, an individual who is six feet tall weighing 220 pounds would have a BMI of approximately 30. BMI is generally accepted within the medical community as a reliable indicator of body fat and is the standard for measurement used to determine if a person is overweight or obese, according to the National Institutes of Health, or NIH. Moreover, it is a relative risk predictor of the morbidity and mortality associated with being obese.

The growing prevalence of obesity has increasingly been recognized as a significant public health problem. In 2004, the Centers for Disease Control and Prevention identified obesity as the number one health threat in the United States. Approximately 300,000 deaths per year in the United States are associated with obesity, according to the Department of Health and Human Services, or HHS. Obesity is also a significant health problem outside of the United States. According to the World Health Organization, there are as many as 1.6 billion people worldwide considered to be overweight, of whom at least 400 million are estimated to be obese. Despite recognition of obesity as a public health crisis, we believe that the obesity epidemic will continue to grow in the United States given the trend towards larger meals, higher calorie foods and a sedentary lifestyle.

Excessive body weight is also associated with various physical complications that are often present and exacerbated by the obese condition. Diabetes, cancer, hypertension, high cholesterol, coronary artery disease, sleep apnea, liver and pulmonary disease, among others, are seen in greater prevalence among the obese than the general population, according to HHS and the North American Association for the Study of Obesity. In addition, research has established a new disease category called metabolic syndrome, which comprises the various co-morbidities, or related conditions, that often accompany obesity. Beyond these consequences, a number of co-morbidities involving the CNS may be complicated by obesity. These co-morbidities include anxiety, depression, substance abuse, chronic pain and insomnia. We believe there is a growing recognition within the medical community that obesity significantly exacerbates these conditions. Obesity and its co-morbidities are believed to cause significant added cost to the health care system. In 2000, HHS estimated the overall economic costs of obesity in the United States to be $117 billion. We expect that more effective treatment of obesity may also be a cornerstone in managing its co-morbidities.

Despite the growing obesity rate, increasing public interest in the obesity epidemic and significant medical repercussions and economic costs associated with obesity, there continues to be a significant unmet need for more effective pharmacological interventions.

Limitations of Current Obesity Therapies

Treatments for obesity consist of behavioral modification, pharmaceutical therapies, surgery and device implantation. Modifications to diet and exercise are the preferred initial treatment in obesity according to the NIH. However, the rigors of behavioral modification often cause significant attrition over time and thus suboptimal weight loss outcomes. Additionally, such an approach is not optimal for every individual. When pharmaceutical therapies are recommended, it is generally after behavioral modification alone has failed. Bariatric surgery, including gastric bypass and gastric banding procedures, is employed in more extreme cases, typically for obese individuals with a BMI over 40. Surgery can be effective in helping patients to lose 50% or more of their total body weight. However, surgery can be associated with significant side effects, potential complications including mortality, and substantial costs and recovery time. In addition, while surgery may be effective in achieving weight loss, recent research has identified "addiction transfer," where patients begin heavy alcohol consumption, drug use or other addictive habits in response to the reduced ability to consume food after gastric bypass surgery. Device implantation, such as neurostimulation, is a newer therapy which has yet to be widely adopted within the medical community.

Several pharmaceutical products have been approved for obesity marketing in the United States. Approved obesity drugs are generally prescribed for short-term use; only a select few have been approved for longer-term maintenance therapy. Several older drugs, indicated for short-term administration, have an amphetamine-like profile, including phentermine, phendimetrazine, benzphetamine and diethylpropion, according to the FDA

approved product information. However, according to that same product information, these drugs have an increased risk for abuse potential and may be associated with adverse cardiovascular or CNS effects. Of these drugs, phentermine, a Class IV controlled substance indicated for short-term use, is the most widely used. Like diet alone, these older treatments, according to a December 1996 issue of the Journal of the American Medical Association, are generally associated with the classic weight loss plateau typically seen after several months of use.

Two drugs approved in the United States for long-term use in the treatment of obesity are sibutramine and orlistat. Sibutramine is marketed in the United States by Abbott Laboratories under the brand name Meridia. An extensive meta-analysis of various clinical trials published in The Annals of Internal Medicine in April 2005 indicates that sibutramine produces average weight loss in patients of approximately 4.5 kg; however, patients typically experience a weight loss plateau after approximately 12 weeks. Sibutramine has been associated with increased risk of hypertension and tachycardia as evidenced in the FDA approved product information.

Orlistat is marketed in the United States by Roche Laboratories, Inc. under the brand name Xenical. The above meta-analysis reported that orlistat produces average weight loss of approximately 2.75 kg. Orlistat is associated with gastrointestinal side effects, the nature of which can be socially constraining, as evidenced in the FDA approved product information. These include flatulence, fecal incontinence and urgency. Orlistat was also launched in 2007 by GlaxoSmithKline in over-the-counter form under the brand name alli.

Due to the side effects and limited efficacy of these approved drugs, less than 2% of the obese population in the United States was treated with a pharmaceutical intervention in 2005, according to a September 2006 report by Frost & Sullivan. This represented approximately five million total U.S. prescriptions, which we believe substantially understates the potential demand for effective treatments. In the mid-1990s, fenfluramine or dexfenfluramine were used off-label in combination with phentermine, together known as "fen-phen," and demonstrated significant weight loss. At its peak in 1996 before fenfluramine and dexfenfluramine were withdrawn for safety issues, fen-phen, along with other prescribed pharmaceuticals, represented over 20 million total U.S. prescriptions, according to IMS Health. We believe this history, combined with the substantial economic cost associated with obesity, underscores the unmet need and the potential for novel therapeutics to dramatically grow the market for obesity therapies.

The Orexigen Solution for Obesity

Obesity is increasingly recognized within the medical community as a disorder of CNS regulation of appetite and energy expenditure. The brain, specifically the hypothalamus, plays a critical role in governing many fundamental processes throughout the body. The hypothalamus receives chemical and hormonal stimuli from various sources, including glucose, insulin, leptin and the peptides secreted by the gut as it processes food. These inputs govern a person's appetite, satiety and energy expenditure. The brain governs body weight by establishing a setpoint, much like a thermostat in an air conditioning system. The body then tries to maintain this value even when the food supply varies a great deal. However, malfunctioning of this system may allow the setpoint to slide up or down, causing overeating and obesity on the one hand or progressive weight loss and cachexia, a physical wasting disorder, on the other.

The brain contains numerous redundant circuits and compensatory mechanisms to preserve body weight, which should not be surprising given that maintenance of body weight is essential to survival. Such mechanisms are invoked in the presence of weight loss whether intentional (in the case of diet) or not (in the case of starvation). This explains the cause of a weight loss plateau. Moreover, in order to appropriately motivate humans to seek food, reward circuitries in the brain stimulate the urge to consume higher calorie food and in turn reward that behavior. The craving cycle is particularly intense with highly palatable foods, such as sweets.

Existing products cause some weight loss for most patients. We believe their modest effect stems from their failure to address these natural compensatory mechanisms in the body. As a result, most of these products have been vulnerable to a classic early weight loss plateau typically seen after several months of therapy. In addition, they generally do not address the psycho-behavioral elements that contribute to unhealthy eating behaviors and, ultimately, obesity. We have designed our product candidates to circumvent the body's natural compensating mechanisms and drive weight loss further, beyond this commonly seen plateau. In addition, with Contrave in

particular, we are attempting to go beyond the traditional approach to weight reduction by also targeting the underlying behavioral mechanisms of craving and reward that drive excess consumption.

The combinations we have chosen are based on the output of a low-throughput screening model developed by our co-founder and Chief Scientific Officer, Michael Cowley, Ph.D. We have obtained an exclusive license to this technology from Oregon Health & Science University, or OHSU. This screening technology uses an *in vitro* model that allows us to quantify firing rates for specific neuronal populations using green fluorescent protein tagging. In particular, research has shown that there is one group of hypothalamic neurons called proopiomelanocortin, or POMC, neurons that play a critical role in managing weight. By exposing POMC neurons in our *in vitro* model to varying concentrations of one or more drug products, we are able to measure the difference in firing activity of these neurons at baseline and over time. This permits us to predict whether a drug will produce weight loss and, more importantly, whether the addition of a second drug has a previously undiscovered synergistic effect on POMC firing rates. We have screened several known compounds as part of the model's validation. Our lead compounds, Contrave and Empatic, both suggested a synergistic profile with respect to POMC firing rates in the model. Additionally, we have verified this predicted synergy in more traditional animal feeding studies. Both combinations have subsequently demonstrated this synergy in human clinical trials.

Our Product Candidates

We are developing Contrave and Empatic for the treatment of obesity. Both of these product candidates have been prepared with combinations of chemical entities that, individually, have already received regulatory approval and have been commercialized previously. If we receive approval to market these product candidates in the United States or elsewhere, we anticipate that they will be produced and sold as single tablets to be taken orally twice a day. In addition, we have begun developing other CNS-related product candidates for the mitigation of weight gain associated with antipsychotic therapy and for the treatment of obsessive-compulsive disorder. Our product pipeline is detailed as follows:

Product Candidate	Drug Components	Indication	Trials Completed	Stage of Development	Commercial Rights
Contrave	Bupropion SR/ Naltrexone SR	Obesity	Phase II, Phase IIb	Phase III	Orexigen (worldwide)
Empatic	Bupropion SR/ Zonisamide SR	Obesity	Phase II, Phase IIb	Phase IIb	Orexigen (worldwide)
OREX-003	Olanzapine/ Zonisamide SR	Mitigation of weight gain associated with antipsychotic therapy	Preclinical	Phase II Planned for 2008	Orexigen (worldwide)
OREX-004	Naltrexone SR/ Fluoxetine	Obsessive-compulsive disorder	Preclinical	Phase II Planned for 2008	Orexigen (worldwide)

Contrave

Contrave is a fixed dose combination of naltrexone SR and bupropion SR. We chose these constituents based on the results of our screening model as well as our understanding of the circuitries in the brain that regulate appetite and energy balance. In particular, naltrexone was chosen as a complement to bupropion in order to block compensating mechanisms that attempt to prevent long-term, sustained weight loss. We hold the exclusive license to two issued U.S. patents covering the Contrave composition, and we have filed additional patents covering various compositions, methods of use and formulations.

Naltrexone was approved in the United States in 1984 for the treatment of opioid addiction and in 1995 for the treatment of alcoholism. It is marketed under the brand names Trexan, Depade, Revia, and in an injectable extended release formulation, Vivitrol. Naltrexone IR became available in generic form in the United States in 1998. Naltrexone works by blocking opioid receptors in the brain and inhibits the reinforcing aspects of addictive substances, reducing their perceived reward. Naltrexone was evaluated in the 1980s for weight loss and was shown

to have negligible effects in clinical trials. However, it has been shown to negatively alter the palatability of many foods, particularly sweets, including, for example, in a study published in the October 2002 issue of Neuroscience and Biobehavioral Reviews. Nausea is a well-known side effect associated with IR naltrexone that affects its tolerability. In our Contrave Phase II clinical trials, we used the generic IR formulation of naltrexone. Commencing with our Phase III clinical trials, naltrexone is being delivered in our proprietary SR formulation in order to improve its tolerability.

Bupropion was approved for marketing in the United States in 1985 for depression, marketed under the brand name Wellbutrin, and in 1997 for smoking cessation, marketed under the brand name Zyban. The IR version became available in generic form in the United States in 1999. Bupropion SR became available in generic form in the United States in 2004 and bupropion XL became available in generic form in the United States in December 2006. Bupropion is active at the neuronal uptake site for the neurotransmitters dopamine and norepinephrine. Functionally, bupropion is thought to increase the level of dopamine activity at specific receptors in the brain, which appears to lead to a reduction in appetite and increase in energy expenditure. Bupropion is currently among the most commonly prescribed antidepressants in the United States; in 2006, its sales totaled approximately $2.4 billion and approximately 9% of the total prescriptions written for depression, according to IMS Health. Bupropion has become popular in the treatment of depression not only for its clinical efficacy, but also its attractive side effect profile relative to other antidepressants on the market. One of the reported side effects of bupropion clinical trials was modest weight loss. Subsequently, bupropion has been studied for weight loss; results have shown approximately 3% weight loss before reaching plateau, according to a study published in the October 2002 issue of Obesity Research.

Scientific Rationale

The two drug constituents of Contrave were chosen in order to leverage the brain's normal circuitry and biochemistry to reduce appetite, expend more calories, diminish food craving and food-based reward, and block compensating mechanisms that attempt to prevent long-term, sustained weight loss. Bupropion has been shown in studies to activate the POMC neurons within an area in the hypothalamus known as the arcuate nucleus. As bupropion increases firing of POMC neurons, two important chemical products are released. One is alpha-Melanocyte Stimulating Hormone, or α-MSH, which activates a receptor in the hypothalamus known as the melanocortin-4, or MC-4, receptor which appears to lead to a reduction of appetite and an increase in energy expenditure. This is a major pathway by which naturally occurring peptides such as leptin regulate body weight. However, in obese patients, a resistance to circulating leptin prevents the body from acting in its normal way to regulate weight. Bupropion-induced stimulation of POMC circumvents leptin resistance and activates this weight loss pathway.

In addition to α-MSH, stimulation of POMC also produces beta-endorphin, an opioid occurring naturally in the body. Our co-founder and Chief Scientific Officer, Michael Cowley, Ph.D., identified an auto-receptor on the POMC neuron that recognizes beta-endorphin. Dr. Cowley discovered that by binding to this receptor, beta-endorphin serves as a brake on the POMC system. Left unchecked, this braking system acts to reduce POMC firing rates, thus moderating potential weight loss and likely explaining the characteristic plateau in weight loss. Based on this discovery, we chose naltrexone as the second component in Contrave. Naltrexone is a potent opioid receptor antagonist which competes with beta-endorphin, thus limiting its access at the auto-receptor on the POMC neuron. When bupropion and naltrexone are co-administered, they both induce an increase in POMC firing that is maintained for an extended duration. This is expected to translate into a greater weight loss that should be sustained over an extended time period.

As a second benefit, both bupropion and naltrexone are known to act on the reward pathways in the brain that have been implicated in addiction to a number of substances, including food. These reward pathways are primarily regulated by dopamine and endogenous opioids, which are the targets of bupropion and naltrexone, respectively. Given that both drugs are approved for addiction-related disorders, we expect that together they may attenuate food craving and reward. As a result, we expect that Contrave may have an additional therapeutic benefit in patients who report food craving or obsession, which drives them to eat even when not hungry.

Contrave Clinical Results

Phase II Clinical Trial. We initiated clinical testing of Contrave with a Phase II clinical trial in 2004. This trial enrolled 238 patients at eight U.S. clinical trial sites to evaluate the safety and efficacy of the Contrave combination. Patients accepted for the trial had a BMI in the range of 30 to 40, were non-smokers and did not have diabetes or other significant medical complications. On average, patients enrolled in this trial weighed approximately 95 kilograms, or 209 pounds, at the beginning of the trial, or baseline. Patients were randomly placed into one of four treatment groups:

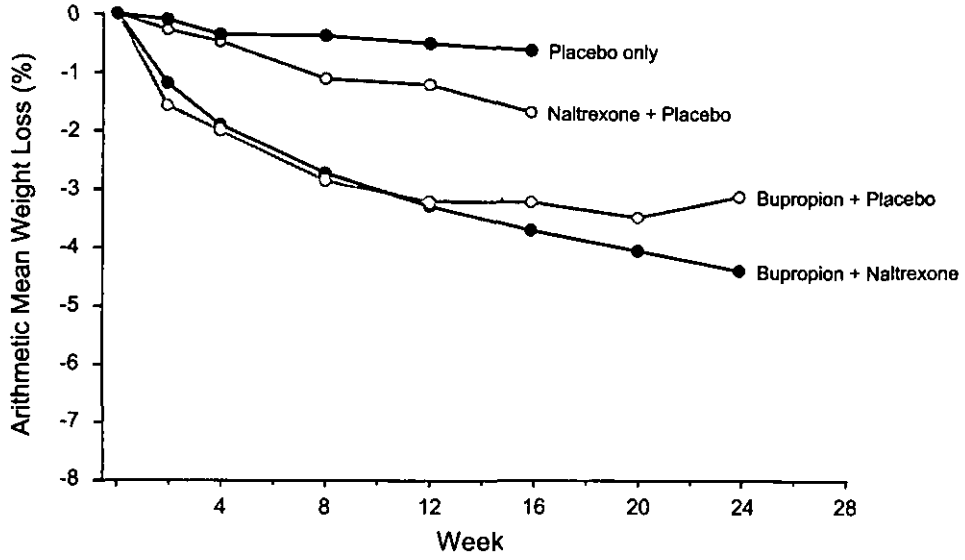
- combination therapy, which consisted of 50mg naltrexone IR plus 300mg bupropion SR;
- bupropion monotherapy, which consisted of 300mg bupropion SR plus placebo;
- naltrexone monotherapy, which consisted of 50mg naltrexone IR plus placebo; and
- placebo, which consisted of two placebo pills.

The primary endpoint for this trial was percent change in body weight measured 16 weeks after the start of treatment, with secondary endpoints that included the percent change in body weight 24 weeks after the start of treatment and response rates based on the percentage of patients who lost at least 5% and 10% of their baseline weight 16 and 24 weeks after the start of treatment. The outcomes for patients receiving the combination regimen were compared to each individual monotherapy and placebo. We also monitored the safety and tolerability of Contrave in this trial. The statistical analysis plans for the first Phase II clinical trials for Contrave and Empatic specified the use of an adjusted least-squares mean methodology for analysis of the primary endpoints. Accordingly, we have reported our results for these trials using this methodology. Least-squares mean methodology is based on a linear regression technique applied by statisticians to clinical trial data. We note, however, that graphs that show weight loss over time for each treatment group in our Contrave and Empatic clinical trials utilize arithmetic mean data.

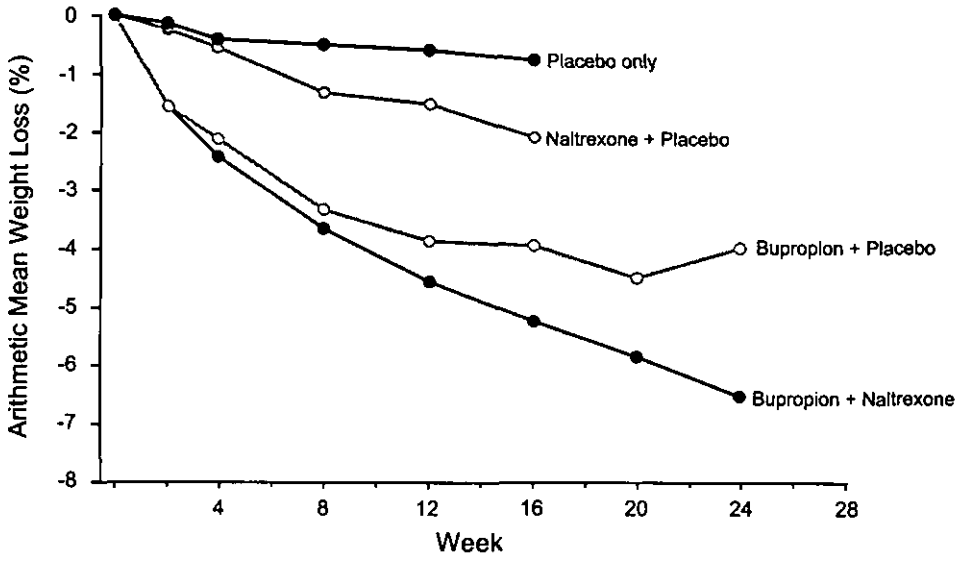
On an intent-to-treat basis, which includes all randomized patients who recorded at least one post-baseline body weight measurement, Contrave demonstrated in this trial mean weight loss of 4.0% of baseline body weight at 16 weeks, compared to 3.6% for bupropion alone, 2.0% for naltrexone alone and 1.0% for placebo. One important observation in this trial was that the benefit of adding naltrexone became more apparent over time, as weight loss curves for the combination therapy group gradually diverged from the bupropion monotherapy group. Accordingly, by 24 weeks, Contrave showed 5.2% weight loss on an intent-to-treat basis, compared to 4.0% for bupropion alone. When this analysis is restricted to those patients who completed 16 weeks of treatment, Contrave demonstrated mean weight loss of 4.8% of baseline body weight, compared to 3.9% for bupropion alone, 2.3% for naltrexone alone and 1.0% for placebo. By 24 weeks, Contrave showed 6.8% weight loss among completers, compared to 4.5% for bupropion alone.

Weight loss, plotted over time on both an intent-to-treat basis as well as for completers, is as follows:

Contrave Phase II Mean Weight Loss through 24 Weeks
Intent-to-Treat Population



Contrave Phase II Mean Weight Loss through 24 Weeks
Completer Population



There were three serious adverse events identified in this trial, all reported by the investigators as unrelated to the study drugs. At 16 weeks, approximately 17.6% of the patients receiving Contrave had discontinued its use due to a treatment-related adverse event, compared to 16.4% for the bupropion monotherapy group, 24.1% for the naltrexone monotherapy group and 9.4% for the placebo group. The most common side effect reported for Contrave was nausea, which was experienced early in treatment and generally resolved over time. Most cases of nausea were reported to be mild; a few were rated as moderate. Nausea is a well-known side effect associated with naltrexone.

Phase IIb Clinical Trial. Based on the results of our initial Phase II clinical trial for Contrave, we concluded that Contrave showed sufficient efficacy and an acceptable safety and tolerability profile to warrant continued development. In July 2005, we proceeded to study Contrave in a larger Phase IIb trial exploring a higher dose of bupropion SR and lower doses of naltrexone IR. This trial enrolled 419 patients at eight clinical sites in the United States. This trial was submitted to the FDA as a Phase II clinical trial. However, because we believe that the results from this clinical trial provide sufficient evidence of the superiority of the combination drug therapy to the individual monotherapies and placebo in the treatment of obesity, we have characterized this study as a Phase IIb clinical trial. In correspondence with the FDA, the agency has indicated that the results from this trial enable future pivotal studies to be conducted based on a comparison of the combination therapy to placebo only. This determination will limit the amount of additional data we need to collect to support our future NDA filing. Furthermore, we believe that the use of placebo as a comparator for evaluating the efficacy of Contrave should increase the likelihood that Contrave will demonstrate efficacy in our Phase III program.

Prior to the commencement of the Phase IIb clinical trial, in an effort to determine the optimal dose of naltrexone, we evaluated in a Positron Emission Tomography, or PET, study three doses that were lower than the 50mg employed in the previous Phase II clinical trial. PET permits quantification of the extent to which a given drug dosage occupies its target receptors. In general, an antagonist such as naltrexone should occupy 70% to 80% of the relevant receptor population in order to be functionally effective. We tested naltrexone dosages of 16mg, 32mg and 48mg in this PET trial. Results indicated that each of these three doses would be predicted to be effective and we therefore believed that there was little rationale to go either above or below this dose range. Accordingly, these three doses were taken into our Phase IIb clinical trial for Contrave.

The Phase IIb clinical trial was designed to evaluate patients for 24 weeks under double-blind conditions. Patients accepted for the trial had a BMI in the range of 30 to 40, were non-smokers and did not have diabetes or other significant medical complications. On average, patients enrolled in this trial weighed approximately 95 kilograms, or 209 pounds, at baseline. Patients were initially placed randomly into one of five treatment groups:

- 48mg naltrexone IR plus 400mg bupropion SR;
- 16mg naltrexone IR plus 400mg bupropion SR;
- bupropion monotherapy, which consisted of 400mg bupropion SR plus placebo;
- naltrexone monotherapy, which consisted of 48mg naltrexone IR plus placebo; and
- placebo, which consisted of two placebo pills.

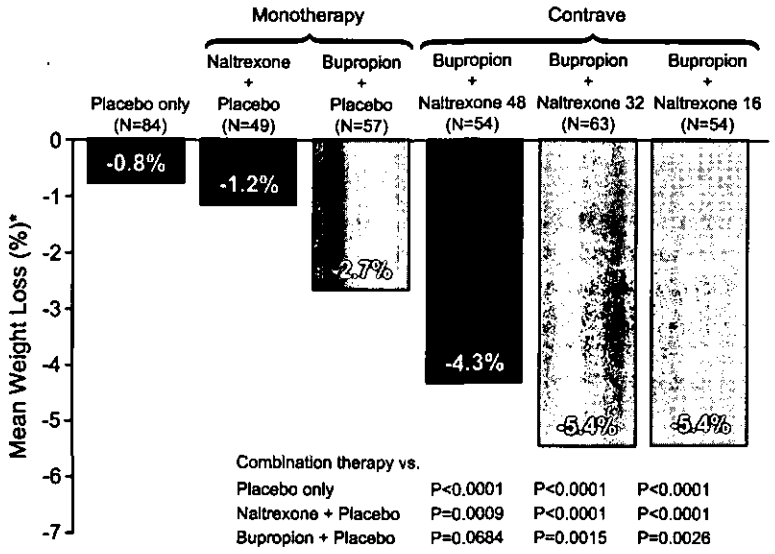
The primary endpoint for this trial was percent change in body weight measured 24 weeks after the start of treatment, with secondary endpoints that included the percentage of patients who lost at least 5% and 10% of their baseline weight 24 weeks after the start of treatment. The outcomes for patients receiving the combination regimen were compared to each individual monotherapy and placebo. We also monitored the safety and tolerability of Contrave in this trial. For the Contrave Phase IIb clinical trial, the statistical analysis plan specified the use of an unadjusted least-squares mean methodology for analysis of the primary endpoint. Accordingly, we have reported our results for this trial using this methodology.

In addition, on the basis of the PET results, we added a second set of patients randomized either to 32mg naltrexone plus 400mg bupropion SR or a double placebo. While these patients were enrolled subsequent to the initial group of patients, the clinical sites, investigators and study procedures remained constant. The statistical analysis plan submitted to the FDA included specifications for a pooled analysis of both groups of patients. In total, 361 patients between the two sets were randomized and had at least one post-baseline body weight measurement. These patients represent the intent-to-treat population.

After 24 weeks, patients were permitted to continue in the study for an additional 24 weeks of open-label treatment. Patients that were initially randomized to placebo or naltrexone monotherapy were crossed over to naltrexone 32mg plus bupropion 400mg therapy; all other patients that remained with the study continued to receive their originally assigned treatment. Data for the crossover group have been segregated and are not considered in the 48 week efficacy analyses presented below.

We believe the 24 week data show significant advantages of Contrave therapy for the treatment of obesity compared to the efficacy demonstrated by the respective monotherapies and placebo. The 24 week results are depicted graphically for the intent-to-treat and completer populations as follows:

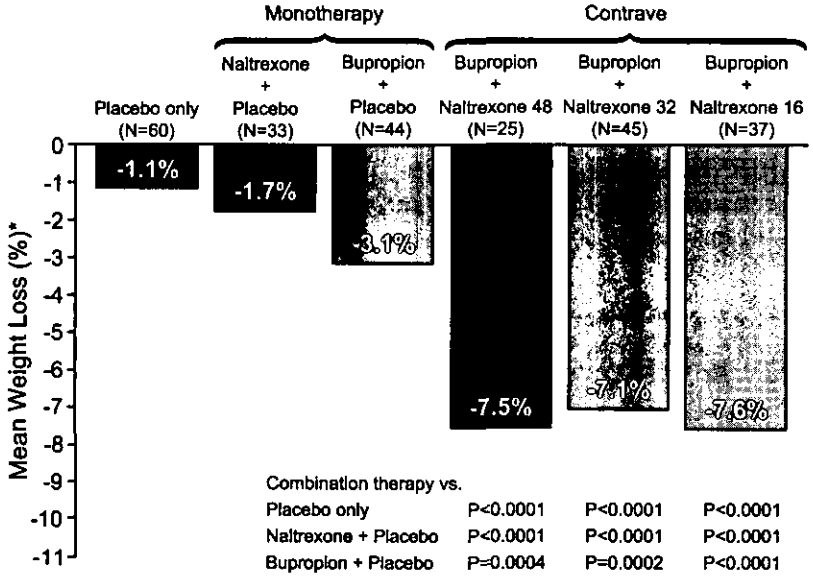
Contrave Phase IIb Mean Weight Loss at 24 Weeks
Intent-to-Treat Population



* Calculated on the basis of unadjusted least-squares mean methodology.

"N" indicates the number of patients in the treatment group. "P"-values indicate the likelihood that clinical trial results were due to random statistical fluctuations rather than true cause and effect. The lower the p-value, the more likely there is a true cause-and-effect relationship. Typically, the FDA requires a p-value of less than 0.05 to establish the statistical significance of a clinical trial.

Contrave Phase IIb Mean Weight Loss at 24 Weeks
Completer Population



* Calculated on the basis of unadjusted least-squares mean methodology.

As noted, the p-values were statistically significant among all comparisons (intent-to-treat and completers) with the exception of a single comparison for the intent-to-treat population between 48mg naltrexone IR plus 400mg bupropion SR compared to 400mg bupropion SR alone where the p-value was 0.0684.

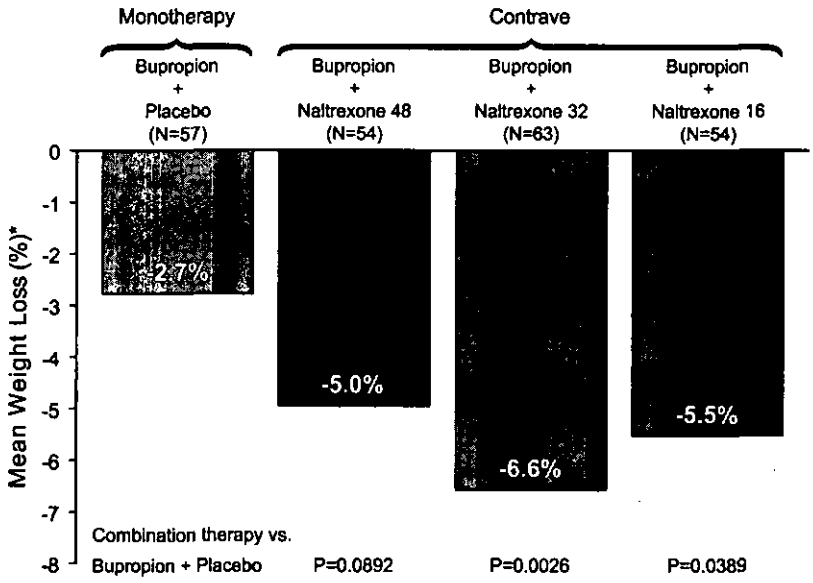
With regard to the 5% and 10% categorical response rates, patients in the three Contrave combination therapy groups performed substantially better than monotherapy as well as placebo patients. For the intent-to-treat population at 24 weeks, between 39% and 52% of patients on the three dosages of Contrave lost at least 5% of their body weight, compared to 26% for bupropion alone, 10% for naltrexone alone and 15% for placebo. Between 15% and 19% of patients on the three dosages of Contrave in the intent-to-treat group lost at least 10% of their body weight, compared to 7% for bupropion alone, 2% for naltrexone alone and 2% for placebo. For the completer population, between 64% and 70% of patients on the three dosages of Contrave lost at least 5% of their body weight, compared to 32% for bupropion alone, 15% for naltrexone alone and 20% for placebo. Between 24% and 32% of patients on the three dosages of Contrave in the completer group lost at least 10% of their body weight, compared to 9% for bupropion alone, 3% for naltrexone alone and 3% for placebo.

There were three serious adverse events in this trial through the 24-week primary endpoint, all reported by investigators as unrelated to the study drugs. There were five additional serious adverse events in four patients in the 24-week continuation period. One of these, atrial fibrillation, in a patient receiving bupropion monotherapy, was considered by the investigator as possibly related to the bupropion monotherapy; the others were all considered to be unrelated to any of the study drugs. Of the intent-to-treat population, approximately 68% of patients completed treatment through 24 weeks. The rates of discontinuation of study drug due to adverse events at 24 weeks ranged from 15.9% to 29.5% for the three Contrave dosages, compared to 8.3% for bupropion monotherapy, 10.7% for naltrexone monotherapy and 8.2% for placebo. As in the previous Phase II clinical trial with naltrexone IR, nausea was the most common adverse event leading to discontinuation of therapy. The rate of discontinuation of study drug due to nausea appeared to be dose-dependent, with the lower doses of naltrexone demonstrating a substantially lower rate of discontinuation at 24 weeks than the highest Contrave dose (48mg naltrexone IR/400mg bupropion SR). All other adverse event-related causes of study drug discontinuation at 24 weeks were below a 7% frequency.

Discontinuation of study drug due to an adverse event generally occurred early in treatment. As a result, in the intent-to-treat analysis, the 48mg naltrexone IR plus 400mg bupropion SR treatment appears somewhat less effective than other Contrave dosages. Use of the last-observation-carried-forward, or LOCF, method implies that data for patients who drop out of the study prior to completion are carried forward in the analysis. Thus, limited weight loss observed early in the course of treatment in patients who discontinue treatment early averages down the efficacy observed in patients who remained on therapy for longer periods of time. This effect is illustrated when comparing the intent-to-treat results to the completer analysis.

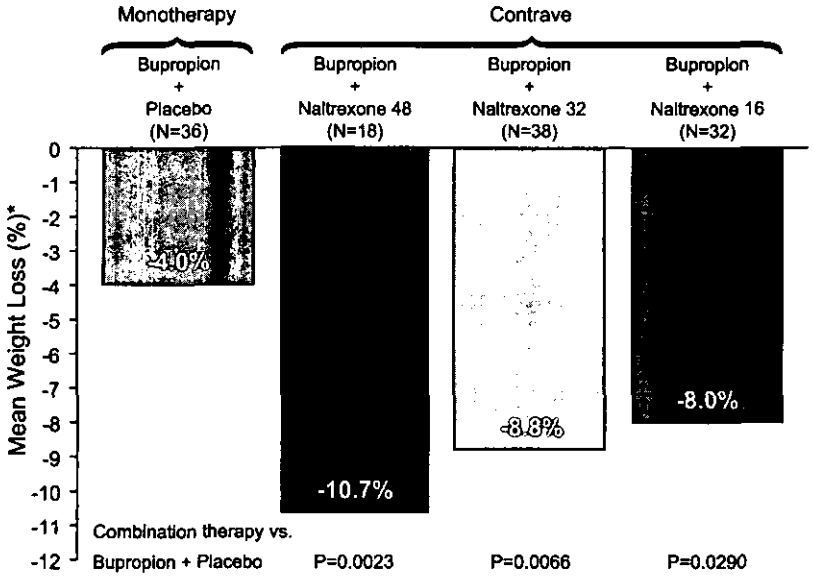
As noted, weight loss at 24 weeks was the primary endpoint for this trial. However, the protocol permitted study participants to continue on Contrave or bupropion for an additional 24-week period. Data through 48 weeks of treatment indicates that patients, particularly those assigned to the Contrave treatment groups with the two highest naltrexone dosages (48mg and 32mg), continued to lose weight in the interval from weeks 24 to 48. For the intent-to-treat and completer populations, the results were as follows:

Contrave Phase IIb Mean Weight Loss at 48 Weeks
Intent-to-Treat Population



* Calculated on the basis of unadjusted least-squares mean methodology.

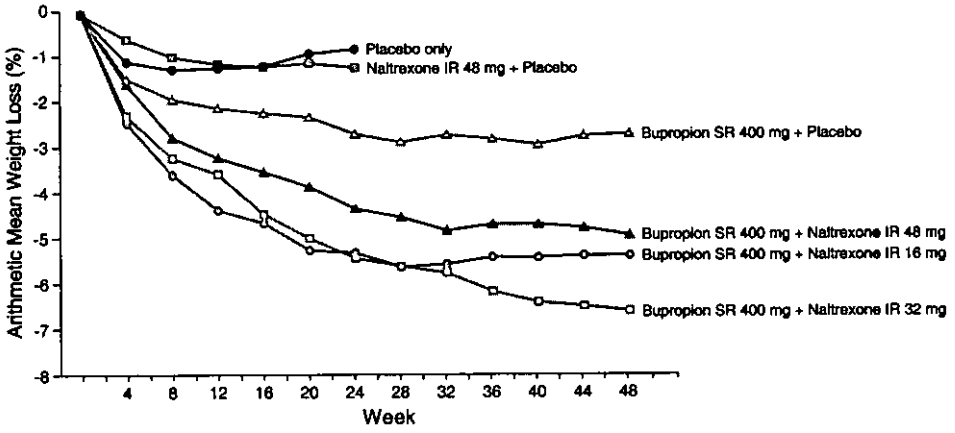
Contrave Phase IIb Mean Weight Loss at 48 Weeks
Completer Population



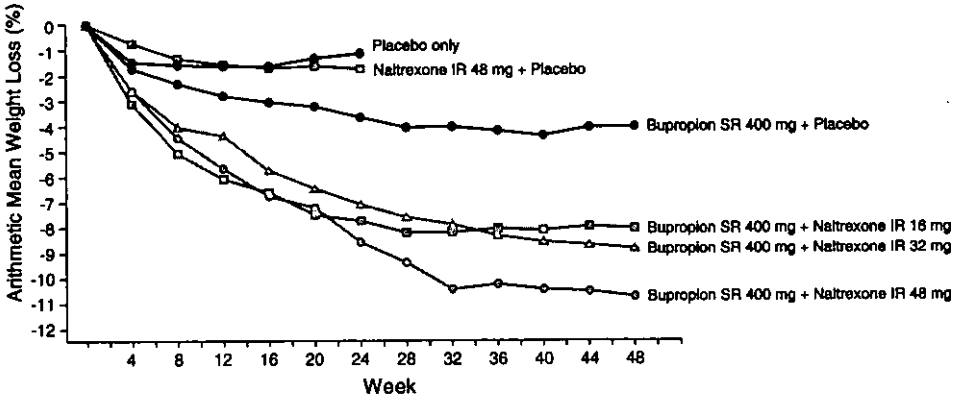
* Calculated on the basis of unadjusted least-squares mean methodology.

As noted, the p-values were statistically significant among all comparisons (intent-to-treat and completers) with the exception of a single comparison for the intent-to-treat population between 48mg naltrexone IR plus 400mg bupropion SR compared to 400 mg bupropion SR alone where the p-value was 0.0892. Weight loss through 48 weeks, plotted for the intent-to-treat and completer populations, is as follows:

Contrave Phase IIb Mean Weight Loss Over 48 Weeks
Intent-to-Treat Population



Contrave Phase IIb Mean Weight Loss Over 48 Weeks
Completer Population



As these results imply, most patients continued to lose weight between 24 weeks and 48 weeks. No serious adverse events related to the Contrave combination occurred during this trial.

A subset of patients participating in our Phase IIb clinical trial for Contrave also participated in a study assessing the effects of Contrave therapy on visceral fat. Visceral fat is the fat that surrounds the organs in the

abdomen, and is particularly worrisome as it is associated with increased risk for cardiovascular disease, insulin resistance, hypertension and hyperlipidemia. In this sub-study, patients from all study arms (Contrave at three different naltrexone dosages, bupropion monotherapy, naltrexone monotherapy and placebo) received body scans to measure body composition at the start of treatment and 24 weeks after the start of treatment. These measurements enabled determination of patients' total fat, visceral fat and lean tissue composition at the beginning of treatment and at the 24-week point. Of the patients analyzed, the three Contrave-treated groups experienced a mean decrease in total body fat at 24 weeks of between 12.2% and 16.0%, compared to a 3.2% to 4.1% mean decrease for patients receiving either of the monotherapies or placebo. Patients in the three Contrave therapy groups experienced a mean decrease in visceral body fat at 24 weeks of between 13.7% and 16.7%, compared to a 0.1% to 4.6% mean decrease for patients receiving either of the monotherapies or placebo. These results suggest that weight loss associated with Contrave therapy results primarily from fat tissue loss, including loss of visceral fat.

In addition, Contrave demonstrated improvements in both serum lipids and glycemic indices at week 24. In particular, the Contrave 32/400mg dose group demonstrated statistically significantly greater improvement compared to either the placebo or monotherapy groups on measures of fasting glucose and insulin resistance (log (HOMA)) and the insulin check index (QUICKI). Significant improvements were also observed when compared with the control groups in waist circumference, insulin and triglycerides.

We are conducting additional clinical trials as described below, the results of which may not corroborate our earlier results, in order to provide enough evidence regarding efficacy and safety to submit an NDA to the FDA for potential regulatory approval. In addition, the occurrence of one or more serious side effects associated with Contrave may delay or prevent regulatory approval. The most common side effects observed in our clinical trials of Contrave to date include nausea, dizziness, insomnia and headaches, all of which were considered non-serious.

Contrave Phase III Clinical Development Program

In April 2006, we met with the FDA to discuss the clinical trial requirements for submission of NDA filings for both Contrave and Empatic. Based on feedback from the FDA, we are conducting clinical trials for Contrave, and intend to conduct clinical trials for Empatic, to provide substantial evidence of their safety and effectiveness in treating obesity. Our understanding of the NDA filing requirements for Contrave was confirmed in our end-of-Phase-II meeting with the FDA in October 2007. Accordingly, our clinical development plan for Contrave is designed to obtain data on 1,500 patients exposed to drug for one year, under double-blind, placebo-controlled conditions. We expect the Phase III clinical development plan for Empatic will follow a similar design. Our clinical trials may not corroborate our earlier results. In addition, undesirable side effects of Contrave and Empatic may delay or prevent their regulatory approval. We expect to file an NDA with the FDA in late 2009 for Contrave and in early 2012 for Empatic, assuming that our clinical trials proceed as planned and are successful.

We are currently conducting four Phase III clinical trials for Contrave. Based on our Phase II and Phase IIb trial results and feedback from the FDA, these Phase III clinical trials are designed to assess three doses of naltrexone SR (16mg, 32mg and 48mg) in combination with a 360mg dose of bupropion SR. We believe this dose of bupropion SR, which is in the mid-range of the doses used in our earlier trials, will provide an optimal efficacy-to-side-effects ratio. In addition, as explained further below, we believe that the use of our proprietary naltrexone SR formulation in these trials, as opposed to the IR formulation used in our Phase II clinical trials for Contrave, may lower the incidence of nausea. We believe our Phase III program will provide the required efficacy, safety and exposure data required by the FDA for submission of an NDA. In correspondence with the FDA, the agency agreed that based on the results of our Phase IIb clinical trial for Contrave, our Phase III clinical trials need to evaluate the safety and efficacy of Contrave relative to placebo only, and do not need to compare Contrave to the individual constituent drugs.

Our Phase III clinical trials for Contrave include:

- *NB-301:* This trial is designed to study the effect of Contrave in generally healthy obese patients utilizing the two lower doses of Contrave. We commenced enrollment for this trial in the fourth quarter of 2007 and expect to enroll approximately 1,650 patients at 34 sites. Patients are being blindly randomized to one of two doses of Contrave (16mg naltrexone SR or 32mg naltrexone SR plus 360mg bupropion SR) or placebo. We intend to analyze as co-primary endpoints for this trial the percent change in body weight and percent of patients who achieve 5% weight loss, in each case 56 weeks after the start of treatment.

- *NB-302:* This trial is designed to study the effect of Contrave in generally healthy obese patients in combination with an intensive behavior modification protocol, including dietary counseling, behavioral therapy and exercise. We completed enrollment of this trial in November 2007 with 793 patients at nine sites. Patients have been blindly randomized to one of two treatment arms: Contrave (32mg naltrexone SR plus 360mg bupropion SR) plus behavior modification or placebo plus behavior modification. We intend to analyze as co-primary endpoints for this trial the percent change in body weight and percent of patients who achieve 5% weight loss, in each case 56 weeks after the start of treatment.

- *NB-303:* This trial is designed to study the effect of Contrave in generally healthy obese patients, with a provision for dose escalation for non-responders. We commenced enrollment for this trial in the fourth quarter of 2007 and expect to enroll approximately 1,500 patients at 36 sites. Patients are being blindly randomized initially to either Contrave (32mg naltrexone SR plus 360mg bupropion SR) or placebo. After 28 weeks of treatment, Contrave patients who have not achieved at least 5% weight loss will be blindly re-randomized to receive either a higher dose of Contrave (48mg naltrexone SR plus 360mg bupropion SR) or remain on the original dose. We intend to analyze as co-primary endpoints for this trial the percent change in body weight and percent of patients who achieve 5% weight loss, in each case 56 weeks after the start of treatment.

- *NB-304:* This trial is designed to study the effect of Contrave in obese patients with Type II diabetes. We commenced enrollment for this trial in the second quarter of 2007 and expect to enroll approximately 525 patients at 53 sites. Patients are being blindly randomized to either Contrave (32mg naltrexone SR plus 360mg bupropion SR) or placebo. We intend to analyze as co-primary endpoints for this trial the percent change in body weight and percent of patients who achieve 5% weight loss, in each case 56 weeks after the start of treatment. Recent studies have demonstrated that obesity is a leading risk factor for various metabolic disorders, such as diabetes, and this trial will evaluate several factors related to glucose metabolism as secondary endpoints.

We expect to begin receiving results from Phase III clinical trials of Contrave beginning in late 2008 or early 2009.

We believe that our clinical trial experience with Contrave has demonstrated and replicated the validity of our naltrexone hypothesis, specifically, that the addition of naltrexone to bupropion permits greater weight loss than bupropion alone and sustains weight loss beyond 24 weeks. Moreover, in our clinical trials, Contrave has demonstrated significantly greater weight loss than naltrexone alone as well as placebo. The rate of response (greater than 5% and 10% reduction in body weight from baseline) has also favored Contrave and provides additional support for our belief that Contrave will provide a clinically relevant alternative for clinicians and obese patients.

Contrave SR Formulation Development. While Contrave has generally been well tolerated, the principal adverse event across our trials to date has been nausea. Nausea is typically seen early upon initiating treatment and appears to be transient in most cases. Patients have generally rated their nausea as mild and, on occasion, moderate in severity. Clinical results from our studies suggest that the incidence of nausea has generally been related to the dose of naltrexone IR, particularly at dosages of 48mg or higher. The pharmacology of naltrexone suggests that nausea is related to both gastrointestinal motility and a dose-related CNS effect. There are a number of ways in which we can attempt to address this issue, including lowering the dose, titrating the drug more slowly and adjusting the formulation to release the drug more gradually. Concerning the latter, we hypothesized that, if the drug could be released beyond the stomach, such as in the small bowel, and the maximum blood concentration, or C_{max}, lowered, the incidence and/or intensity of nausea and other adverse events may be reduced.

Accordingly, we have successfully developed and tested an SR formulation of naltrexone which achieves similar exposure or area under-the-curve, referred to as AUC, to that obtained with naltrexone IR but with a lowered C_{max}. This SR preparation is primarily absorbed in the small bowel where the density of opioid receptors is lower, thus reducing the local effects of naltrexone in the gut. In a recent Phase I pharmacokinetic study that we conducted, this SR preparation demonstrated an improvement in tolerability across various measures. These included overall adverse events and gastrointestinal-related events. Not only were the rates of reported adverse events lower in the

SR group, the severity of reported adverse events was also lower. We have incorporated this proprietary SR formulation into the Contrave tablet for our Phase III clinical trials.

Planned Mechanistic Study. As part of the exploration of the putative effect of Contrave on food craving, we plan to initiate a study utilizing functional magnetic resonance imaging, or fMRI. This technique is a brain imaging technology that permits the regional localization and quantification of changes in neuronal activation. Based on emerging literature demonstrating that the brain's basic reward mechanisms are activated when exposed to individualized food cues (picture, image, smell, etc.), we believe the potential exists to demonstrate such a regional activation in select brain centers with select food cues, and in turn, the ability of Contrave to reduce this activation relative to placebo. The constituents of Contrave have been shown individually to be effective in attenuating craving-associated behaviors (bupropion in smoking under the brand name Zyban, and naltrexone in alcoholism and opioid drug addiction under the brand names Vivitrol, Trexan and Revia). Our proposed study would be conducted in a randomized, double-blind fashion at an academic neuroimaging center. Under current plans, patients receiving either Contrave or placebo will receive an fMRI at baseline and at study termination at week eight. It is anticipated that this study, to the extent that it substantiates our hypothesis, may be useful in positioning Contrave as a treatment that reduces the craving-based consumption of select high calorie foods among obese individuals.

Empatic

Empatic is a fixed dose combination of zonisamide SR and bupropion SR. The combination of zonisamide and bupropion, in our screening model, suggested a synergistic increase in POMC neuronal firing, indicating that this drug combination would enhance satiety and energy expenditure. We have also validated this synergy in rodent models of obesity. Based on the strength of these results and the unique mechanism of action of Empatic, we selected this product combination to complement our Contrave clinical development program. We hold an exclusive license to an issued U.S. patent covering the Empatic composition and methods of use in obesity, and we have filed additional patents covering various compositions, methods of use and formulations.

Zonisamide IR was approved in the United States in 2000 for the adjunctive treatment of partial seizures, a form of epilepsy. It is marketed under the brand name Zonegran by Eisai Inc., which acquired the rights to the product from Elan Pharmaceuticals in 2004. Zonegran became available in generic form in the United States in 2005, and at its peak produced approximately $177 million in annual sales, according to IMS Health. The precise mechanism of zonisamide is unknown; however, it is believed that zonisamide has a number of pharmacologic mechanisms including sodium-channel modulation and enhancement of dopamine and serotonin neurotransmission. Zonisamide, given alone, has also shown weight loss in prior clinical trials conducted at Duke University, or Duke.

We have developed a proprietary SR formulation of zonisamide in order to improve its tolerability. Controlling the release of zonisamide via our novel SR formulation reduces the C_{max} while retaining a similar AUC to zonisamide IR. In a single-dose, double-blind, crossover Phase I clinical trial the zonisamide SR formulation that we have chosen to take forward suggested an improved side effect profile compared to the IR form. Our initial Phase II clinical trial of Empatic used an IR formulation of zonisamide. Our more recent Phase IIb clinical trial of Empatic utilized our proprietary zonisamide SR formulation. In commercial form, if approved, zonisamide SR and bupropion SR would be paired in a single tablet given orally twice a day.

Scientific Rationale

Like Contrave, Empatic employs bupropion to increase α-MSH secretion via POMC stimulation. The second component in Empatic, zonisamide, has been shown in our research to synergistically increase the firing rate of POMC neurons by up to eightfold in the presence of bupropion. However, we also believe that zonisamide may have one or more additional effects. Within the hypothalamus, a set of neurons acts in a reciprocal way to POMC. These are referred to as the Neuropeptide Y/Agouti-related peptide, or NPY/AgRP, neurons. Stimulation of NPY/AgRP neurons results in the release of AgRP, which competes with α-MSH for access to the MC-4 receptor. Binding of AgRP at the MC-4 receptor results in an increase in appetite and energy conservation, which tends to counteract the weight loss promoting activity of α-MSH. The pharmacology of zonisamide has been hypothesized to also inhibit

the firing of NPY/AgRP neurons. Strategies that minimize AgRP competition for the MC-4 receptor and maximize α-MSH activation of the MC-4 receptor thus may have the potential to lead to substantive weight loss. We plan to continue to explore the combination of increased POMC firing and reduced NPY/AgRP activity in our clinical development of Empatic.

Empatic Clinical Results

Phase II Clinical Trial. We initiated clinical testing of Empatic with a Phase II proof-of-concept clinical trial in 2004. This trial enrolled 127 patients across five clinical sites in a similar protocol to our Phase II clinical trial of Contrave. Patients accepted for the Empatic Phase II clinical trial had a BMI between 30 to 40, were non-smokers and did not have diabetes or other significant medical complications. On average, patients enrolled in this trial weighed approximately 94 kilograms, or 207 pounds, at baseline. Patients were randomly placed into one of two treatment groups:

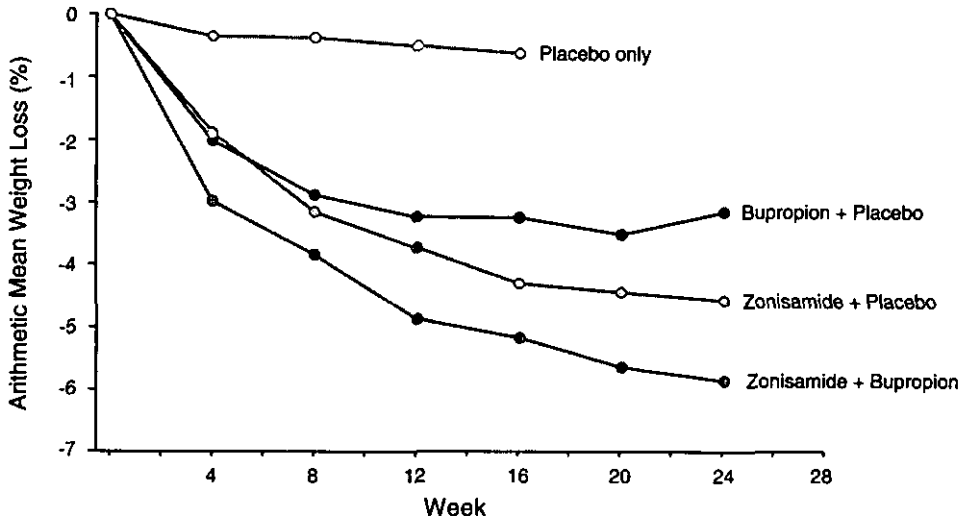
- combination therapy, which consisted of 300mg bupropion SR plus 400mg zonisamide IR; or
- zonisamide monotherapy, which consisted of 400mg zonisamide IR plus placebo.

Since the design was nearly identical to our Phase II clinical trial of Contrave, and because it was performed immediately following that trial and conducted at a subset of the same investigative sites, the analysis plan anticipated utilizing the placebo and bupropion monotherapy data from the Contrave Phase II clinical trial for comparative purposes. The primary endpoint for the Empatic Phase II clinical trial was percent change in body weight measured 16 weeks after the start of treatment, with secondary endpoints that included the percent change in body weight 24 weeks after the start of treatment and the percent of patients who lost at least 5% and 10% of their baseline weight 16 and 24 weeks after the start of treatment.

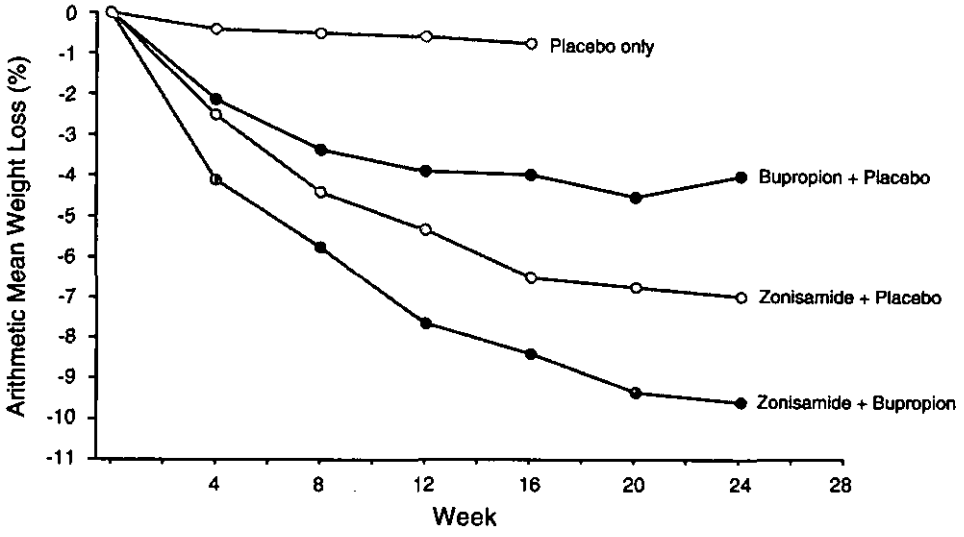
On an intent-to-treat basis, Empatic demonstrated in this trial mean weight loss of 5.2% from baseline at 16 weeks, compared to 4.3% for zonisamide alone. On a completers analysis, Empatic patients demonstrated mean weight loss of 8.3% from baseline 16 weeks after the start of treatment, compared to 5.7% for zonisamide alone. At 24 weeks, the advantage of Empatic treatment in weight loss became more apparent. By 24 weeks, Empatic showed 5.8% weight loss on an intent-to-treat basis, compared to 4.5% for zonisamide alone. When this analysis is restricted to those patients who completed 24 weeks of treatment, Empatic demonstrated mean weight loss of 9.2% of baseline body weight, compared to 6.5% for zonisamide alone.

Weight loss, plotted over time for the intent-to-treat and completer populations, was as follows:

Empatic Phase II Mean Weight Loss Over 24 Weeks
Intent-to-Treat Population



Empatic Mean Weight Loss Over 24 Weeks
Phase II Completer Population



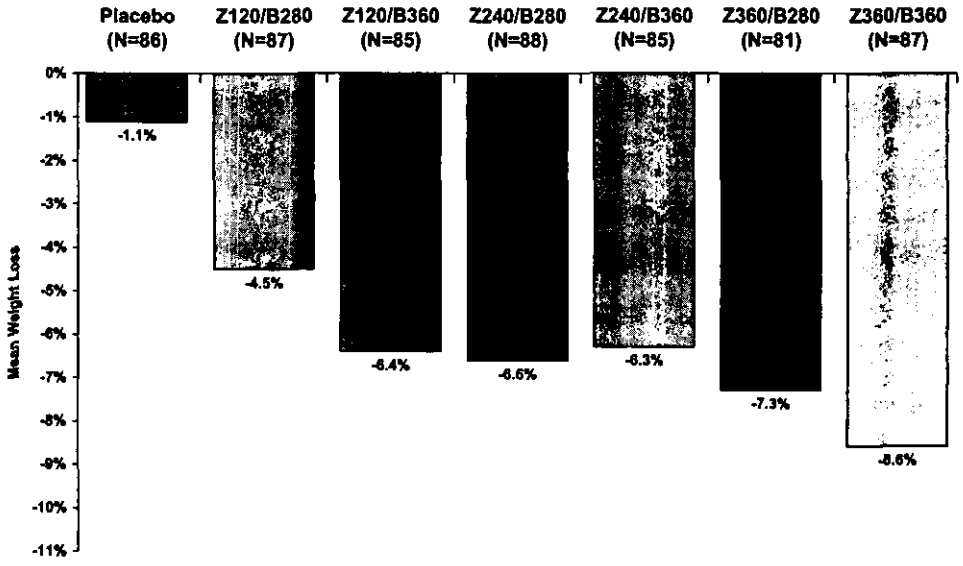
There were two serious adverse events reported in this trial, both of which were designated by the investigators as unrelated to the study drugs. In addition, two patients (one patient in the combination group and one patient in the zonisamide plus placebo group) experienced suicidal ideation, which is a labeled adverse event for both bupropion and zonisamide. The symptoms resolved after discontinuation of study drugs. Among patients receiving Empatic, the rate of discontinuation of the trial at 24 weeks due to an adverse event was 37.3%, compared to 20.3% for the zonisamide IR monotherapy group. Adverse events were typically reported shortly after initiation of therapy and tended to resolve over time.

Phase IIb Clinical Trial. Based on the results of our initial Phase II clinical trial for Empatic, we concluded that Empatic showed sufficient efficacy and an acceptable safety and tolerability profile to warrant continued development. In June 2006, we proceeded to study Empatic in a larger Phase IIb clinical trial exploring several different dosage combinations of bupropion and zonisamide at 15 clinical sites in the United States. Prior to the commencement of the Phase IIb clinical trial, in an effort to improve the tolerability profile of the Empatic combination, we developed and tested a proprietary SR formulation of zonisamide. We employed this SR formulation in three dosages of zonisamide SR paired with one of two dosages of bupropion SR. Patients accepted into this randomized, double-blind, placebo-controlled clinical trial had a BMI between 29 to 45, were non-smokers and did not have diabetes or other significant medical complications. On average, patients enrolled in this trial weighed approximately 100 kilograms, or 220 pounds, at baseline. The trial enrolled 623 patients, of which 599 are included in the intent-to-treat population, meaning they received at least one post-baseline measurement. The trial included only minimal diet and exercise intervention. Patients were randomized into seven treatment groups:

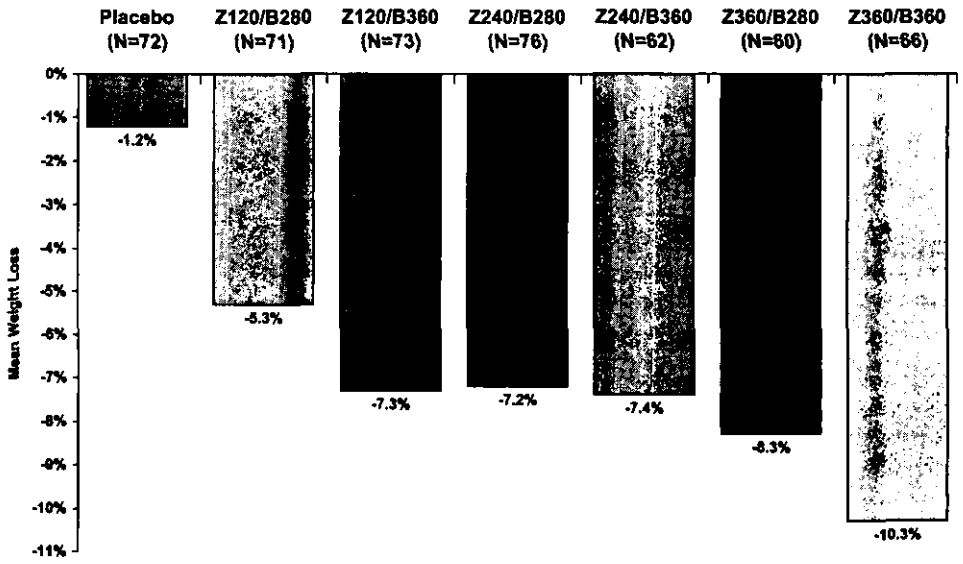
- 120mg zonisamide SR plus 280mg bupropion SR;
- 240mg zonisamide SR plus 280mg bupropion SR;
- 360mg zonisamide SR plus 280mg bupropion SR;
- 120mg zonisamide SR plus 360mg bupropion SR;
- 240mg zonisamide SR plus 360mg bupropion SR;
- 360mg zonisamide SR plus 360mg bupropion SR; and
- placebo, which consisted of two placebo pills.

The primary endpoint for this trial was percent change in body weight measured 24 weeks after the start of treatment. For the intent-to-treat and completer populations, the results at 24 weeks were as follows:

Empatic Phase IIb Mean Weight Loss at 24 Weeks
Intent-to-Treat Population



Empatic Phase IIb Mean Weight Loss at 24 Weeks
Completer Population

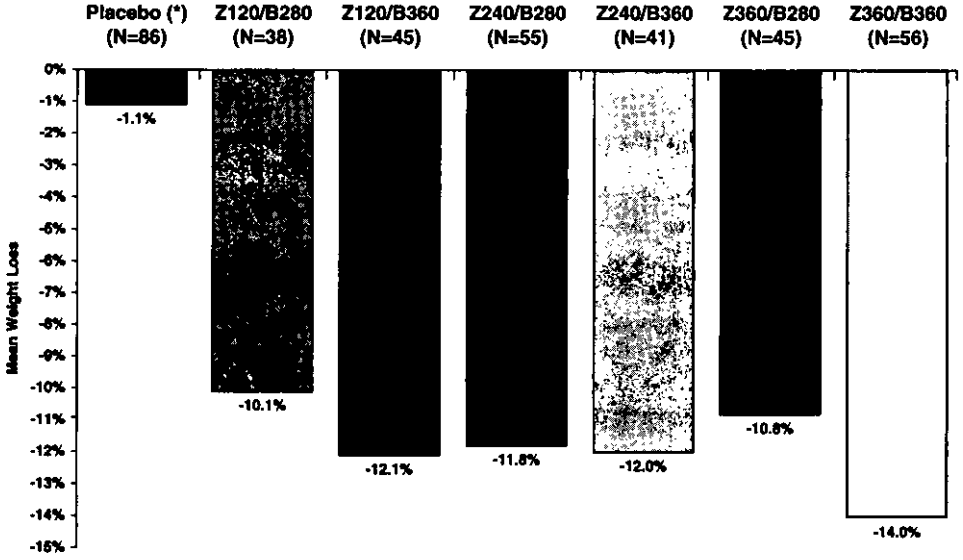


Results of the trial indicated that Empatic was safe and generally well tolerated. The discontinuation rate for spontaneously reported adverse events across the six Empatic dosages ranged from 9.2% to 20.7% through 24 weeks, with an average of 14.0%, which was meaningfully lower than the rate in our earlier Phase II clinical trial employing an older IR form of zonisamide (37.3%). The discontinuation rate due to adverse events through 24 weeks for the dose combination that we intend to continue in clinical trials was 16.9%, which was not statistically different than the 9.1% rate seen with placebo. Adverse events were consistent with the existing

package labels for the two constituents and most commonly included headache, nausea, insomnia, anxiety or dry mouth. Of the intent-to-treat population, approximately 80.0% of patients completed treatment through 24 weeks.

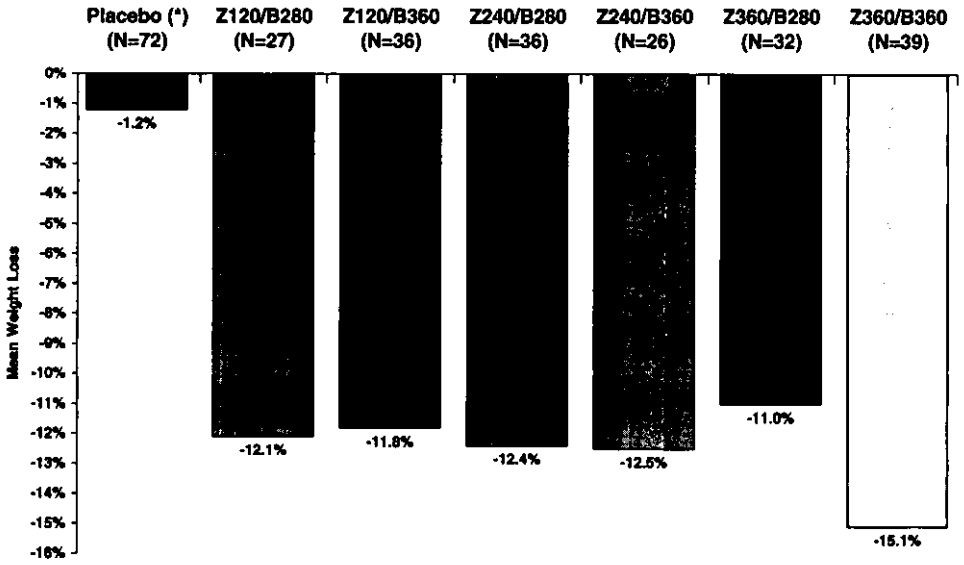
As noted above, weight loss at 24 weeks was the primary endpoint for this trial. However, the trial protocol permitted all patients who completed 24 weeks of treatment to continue on their existing double-blind therapy for an additional 24 weeks. Alternatively, patients who failed to achieve at least a 5% response 24 weeks after the start of treatment were permitted to switch to the highest Empatic dose in a 24-week open label extension. Most patients receiving Empatic therapy elected to continue on their existing double-blind therapy for an additional 24 weeks and continued to lose weight in the time period from weeks 24 to 48. Analysis of their weight loss, as specified by the study protocol, is referred to as the intent-to-treat — double blind extension. Patients from this group who completed treatment through week 48 are referred to as completer — double blind extension. Except with respect to the placebo patients, as explained below, only data for patients remaining on double-blind treatment beyond week 24 were included in the analysis and data from patients discontinuing blinded therapy through week 24 were not imputed. The double-blind extension results are detailed as follows:

Empatic Phase IIb Mean Weight Loss at 48 Weeks
Intent-to-Treat — Double Blind Extension Population



* Placebo weight loss at 24 weeks; see discussion of study design below.

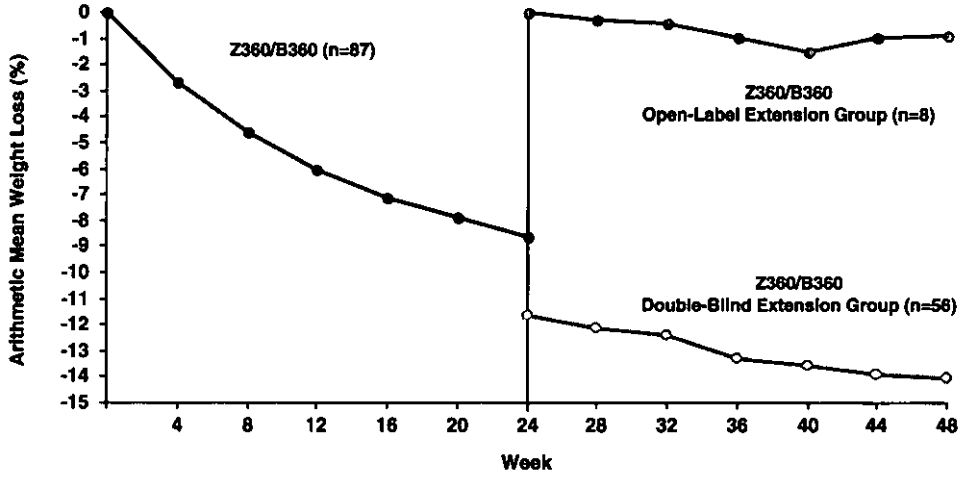
Empatic Phase IIb Mean Weight Loss at 48 Weeks
Completer — Double Blind Extension Population



* Placebo weight loss at 24 weeks; see discussion of study design below.

The study design for the trial permitted patients who did not achieve a 5% weight loss from baseline to switch to the highest Empatic dose after 24 weeks. Because most (approximately 88%) of the placebo patients did not achieve a 5% clinical response at 24 weeks, most (approximately 79%) of the placebo patients who completed 24 weeks switched to the highest Empatic dose. This aspect of the trial, which permitted patients not achieving a 5% response to switch to the highest Empatic dose after 24 weeks, introduces selection bias for patients most likely to lose weight and enhances the results for all groups in the trial. However, the impact is greatest in the placebo arm because of the significantly higher proportion of placebo patients who switched to the highest Empatic dose after 24 weeks. As such, data for the actual 48-week double-blind placebo treatment arm are not presented.

Weight loss, plotted over time for the highest dosage group on an intent-to-treat basis, was as follows:



The discontinuity after 24 weeks in the above graph relates to the trial design. As noted above, patients who did not achieve 5% weight loss after 24 weeks were permitted to switch to the highest dosage group (Z360/B360).

Hence, we show the group of patients who remained in the highest dosage group, in double-blind treatment, separately from those who opted to enter the open label extension after week 24.

Results of this trial also indicated that Empatic was safe and generally well tolerated. Between 24 and 48 weeks, the overall rate of discontinuation due to adverse events among the double-blind extension group receiving Empatic was less than 2.0%. Moreover, the discontinuation rate due to adverse events in each of the Empatic treatment arms was lower than placebo, with the exception of the zonisamide 240mg plus bupropion 360mg dose, where the rate was slightly higher than placebo. The discontinuation rate due to adverse events in the double-blind extension group receiving the highest Empatic dose between weeks 24 and 48 was 0%. Adverse events were consistent with the existing package labels for one or both of the Empatic constituents and most commonly included headache, insomnia, nausea or dry mouth. There were no serious adverse events that were attributed by investigators to Empatic, and there was no statistically significant increase in treatment-associated depression or suicidality with Empatic relative to placebo.

We will need to conduct additional clinical trials of Empatic, the results of which may not corroborate our earlier results, in order to provide enough evidence regarding efficacy and safety to submit an NDA to the FDA for potential regulatory approval. In addition, the emergence of serious side effects associated with Empatic may delay or prevent regulatory approval. The most common side effects observed in our clinical trials of Empatic to date include headache, insomnia, nausea and dry mouth, all of which were considered non-serious.

Future Empatic Clinical Development Plans

We recently submitted to the FDA the results of this trial at 24 weeks, the primary endpoint. In subsequent correspondence, the FDA confirmed the design of our next planned Phase IIb clinical trial. We plan to initiate this trial in mid-2008, evaluating Empatic against individual monotherapies and placebo. Based on the above results of our completed Phase IIb clinical trial, we expect to take the highest dose ratio of Empatic, potentially with one lower dose ratio, into this upcoming clinical trial.

Based on our correspondence with the FDA and the FDA's recent draft guidance, we expect that our Phase III clinical development program for Empatic will be designed, similar to the Contrave Phase III program, to provide exposure for approximately 1,500 patients for one year under double-blind, placebo-controlled conditions. Given the clinically significant magnitude of weight loss experienced in our Phase II clinical trials to date, we anticipate including patients in future pivotal trials with higher BMI levels, including, for example, patients who might be candidates for surgical intervention. We may also conduct studies that include patients with dyslipidemia, hypertension and/or diabetes. In addition, zonisamide carries a Category C pregnancy rating and there have been published concerns in academic journals regarding the possible developmental effects of zonisamide in animals as well as reports from Japan in which women receiving zonisamide combined with other anticonvulsants had children with birth defects. It is therefore likely that Empatic, if approved, will receive a Category X pregnancy precaution and thus, would be contraindicated for use by pregnant or nursing women with warnings about use of Empatic by women of childbearing age. As a result, women of childbearing age will be required to meet pre-stated pregnancy prevention criteria. We expect that we will initiate our Phase III clinical trials in 2009 and expect that these trials would compare Empatic to placebo. We anticipate that the results of these trials, if they commence and progress as we anticipate, will begin to become available in mid-2011 and provide the basis of an NDA submission for Empatic in early 2012.

Earlier Stage Programs

We have begun developing two additional product candidates: one in mitigation of weight gain associated with antipsychotic therapy and the other for the treatment of obsessive-compulsive disorder. We believe there is a substantial unmet medical need in both of these areas, and we expect that a combination approach may improve the therapeutic options available for both patient groups.

OREX-003: Olanzapine/Zonisamide SR for the Mitigation of Weight Gain Associated with Antipsychotic Therapy

OREX-003 is the working name we have given to the olanzapine/zonisamide SR combination product candidate that we are currently developing for the mitigation of weight gain associated with antipsychotic therapy. We own or have exclusive rights to two patent applications currently pending in the United States and a number of corresponding patent applications currently pending in various foreign countries with respect to various compositions, methods of use and formulations relating to this product candidate.

The market for antipsychotic medications has grown dramatically over the last 10 years, as the second generation or "atypical" group of medications has been increasingly prescribed for schizophrenia and bipolar disorder. These are severe, chronic and often disabling disorders that affect over 8.0 million adults in the United States, according to the National Institute of Mental Health. The current group of medications has been called atypical because they are not associated with the adverse event profile of the first generation antipsychotic agents, which have been prescribed since the 1950s. The antipsychotic drug with the highest sales over the last five years has been olanzapine, which is marketed under the brand name Zyprexa. At its peak in 2004, worldwide Zyprexa sales totaled approximately $4.4 billion, according to Eli Lilly and Company. Despite the historical commercial success of Zyprexa, new prescriptions have declined as a result of its side effects, particularly excessive weight gain and metabolic effects. The Zyprexa package insert reports that in an analysis of 13 placebo-controlled trials of olanzapine, 56% of patients gained 7% or more of baseline body weight in long-term trials. Consequently, we believe there is currently a high degree of concern about Zyprexa among patients and physicians, resulting in poor compliance and a growing reluctance to prescribe it.

Evidence that zonisamide could be an effective complement to address olanzapine-associated weight gain and related metabolic effects derives from human and animal studies. According to a study published by Wang et al. in the July 2007 issue of the Journal of Psychiatric Research, zonisamide has shown potential as an effective and generally well-tolerated treatment for psychotropic-induced weight gain in bipolar disorder patients. Further evidence for the potential benefit of zonisamide use in conjunction with olanzapine derives from a preclinical animal study led by Michael A. Cowley, Ph.D., our co-founder and Chief Scientific Officer, in which zonisamide attenuated olanzapine-associated increase in appetite, weight gain and elevated blood glucose. The study also showed that zonisamide normalized the activation of the appetite-associated orexin circuitry in the rat brain associated with olanzapine treatment.

We plan to initiate a Phase II proof-of-concept clinical trial for OREX-003 in the third quarter of 2008. We anticipate that this trial will be designed to enroll approximately 75 patients across multiple sites. Patients will be randomized to receive olanzapine plus zonisamide SR or olanzapine alone (plus placebo). The primary objective of this clinical trial is to compare the change in body weight of the two treatments at Week 16. We anticipate that the results of this clinical trial, if it progresses as we anticipate, will be available in late 2009.

OREX-004: Naltrexone SR/Fluoxetine for Obsessive-Compulsive Disorder

OREX-004 is the working name we have given to the naltrexone SR/fluoxetine combination product candidate that we are currently developing for the treatment of obsessive-compulsive disorder, or OCD. We hold the exclusive license to two issued U.S. patents covering the Contrave composition and expect that they will similarly cover OREX-004, and we own or have exclusive rights to two patent applications currently pending in the United States and a number of corresponding patent applications currently pending in various foreign countries with respect to various compositions, methods of use and formulations relating to this product candidate.

OCD is an anxiety disorder characterized by recurrent, unwanted thoughts (obsessions) and/or repetitive behaviors (compulsions) that lead to significant psychological stress. Individuals with OCD may be plagued by persistent, unwelcome thoughts or images, or by the urgent need to engage in certain rituals. Such rituals may take the form of repetitive behaviors such as hand washing, counting, checking or cleaning and are often performed with the hope of preventing obsessive thoughts or making them go away. Performing these rituals, however, provides only temporary relief, and not performing them markedly increases anxiety. In the United States, OCD is a common mental disorder, affecting approximately 2.2 million adults, according to the National Institute of Mental Health.

The disorder is often under-diagnosed and untreated and it is estimated that at least half of those with OCD receive no treatment.

OCD is often treated with behavioral therapy and medication, usually a selective serotonin reuptake inhibitor, or SSRI, such as fluoxetine. SSRIs are a class of medication that is typically used for treating depression. Use of an SSRI for OCD ordinarily requires a higher dose administered for a longer duration than is typically used for depression. Many patients do not respond to SSRIs, and those who do respond often achieve only a partial response. In particular, the compulsive symptoms of the condition tend to be less well controlled by SSRI therapy.

We believe that the addition of naltrexone to an SSRI may improve outcomes for some sufferers of OCD. The compulsive features of the disease have been theorized to have a reward-based component, which is likely influenced by a balance of endogenous dopamine and opioids. The addition of an opioid antagonist such as naltrexone may dampen dopamine-based reward and thereby decrease compulsive behaviors. Naltrexone, in particular, has been reported to be useful with repetitive and impulsive behaviors including alcoholism, self-injurious behavior, kleptomania, trichotillomania (hair pulling) and compulsive gambling.

We have conducted a preclinical study examining the effect of the combination of naltrexone and fluoxetine, a commonly prescribed SSRI marketed under the brand name Prozac, in an established animal model of OCD. In this study, we showed a statistically significant reduction of compulsive behavior compared to either naltrexone or fluoxetine alone after seven days of treatment. In addition, the combination suggested a synergy in behavior improvement relative to either naltrexone or fluoxetine alone. We believe that this preclinical model may have validity in terms of predicting efficacy in humans.

We plan to initiate a Phase II proof-of-concept clinical trial for OREX-004 in the third quarter of 2008. We anticipate that this trial will be designed to enroll approximately 90 patients across multiple sites. Patients will be randomized to receive the naltrexone SR/fluoxetine combination therapy, naltrexone SR alone (plus placebo), fluoxetine alone (plus placebo) or placebo. We anticipate that the primary endpoint will be a measurement of change in OCD symptoms at 10 weeks. We anticipate that the results of this clinical trial, if it progresses as we anticipate, will be available in mid-2009.

Sales and Marketing

We maintain worldwide commercial rights to our product candidates, and have the opportunity to build a specialty sales force to market and sell these products independently. However, we expect that Contrave and Empatic, if approved, will be prescribed predominantly by primary care physicians, including general practitioners, family practitioners and internists. In order to target this large group of potential prescribers, we may consider entering into a collaboration, either in the United States, outside the United States or both, with a pharmaceutical company that has the sales force and marketing resources to adequately address this physician audience. We may also consider a collaboration with a pharmaceutical company that has greater development resources than we do to expand or accelerate one or both of our clinical development programs. However, we cannot assure you that we will complete any collaboration or other strategic transaction, or that, if completed, any collaboration or other strategic transaction will be successful or on attractive terms. For the foreseeable future, we expect to maintain commercial rights to our product candidates and to continue to develop them independently.

While both Contrave and Empatic are designed to produce weight loss, we expect to position them to target different segments of the obese population. The two components of Contrave, bupropion and naltrexone, are both approved to treat addictive disorders: smoking in the case of bupropion, and alcoholism and opioid addiction in the case of naltrexone. Recent research suggests that for many obese patients, overconsumption of food is an addiction, much like smoking and alcoholism. Notably, women report substantially greater food craving than men, according to a 1991 study. In addition, women were responsible for 90% of all weight loss prescriptions written in the United States from 1998 to 2003, according to IMS Health. Given its profile, we believe that Contrave may be particularly well-suited for mild-to-moderately obese women who report food cravings.

We believe that Empatic, given its profile, may be more effective than Contrave in reducing weight, at least in the early stages of treatment. The overall tolerability of Empatic has yet to be determined. However, it is likely to have labeling which would recommend appropriate birth control for women of childbearing age and to be

contraindicated in women who are pregnant or breast feeding. As a result, we believe that Empatic may be especially well-suited for men and post-menopausal women who are heavier and require greater weight reduction. We expect that the experience gained from future clinical trials will enable us to further refine the positioning and brand characteristics of both products.

To date, we have focused our clinical development efforts exclusively in the United States. This appears to be the largest commercial market for obesity therapeutics and the market which we believe we best understand. However, we have also sought to establish intellectual property covering our obesity product candidates, primarily in the form of patent application filings, in various foreign markets. We recognize that there is a significant emerging obesity market in Europe, Asia and Latin America. We believe that conducting the necessary supplemental trials, engaging in local regulatory dialogue and conducting local market research is likely best done through strategic collaborators in territories outside the United States or possibly in partnership with a global pharmaceutical company. We will continue to consider international opportunities, and appropriately prioritize these opportunities in the context of the opportunity in the United States.

Intellectual Property

We rely on a combination of in-licensed patent rights, our own patent rights, trademarks, trade secrets and know-how to protect Contrave and Empatic. We own or have exclusive rights to 13 patent application families currently pending in the United States with respect to various compositions, methods of use and formulations relating to Contrave and/or Empatic. We also have a number of patent applications currently pending in various foreign countries that correspond to some of the pending U.S. applications. We also seek to protect our trade secrets and our know-how relating to our products and our business. These intellectual property rights are in addition to any regulatory exclusivity that we may be able to obtain.

Contrave is currently protected in the United States by U.S. Patent Nos. 5,817,665 and 5,512,593, which we have in-licensed on an exclusive basis from Dr. Lee Dante pursuant to a patent license agreement described in further detail below. These patents, which we refer to as the Dante patents, provide basic composition of matter coverage for the Contrave naltrexone/bupropion combination, and are also expected to provide similar coverage for our OREX-004 product candidate.

In addition to the Dante patents, we own a U.S. patent application and a related continuation patent application, each of which stem from a provisional patent application that we own but that is the subject of agreements with OHSU and Duke requiring us to pay them specified royalties on sales of products covered by the patent applications. These agreements are described in further detail below. These patent applications, which we refer to as the Weber/Cowley patent applications, are directed to the current composition of our Contrave product candidate, including our SR formulation of naltrexone, and methods for using that composition to effect weight loss. We have received a Notice of Allowance from the U.S. Patent and Trademark Office, or PTO, for the Weber/Cowley patent application covering the composition of Contrave. The allowed claims cover certain sustained release compositions of bupropion and naltrexone combined in a single dosage form. If the issue fees for this application are timely paid for, and if the application is not withdrawn from issue by us or by the PTO, we would expect a U.S. patent to issue on this application in due course. If and when a U.S. patent issues as we anticipate based on the Notice of Allowance, we expect to have protection for Contrave extended from 2013 through at least 2024. Although withdrawal from issue is not common, no assurance can be given that this patent application will not be withdrawn from issue, nor can there be any assurance that any patent claims issuing from this application will be sufficiently broad to protect Contrave in the United States. We and/or our licensors have also filed a number of international counterparts to these patent applications in foreign countries. We have also received a Decision to Grant a Patent covering compositions and uses of bupropion and naltrexone for affecting weight loss from the European Patent Office, or EPO. If patents ultimately issue from these U.S. patent applications and their international counterparts, we expect to have additional coverage to at least 2024.

The PTO has allowed our intent-to-use trademark application for the CONTRAVE mark for registration in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss, and a registration is expected to issue shortly. An application for the CONTRAVE mark remains pending in connection with certain printed materials and medical information services. We have also obtained foreign trademark

registrations for the mark CONTRAVE in Europe and Japan. The CONTRAVE mark is also the subject of a pending trademark application in Canada.

Empatic is currently protected in the United States by U.S. Patent Number 7,109,198, which is based on the work of Dr. Kishore Gadde, and which we refer to as the Gadde patent and have licensed on an exclusive basis from Duke pursuant to a patent license described in further detail below. The Gadde patent, which is expected to expire in 2023, provides basic composition of matter coverage for the Empatic zonisamide/bupropion combination and also covers methods of using Empatic to treat obesity and to reduce the risk of hypertension, diabetes or dyslipidemia. Duke has received a Notice of Allowance from the PTO for a continuation patent application, related to the Gadde patent and also exclusively licensed to us, that covers methods of using zonisamide (including in combination with bupropion) to cause weight loss. If a patent ultimately issues from this allowed continuation application, it will provide additional coverage for methods of using Empatic to treat obesity until 2023. We have also exclusively licensed from Duke an international patent application that was filed as a counterpart to the Gadde patent in foreign countries, and this international application has now matured into national applications pending in several foreign countries. We have received a Notice of Allowance from the PTO for the intent-to-use trademark application for the EMPATIC mark. The EMPATIC mark is also the subject of trademark applications that we have filed in certain countries overseas.

We own or have exclusive rights to two patent applications currently pending in the United States with respect to various compositions, methods of use and formulations relating to our OREX-003 product candidate (olanzapine/zonisamide SR). One of the applications is directed to the olanzapine/zonisamide combination and methods of using it, and the other is directed to the zonisamide SR formulation. We also have a number of patent applications currently pending in various foreign countries that correspond to the pending U.S. applications. In addition, if a patent ultimately issues from the allowed continuation application that covers methods of using zonisamide (including in combination with bupropion) to cause weight loss, it will provide additional coverage for our OREX-003 product candidate. Likewise, in addition to the coverage provided by the Dante patents mentioned above, we own two patent applications currently pending in the United States with respect to various compositions, methods of use and formulations relating to our OREX-004 product candidate (naltrexone SR/fluoxetine). One of the applications contains claims directed to the naltrexone/fluoxetine combination and methods of using it to treat OCD, and the other is directed to the naltrexone SR formulation. We also have a number of patent applications currently pending in various foreign countries that correspond to the pending U.S. applications.

Licensing Agreements

Oregon Health & Science University License Agreement

In June 2003, we entered into a license agreement with OHSU whereby we acquired an assignment of any rights OHSU may have to a U.S. provisional patent application that we filed, which formed the basis for our subsequently filed and currently pending Weber/Cowley patent applications. These applications cover the current composition of our Contrave product candidate, including our SR formulation of naltrexone and methods for using that composition to effect weight loss. OHSU and the inventors have assigned all rights in the underlying invention to us. This license agreement was amended in November 2003, December 2006 and December 2007.

As consideration for this license agreement, we paid an upfront fee of $65,000 and issued 76,315 shares of our common stock to OHSU. We are also obligated to pay a royalty to OHSU on net sales for Contrave and any other products covered by the assigned patent rights.

The term of the agreement generally extends until the last of the subject patent rights expire, which is expected to occur in 2024 assuming patents issue with respect to our pending Weber/Cowley patent applications. We may unilaterally terminate the agreement and/or any licenses in any country upon specified written notice to OHSU. OHSU may terminate the agreement upon delivery of written notice if we commit a material breach of our obligations and fail to remedy the breach within a specified period or may immediately terminate the agreement upon the delivery of written notice concerning the occurrence of specified bankruptcy proceedings. In addition, upon written notice and our failure to remedy any of the following breaches within a specified period, OHSU may terminate or modify the agreement: if we cannot demonstrate to OHSU's satisfaction that we have taken, or can be expected to take within a reasonable time, effective steps to achieve practical application of the licensed products

and/or licensed processes; or if we have willfully made a false statement of, or willfully omitted, a material fact in any report required by the agreement; or if we commit a substantial breach of a covenant or agreement contained in the license. Under the terms of the agreement, we are responsible for all prosecution and maintenance (including all costs associated with the enforcement) of any patent applications, including the Weber/Cowley patent applications, that stem from the assigned rights, and for any patents that may issue with respect thereto. If and when issued, we will also be responsible for enforcing any such patents.

In addition to assigning us any rights it had in our provisional patent application directed to the Contrave combination of naltrexone and bupropion, OHSU has licensed to us, on an exclusive basis, the issued patent underlying the *in vitro* model that we have used for screening combination therapies for impact on neuronal activity. Our rights to this model extend through the expiration of the patent, which is expected to occur in 2024. We have the right to grant sublicenses to third parties for this patented technology, subject to our obligation to pay OHSU a royalty on revenue received by us from the sale of any products covered under such sublicensing arrangements. Under the terms of the agreement, OHSU is solely responsible for the prosecution, maintenance and enforcement (including all costs associated therewith) of this patent; however, we are required to pay 100% of the prosecution and maintenance expenses incurred by OHSU in connection with these patent rights. As of December 31, 2007, we have paid a total of approximately $36,000 in connection with the maintenance and prosecution of this patent and owe OHSU an additional $42,000 in connection with the amendment to the agreement effected in December 2007. In addition, OHSU has the right to not file any patent application or to abandon any patent or patent application included in the patent rights, in which case it must provide us 60 days' prior written notice and, in response, we may elect at our sole cost to pursue these actions.

In August 2006, we entered into a research agreement with OHSU for the continuation of the original research underlying the Weber/Cowley patent applications. This agreement was terminated in February 2008. Prior to its termination, we paid OHSU approximately $556,000 in accordance with the terms of the agreement.

Lee Dante License Agreement

In June 2004, we entered into a patent license agreement with Lee G. Dante, M.D., whereby we acquired an exclusive worldwide license to two U.S. patents covering compositions of specified opioid antagonists (including naltrexone) combined with specified antidepressants (including bupropion) and, as such, provide basic composition of matter coverage for the Contrave naltrexone/bupropion combination.

As consideration for this license, we paid upfront fees totaling $100,000 and granted Dr. Dante an option to purchase 73,448 shares of our common stock at an exercise price of $0.10 per share which expires in April 2014. In April 2006, Dr. Dante exercised options with respect to 35,000 of these shares. We are also obligated to pay a royalty on net sales of products covered by the license. We will be required to make a one-time milestone payment to Dr. Dante in the amount of $1.0 million upon the occurrence of a specified regulatory event. We have the right to grant sublicenses of the patented technology to third parties, subject to our obligation to pay Dr. Dante a royalty on any revenue we receive from such arrangements.

The term of the agreement generally extends until the last licensed patent right expires, which is expected to occur in 2013. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful misconduct, or illegal conduct with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period. We may also voluntarily terminate the agreement upon delivery of written notice within a specified time period. In addition, Dr. Dante may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Under this agreement, we have the responsibility to defend and/or settle any third-party patent infringement claims, assume all costs associated therewith and, to the extent these claims result from our activities or those of our sublicensees and not from Dr. Dante's activities, indemnify him for any damages resulting therefrom. In the case of third-party infringement of the licensed patents, we have the right, but not the obligation, to either settle or prosecute at our own expense any such infringement. Dr. Dante has the right, but not the obligation, to join any suit we commence at our expense and, if we do not undertake action within three months of being made aware of infringing activity, the right to commence his own suit at his expense.

Duke University License Agreement

In March 2004, we entered into a patent license agreement with Duke whereby we acquired an exclusive worldwide license to the Gadde patent. The Gadde patent is a U.S. patent covering the composition of our Empatic product candidate and methods for using Empatic to treat obesity and reduce the risk of hypertension, diabetes or dyslipidemia. Under the agreement, we also acquired a license to several related patent applications, including an international patent application, and any patents or patent applications that ultimately issue therefrom. The license agreement was amended in December 2004 and July 2006.

As consideration for this license, we issued 442,624 shares of our common stock to Duke and may be required to make future milestone payments totaling $1.7 million upon the achievement of various milestones related to regulatory or commercial events. We are also obligated to pay a royalty on net sales of products covered by the license. We have the right to grant sublicenses to third parties, subject to our obligation to pay Duke a royalty on any revenue we receive from such sublicensing arrangements. In addition, under this agreement we are obligated to pay Duke a specified royalty on sales of products covered by the Weber/Cowley patent applications.

The term of the agreement generally extends until the last licensed patent right expires, which is expected to occur in 2023. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful misconduct, or illegal conduct of the other party with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period. We may also voluntarily terminate the agreement upon delivery of written notice within a specified time period. Duke may terminate the agreement upon delivery of written notice if we fail to meet certain specified milestones of the agreement and fail to remedy such a breach within the specified period. In addition, Duke may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Under this agreement, we have the responsibility to defend and/or settle any third-party patent infringement claims, assume all costs associated therewith and, to the extent these claims result from our activities or those of our sublicensees and not from Duke's activities, indemnify Duke for any damages resulting therefrom. In the case of third-party infringement of the licensed patents, we have the right, but not the obligation, to either settle or prosecute at our own expense any such infringement. Duke has the right, but not the obligation, to join in any suit we commence at our expense and, if we do not undertake action within three months of being made aware of infringing activity, the right to commence its own suit at Duke's expense.

Cypress Bioscience, Inc. License Agreement

In January 2005, we entered into a license agreement with Cypress Bioscience, Inc., or Cypress, whereby we sublicensed certain of our rights under the Duke agreement to Cypress for specified uses. The technology sublicensed relates to the use of zonisamide with either of two specified therapeutics: mirtazapine and setipiline. As consideration for this license, Cypress paid us non-refundable upfront fees of $1.5 million. In addition, Cypress is obligated to pay us a royalty on net sales of any products covered by the sublicensed technology. Cypress may also be required to make future milestone payments to us of up to $57.0 million upon its achievement of various regulatory milestones. In June 2006, Cypress announced that the results of a completed Phase IIa trial did not support continuing its development program for obstructive sleep apnea, one of the specified uses under the agreement. Therefore, we do not expect to be paid the $20.0 million portion of the milestones related to sleep apnea.

The term of the Cypress agreement generally extends until the last licensed patent right expires, which is expected to occur in 2023. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful misconduct, or illegal conduct of the other party with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period. Cypress may terminate the agreement for any reason upon delivery of written notice within the specified period. Cypress may also terminate with no notice if an unfavorable judgment is entered against us or any other party relating to the patents we have sublicensed to Cypress. In addition, Cypress may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Under this agreement, each party has the sole right to control the defense, at its own expense, of any third-party patent infringement claim asserted against it. In the case of third-party infringement of the licensed patents, Cypress has the right, but not the obligation, to settle or prosecute at its own expense any such infringement. We have the right, but not the obligation, to join any suit commenced by Cypress, at its expense, and if Cypress does not undertake action within three months of having been made aware of infringing activity, the right to commence suit ourselves at our expense.

As a result of our sublicensing of the Duke technology to Cypress for specified uses, we may be required to make future payments to Duke of up to $5.7 million ($3.7 million, excluding those related to sleep apnea) upon Cypress's achievement of various regulatory milestones.

Manufacturing

To date, our products used in clinical trials have been produced by outside contractors under our supervision. PharmaDirections, Inc. is our drug development consultant and manages subcontractors on our behalf.

In December 2005, we entered into a consulting agreement with PharmaDirections under which PharmaDirections agreed to serve as our primary drug development consultant with responsibility for managing subcontractors and assisting us with management and coordination of regulatory matters, new formulation development, chemistry, manufacturing and research, among other matters. Under this agreement, we pay fees to PharmaDirections on a per-project basis as approved on corresponding work orders. In addition, during any wind-down period in connection with the termination of the agreement, we will be required to make specific minimum monthly payments. This agreement was amended in January 2006 and June 2007. The term of this agreement generally extends until June 15, 2008. However, we may terminate the agreement upon 30 days' written notice.

The University of Iowa developed the existing bupropion SR formulation and manufactured it for our Contrave Phase II clinical trials as well as for portions of our first two Phase III trials. The University of Iowa also manufactured the bupropion SR formulation for our previous Phase II Empatic clinical trials using bupropion active pharmaceutical ingredient, or API, from Solmag S.p.A., which also continues to provide bupropion API to our manufacturers for all of our ongoing clinical trials. Previously, the bupropion SR formulation used in our Phase III clinical trials for Contrave was also manufactured by Pharmaceutical Manufacturing Research Services, Inc. or PMRS, and Patheon Pharmaceuticals, Inc., or Patheon. Patheon is currently, and we expect going forward will continue to be, the manufacturer of our long-term clinical and commercial quantities of bupropion SR, naltrexone SR and finished Contrave tablets. To date, all of our contract manufacturers have performed services under short-term purchase order or similar arrangements. We have no long-term commitments or supply agreements with these contract manufacturers. For example, Patheon currently provides our clinical quantities on a proposal-by-proposal basis under a master agreement for pharmaceutical development services that we entered into in February 2007. Either party may terminate the agreement upon notice if the other party commits a material breach of its obligations and fails to remedy the breach within 30 days. In addition, we may terminate the agreement immediately for any business reason.

PMRS will provide bupropion SR, zonisamide SR and finished Empatic tablets for use in our upcoming Empatic Phase IIb clinical trial. We have not yet selected a finished tablet manufacturer for our Phase III Empatic clinical trials or for Empatic commercial supply.

Patheon produces our naltrexone SR requirements using API supplied by Organon Biosciences (formerly known as Diosynth). Previously, Pharm Ops Inc. produced our naltrexone SR using API from Organon Biosciences and zonisamide SR using API from Chemagis Ltd. In addition, Pharm Ops produced our finished Contrave tablets for our earlier clinical trials. We utilize the services of Almac Clinical Services to package our clinical supplies into Contrave Titration Packs, Empatic Titration Packs and bottles for use in our clinical trials. To date, all of our purchases of API have been completed by purchase order. We have no long-term commitments or supply agreements with any of our API suppliers. Although we may seek to establish long-term supply commitments in the future, we may be required to agree to minimum volume requirements, exclusivity arrangements or other restrictions. We may not be able to enter into long-term agreements on commercially reasonable terms, or at all.

In the future, if we are able to achieve approval in the United States or other countries to market and sell our products, we intend to continue to rely on outside contractors for the production of necessary supplies. We do not currently intend to establish our own manufacturing capabilities.

Competition

Treatments for obesity consist of behavioral modification (diet and exercise), pharmaceutical therapies, surgery and device implantation. Modifications to diet and exercise are the preferred initial treatment in obesity. However, the demands of behavioral modification tend to cause significant attrition over time and, frequently, suboptimal weight loss outcomes. When pharmaceutical therapies are recommended it is generally after behavioral modification alone has failed. Bariatric surgery, including gastric bypass and gastric banding procedures, is employed in more extreme cases, typically for patients with a BMI exceeding 40 or who are experiencing obesity-related complications such as diabetes. Surgery can be effective in helping patients to lose 50% or more of their body weight. However, surgery is associated with significant side effects, potential complications and high costs. In addition, while surgery may be effective in achieving weight loss, recent research has identified "addiction transfer," where patients begin heavy alcohol consumption, drug use or other addictive habits in response to the reduced ability to consume food following gastric bypass surgery. Device implantation is a newer therapy which has yet to be widely adopted within the medical community.

Several pharmaceutical products are approved for marketing in the United States with an obesity indication. These pharmaceutical products generally are prescribed for short-term use; fewer agents have been approved for longer-term maintenance therapy. Several older agents, indicated for short-term administration, are amphetamine-like compounds including phentermine, phendimetrazine, benzphetamine and diethylpropion. Of these, phentermine is the most widely used, accounting for approximately 3,456,000 prescriptions in the United States in 2006, or approximately $35 million in sales, according to IMS Health.

Sibutramine is marketed in the United States by Abbott Laboratories under the brand name Meridia. Sibutramine appears to suppress appetite by inhibiting the reuptake of serotonin, norepinephrine and dopamine in the brain. In 2006, Meridia accounted for approximately 542,000 prescriptions in the United States, or approximately $59 million in sales, according to IMS Health.

Orlistat is marketed in the United States by Roche Laboratories, Inc. under the brand name Xenical. Orlistat works by inhibiting lipase, an enzyme that blocks the absorption of fat in the gastrointestinal tract. In 2006, Xenical accounted for approximately 623,000 prescriptions in the United States, or approximately $93 million in sales, according to IMS Health. Orlistat was launched in 2007 over-the-counter in the United States by GlaxoSmithKline under the brand name alli.

Despite the large market opportunity for anti-obesity agents, there are relatively few competitive products in late stage clinical development. In June 2007, an FDA advisory panel determined not to recommend approval for rimonabant, which was developed by Sanofi-Aventis under the brand name Acomplia. Subsequently, Sanofi-Aventis has withdrawn the U.S. application for rimonabant. Rimonabant is part of a new class of anti-obesity drugs that work as antagonists at the cannabinoid type 1, or CB-1, receptor. Other pharmaceutical companies, including Merck & Co., Inc. and Pfizer Inc., continue late stage testing of obesity product candidates targeting this receptor.

A number of other biotechnology and pharmaceutical companies have drugs in development for obesity. These include Arena Pharmaceuticals, Inc., Amgen Inc., Amylin Pharmaceuticals, Inc., Alizyme plc, Nastech Pharmaceutical Co., Inc., Neurosearch A/S, Peptimmune, Inc. and Vivus, Inc., among others. With the exception of Vivus, Inc., most of these efforts are directed toward a monotherapeutic approach which we would expect to be subject to the same early plateau typically seen.

In addition, we may face competition from generic products. Each of bupropion, naltrexone and zonisamide is available in generic form. However, we have undertaken strategies which we believe may impede potential competition from generic products. Supplementing our existing composition patents and patent applications, we have developed formulations and dosages of Contrave and Empatic that we believe may improve patient outcomes and provide further barriers to entry for potential competitors. We believe there cannot be an AB-equivalence designation for the generic versions of the constituents comprising Contrave and Empatic because of differences in

pharmacokinetics between the existing generically available formulations and doses and the formulations and doses we plan to use. For naltrexone and zonisamide, we have selected dosages and are using formulations that are not currently available in generic form and create a different pharmacokinetic profile from the generic forms of these drugs. For bupropion, we are utilizing dosages that are not currently generically available. We believe that our existing in-licensed composition patents and, if issued, our pending composition patents, will prevent generic firms from manufacturing comparable formulations and from marketing the constituent compounds together. In addition, we believe that practitioners who are seeking to prescribe safe and effective therapy are not likely to prescribe off-label generics in place of Contrave or Empatic because the dosages, pharmacokinetic profile and titration regimens for our Contrave and Empatic product candidates would not be available using existing generic preparations. Moreover, while general practitioners are the primary prescribers of anti-obesity therapies and are generally familiar with bupropion, they are not the primary prescribers of the other constituents of our product candidates, naltrexone and zonisamide. Accordingly, we believe that general practitioners will be unlikely to prescribe generic compounds with which they are unfamiliar. As a result, we believe that we have established a position with both Contrave and Empatic that will limit generic competition.

Third-Party Reimbursement

Despite the recognition of obesity as a chronic disease and its enormous cost to our health care system, universal coverage of and reimbursement for drugs to treat obesity by both public and private payors is lacking. However, third-party reimbursement for anti-obesity drugs appears to be evolving, including among state Medicaid programs and private commercial plans and pharmacy benefit managers.

Medicaid

The Medicaid program provides health insurance coverage for individuals who are poor and meet certain other eligibility criteria. The program is a federal and state partnership. Within broad federal parameters, each state designs and administers its own program. The federal government shares in the cost of the program by reimbursing states a percentage of their costs.

States provide outpatient prescription drug coverage under their Medicaid programs, although it is an optional service. States that elect to offer outpatient prescription drug coverage must do so through the Medicaid Rebate Program. Under the Medicaid Rebate Program, states must provide coverage for all FDA-approved drugs of every manufacturer that has entered into a rebate agreement with HHS. However, states may exclude coverage for certain drugs including drugs to treat anorexia, weight gain and weight loss. In 2000, 32 out of 44 Medicaid programs surveyed by the Kaiser Commission excluded these drugs. More recent data suggests that state Medicaid programs may have increased coverage for certain anti-obesity drugs. For example, Meridia (sibutramine) and Xenical (orlistat) are listed on the formularies of 52% and 58% of state Medicaid programs, respectively.

Medicare

The Medicare program provides health insurance for individuals aged 65 and over and those with serious disability or end-stage renal disease, regardless of income. However, Medicare coverage of obesity treatments is limited. Current policy authorizes coverage of non-pharmacologic obesity treatments but only when such treatments are an integral and necessary part of a course of treatment for a co-morbid medical condition. Pursuant to this policy, in February 2006, Medicare began covering certain designated bariatric surgical services for Medicare patients with a BMI equal to or greater than 35, who have at least one co-morbidity and have been previously unsuccessful with the medical treatment of obesity. However, the policy reiterates that treatments for obesity alone are not covered because such treatments are not considered reasonable and necessary. In addition, by statute, Medicare's prescription drug benefit does not cover either outpatient prescription weight loss drugs or over-the-counter drugs.

Private Commercial Plans

There is a wide range of coverage by private commercial plans for Meridia and Xenical. Based on data obtained from Fingertip Formulary databases, almost half of commercial plans reviewed (excluding Blue Cross

Blue Shield) listed Meridia and Xenical on their formularies. Over 85% of the Blue Cross Blue Shield plans reviewed listed Meridia and over 90% listed Xenical. In addition, over 90% of the pharmacy benefit management companies, or PBMs, reviewed listed both Meridia and Xenical on their formularies. The amount of coverage provided by these commercial plans varies, however, and significant out-of-pocket payments are often still required.

Although third-party payor attitudes regarding obesity-related products and services appear to be changing, as exemplified by the coverage of Meridia and Xenical by PBMs and Blue Cross Blue Shield plans, our product candidates for obesity, if approved, may not achieve broad coverage. Moreover, the amount of any coverage provided under the various plans may be minimal. We do not, however, expect the success of our obesity product candidates to be contingent upon third-party payor coverage and reimbursement, but rather on their acceptance by physicians and by people who want to lose weight and are willing to pay for the drugs out of pocket.

Government Regulation

Prescription drug products are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising and promotion of such products under the Federal Food Drug and Cosmetic Act, or FFDCA, and its implementing regulations, and by comparable agencies and laws in foreign countries. Failure to comply with applicable FDA or other requirements may result in civil or criminal penalties, recall or seizure of products, partial or total suspension of production or withdrawal of the product from the market.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. All applications for FDA approval must contain, among other things, information relating to pharmaceutical formulation, stability, manufacturing, processing, packaging, labeling, and quality control.

New Drug Approval (NDA)

A new drug approval by the FDA is generally required before a drug may be marketed in the United States. This process generally involves:

- completion of preclinical laboratory and animal testing in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application for human clinical testing which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug product for each intended use;
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is produced to assess compliance with the FDA's current Good Manufacturing Practice, or cGMP, regulations; and
- submission to and approval by the FDA of an NDA application.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30 day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. A

separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the study until completed. The FDA, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, regulations, including regulations for informed consent.

For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following three sequential phases, which may overlap:

- *Phase I:* Studies are initially conducted in a limited population to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase II:* Studies are generally conducted in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trials.
- *Phase III:* These are commonly referred to as pivotal studies. When Phase II evaluations demonstrate that a dose range of the product is effective and has an acceptable safety profile, Phase III clinical trials are undertaken in large patient populations to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.
- *Phase IV:* In some cases, FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. Such post approval trials are typically referred to as Phase IV studies.

Because our product candidates are fixed-combination prescription drugs, we will need to comply with the FDA's regulation that requires each component of each product to make a contribution to the claimed effects. This means that our clinical trials for our product candidates will need to evaluate the combination as compared to each component separately and to placebo. The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive manufacturing information. The cost of preparing and submitting an NDA is substantial. Under federal law the submission of most NDAs is additionally subject to a substantial application fee, currently exceeding $1.17 million. The FDA has agreed to certain performance goals in the review of NDAs. It is likely that the NDAs, if any, for our Contrave and Empatic product candidates will be reviewed on a ten-month cycle by the FDA. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and FDA may interpret data differently than us.

Manufacturers and sponsors of approved drugs are subject to annual product and establishment fees currently exceeding $390,000 per manufacturing establishment and $65,000 per product.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval for modifications to products previously approved by the FDA, an applicant may file an NDA under Section 505(b)(2) of the FFDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act. This statutory provision permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

The Hatch-Waxman Act permits the applicant to rely upon the FDA's findings of safety and effectiveness based on certain preclinical or clinical studies. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. We intend to submit our initial NDAs for Contrave and Empatic under Section 505(b)(2), based on the extensive safety information that has been collected for the approved drug products that are incorporated in these product candidates. To the extent that a Section 505(b)(2) application relies on the FDA's finding of safety and effectiveness of a previously-approved drug, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's publication called "Approved Drug Products with Therapeutic Equivalence Evaluations," otherwise known as the "Orange Book." Specifically, the applicant must certify when the application is submitted that: (1) there is no patent information listed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid or will not be infringed by the manufacture, use or sale of the studies conducted for an approved product. A certification that the new product will not infringe the already approved product's Orange Book listed patents or that such patents are invalid is called a paragraph IV certification. If the applicant has provided a paragraph IV certification to the FDA, the applicant must also send notice of the paragraph IV certification to the patent holder and the NDA holder. If and when we file our NDAs for Contrave and Empatic, we intend to make paragraph IV certifications that our product candidates do not infringe the bupropion patents listed in the Orange Book and send the appropriate notice to the patent holder and NDA holder. In the event that the patent holder or NDA holder files a patent infringement lawsuit against us within 45 days of its receipt of our paragraph IV certification, such lawsuit would automatically prevent the FDA from approving our Section 505(b)(2) NDA until the earliest of 30 months, expiration of the patent (2013), settlement of the lawsuit or a decision in the infringement case that is favorable to us. Any such patent infringement lawsuit could be costly, take a substantial amount of time to resolve and divert management resources.

The Prescription Drug User Fee Act, which has been reauthorized three times by Congress, requires the payment of user fees with the submission of NDAs, including 505(b)(2) NDAs. These application fees are substantial ($1,178,000 in the FDA's Fiscal Year 2008) and will likely increase in future years. The statute provides for waiver of the application fee for the first NDA for a small business under certain circumstances, and we may meet the requirements for this waiver for our first NDA. If we obtain FDA approval for either Contrave or Empatic, we could obtain three years of Hatch-Waxman marketing exclusivity for such product, assuming we obtain the first approval for either product candidate for the indication supported by the clinical studies we conducted. Under this form of exclusivity, the FDA would be precluded from approving a generic drug application or another 505(b)(2) application for a duplicate drug product for the protected indication (for example, a product that incorporates the change or innovation represented by our product) for a period of three years, although the FDA may accept and commence review of such applications. However, this form of exclusivity would not prevent the FDA from approving an NDA that relies on its own clinical data to support the change or innovation. Further, if another company obtains approval for either product candidate for the same indication we are studying before we do, our approval could be blocked until the other company's Hatch-Waxman marketing exclusivity expires.

Manufacturing cGMP Requirements

We and our contract manufacturers are required to comply with applicable FDA manufacturing requirements contained in the FDA's current Good Manufacturing Practice, or cGMP, regulations. cGMP regulations require, among other things, quality control, and quality assurance as well as the corresponding maintenance of records and documentation. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and our third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including Warning Letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, and civil and criminal penalties. Adverse

experiences with the product must be reported to the FDA and could result in the imposition of market restriction through labeling changes or in product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

Other Regulatory Requirements

The recently enacted Food and Drug Administration Amendments Act of 2007, or FDAAA, gives the FDA the authority to require a drug-specific risk evaluation mitigation strategy, or REMS, to ensure the safe use of the drug. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must propose the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug or other measures that the FDA deems necessary to assure the safe use of the drug.

FDAAA also expands the FDA's authority to require post-approval studies and clinical trials if the FDA finds, after approving the drug, that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicates the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet. The FDA has very broad enforcement authority under the FFDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have a material adverse effect on us.

Outside the United States, our ability to market a product is contingent upon receiving marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union registration procedures are available to companies wishing to market a product in more than one European Union member state. The regulatory authority generally will grant marketing authorization if it is satisfied that we have presented it with adequate evidence of safety, quality and efficacy.

DEA Regulation

Naltrexone, one of the components of our Contrave product candidate, is manufactured from semi-synthetic opiates. Although naltrexone is not a narcotic or a controlled substance, manufacturing of naltrexone active pharmaceutical ingredient, or API, is subject to regulation by the U.S. Drug Enforcement Administration, or DEA, because the starting material is regulated. Controlled substances are those drugs that appear on one of five schedules promulgated and administered by the DEA under the Controlled Substances Act, or CSA. The CSA governs, among other things, the distribution, recordkeeping, handling, security, and disposal of controlled substances. Our third-party suppliers of naltrexone must be registered by the DEA in order to engage in these activities, and are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA's regulations. The manufacturers must also obtain an annual quota from the DEA to

obtain sufficient material to manufacture substances derived from opiates. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation, or a denial of renewal, of DEA registration, injunctions, or civil or criminal penalties. The failure to obtain adequate quota can also limit the manufacturing capacity of the manufacturer.

Employees

As of March 14, 2008, we had 25 full-time employees and two part-time employees, consisting of clinical and preclinical development, regulatory affairs, marketing and administration. We consider our relations with our employees to be good.

About Orexigen

We were incorporated in Delaware in September 2002. Our principal offices are located at 12481 High Bluff Drive, Suite 160, San Diego, California 92130, and our telephone number is (858) 436-8600. Our website address is www.orexigen.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

Available Information

We file electronically with the U.S. Securities and Exchange Commission our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed pursuant to Section 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at www.orexigen.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Copies of our annual report will also be made available, free of charge, upon written request.

The public may read and copy any materials filed by us with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at http://www.sec.gov. The contents of these websites are not incorporated into this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

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

You should carefully consider the following risk factors, as well as the other information in this report, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the factors described when evaluating our business.

Risks Related to Our Business and Industry

We are largely dependent on the success of our two obesity product candidates in clinical development: Contrave™ (naltrexone/bupropion, each in a sustained release, or SR, formulation) and Empatic™ (zonisamide SR/bupropion SR). We cannot be certain that either product candidate will receive regulatory approval or be successfully commercialized.

We currently have only a limited number of product candidates in clinical development, and our business currently depends entirely on their successful development and commercialization. We currently have no drug products for sale and we may never be able to develop marketable drug products. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are subject to extensive regulation by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We are not permitted to market our product

candidates in the United States until we receive approval of a new drug application, or NDA, from the FDA, or in any foreign countries until we receive the requisite approval from the regulatory authorities of such countries. We have not submitted an NDA or received marketing approval for any of our product candidates. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA also has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example:

- the FDA may not deem a product candidate safe and effective;
- the FDA may not find the data from preclinical studies and clinical trials sufficient to support approval;
- the FDA may require additional preclinical or clinical studies;
- the FDA may not approve of our third-party manufacturers' processes and facilities; or
- the FDA may change its approval policies or adopt new regulations.

Contrave is currently being evaluated in Phase III clinical trials for the treatment of obesity and will require the successful completion of at least two pivotal clinical trials before we are able to submit an NDA with respect to Contrave to the FDA for potential approval. Empatic is in the later stages of Phase II development and, following its Phase II clinical trials, also will need to successfully complete two or more pivotal trials prior to our submission of an NDA to the FDA for potential approval. Our product candidates may not be approved even if they achieve their specified endpoints in these and future clinical trials. The FDA may disagree with our trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. Any failure to obtain regulatory approval of Contrave or Empatic would limit our ability to ever generate revenues (and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue) and would have a material and adverse impact on our business.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.

Our product candidates are prone to the risks of failure inherent in drug development. Before obtaining regulatory approvals for the commercial sale of Contrave, Empatic or any other product candidate for a target indication, we must demonstrate with substantial evidence gathered in well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA and, with respect to approval in other countries, similar regulatory authorities in those countries, that the product candidate is safe and effective for use for that target indication.

With respect to Contrave, we submitted to the FDA in October 2006 the 24 week results of our Phase II clinical trial, which we characterize as a Phase IIb trial because we believe the results from this clinical trial provide sufficient evidence of the superiority of the combination drug therapy to the individual monotherapies in the treatment of obesity. We received correspondence from the FDA in December 2006 in which the FDA agreed that our future pivotal studies for Contrave could be performed against placebo only. This understanding was confirmed in our end-of-Phase-II meeting with the FDA in October 2007. While the FDA has provided us with guidance on the general efficacy benchmarks required in pivotal trials for comparison against placebo, we may not be able to achieve these requirements or replicate the results observed in our earlier Phase II and IIb clinical trials. Furthermore, the FDA's guidelines were set forth in correspondence and not in the form of a special protocol assessment and, therefore, may change in the future. However, the FDA issued draft guidance on developing products for weight management in February 2007. The draft guidance provides recommendations on the design of studies evaluating the efficacy and safety of products intended to treat obesity. We believe the design of our ongoing and planned pivotal clinical trials for Contrave is consistent with the recommendations made by the FDA in the draft guidance, and we therefore have not revised, and do not intend to revise, the design of our trials in response to the guidance.

With respect to Empatic, we intend to conduct an additional Phase II clinical trial to establish that the combination is more effective than the individual components. It is not clear what magnitude of superiority the FDA will require Empatic to demonstrate versus the most active individual component in order to agree that Phase III clinical trials may be conducted against placebo only. We have not yet commenced any Phase III clinical trials for this product candidate.

In addition, before we can submit an NDA to the FDA for potential regulatory approval, we may need to complete additional preclinical testing of our product candidates to evaluate safety and toxicity. The results from the preclinical and clinical trials that we have completed for Contrave and Empatic may not be replicated in future trials, or we may be unable to demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for either product candidate. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If our drug candidates are not shown to be safe and effective in clinical trials, our clinical development programs could be delayed or terminated. Any delays could also result in the need for additional financing, and our failure to adequately demonstrate the efficacy and safety of Contrave, Empatic or any other product candidates that we may develop, in-license or acquire would prevent receipt of regulatory approval and, ultimately, the commercialization of that product candidate.

Our bioequivalence studies may fail to demonstrate acceptable comparability between different formulations of Contrave used in our Phase III clinical trials and between formulations of Contrave used in our Phase III clinical trials and the formulation of Contrave we intend to launch commercially.

Because different manufacturers and manufacturing methods have been used during the Contrave development program, we will likely need to demonstrate comparable bioavailability and bioequivalence between the differing formulations of Contrave used in our Phase III clinical trials and between the Phase III and commercial formulations of Contrave. If we are unable to demonstrate that the different Contrave formulations used in our Phase III clinical trials are bioequivalent to one another, or if we are unable to demonstrate that the Contrave formulations used in our Phase III clinical trials are bioequivalent to the formulation we intend to launch commercially, then we may be required to repeat some or all of our Phase III clinical trials, or we may need to develop an alternative commercial formulation that is bioequivalent. As a result, our ability to obtain approval of Contrave, if any, may be delayed.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial profile of any approved label.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restricted label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. For example, in each trial evaluating Contrave, some patients experienced nausea. We have developed new formulations and techniques in an effort to reduce the frequency and magnitude of this side effect; however, we are only in the early stages of blinded testing of these methods in four current Phase III clinical trials. Other less common side effects reported in our Contrave trials were dizziness, insomnia and headaches. The most common side effects reported in our Phase IIb trial of Empatic have been headache, nausea, insomnia, anxiety and dry mouth. In addition, the constituent drugs of each of our product candidates each has its own side effect profile that is included in its current product label. If our product candidates are approved by the FDA we would anticipate that their labels would include the side effect profiles of each of the constituent drugs. Moreover, patients in our clinical trials may experience side effects that are indicated in the constituent drugs' labels. In addition, while the constituent drugs that make up Contrave and Empatic have post-marketing safety records and while we have tested these constituent drugs in combination in our clinical trials of Contrave and Empatic to date, the combination of these constituent drugs is still being tested and has not received regulatory approval. Accordingly, the safety of their combined use is not yet fully known. The approvability and eventual labeling of Contrave and Empatic will be determined by the safety experience with the drugs in the context of their relative merits (efficacy) in an obese population. For example, the Endocrinologic and Metabolic Drugs Advisory Committee convened by the FDA recently reviewed another company's obesity product candidate, rimonabant, and determined not to recommend approval of the product candidate to the FDA, based on concerns regarding the safety

profile of the product candidate (in particular, depression, suicidality and seizures) and the potential for long-term use of the product by patients.

A key constituent of Contrave and Empatic is bupropion, which has been approved by the FDA for the treatment of depression and to assist smoking cessation. The FDA has directed manufacturers of all antidepressant drugs to include in their product labels a "black box" warning and expanded warning statements regarding an increased risk of suicidal thinking and behavior in children and adolescents being treated with these drugs. The package insert for bupropion includes such a "black box" warning statement. Although neither Contrave nor Empatic is intended to be promoted for or used in the treatment of primary depression, many obese patients may experience depression and it is likely that there will be depressed obese patients who use these product candidates, if approved. We expect that a similar warning statement will be required on labeling for both Contrave and Empatic. In December 2006, the FDA held an advisory committee meeting regarding suicidal thinking and behavior in adults being treated with antidepressant drugs. The advisory committee recommended that the "black box" warning be extended to cover adults up to their mid-20's. We expect that any additional warnings or other labeling changes related to suicidal thinking and behavior in adults will be required on labeling for both Contrave and Empatic. The FDA has also directed manufacturers of antidepressant drugs to create Medication Guides to be distributed to patients regarding the risk of suicidal thinking and behavior in children and adolescents. Although we have not designed either the Contrave or Empatic programs for the treatment of children or adolescents, it is possible that the FDA will require a Medication Guide for both Contrave and Empatic. These warnings and other requirements may have the effect of limiting the market acceptance by our targeted physicians and patients of Contrave and Empatic, if these product candidates are approved.

In addition, each of the constituent drugs included in the Contrave and Empatic combinations has in its package insert a "Category C" pregnancy precaution. This means that animal studies have shown that each of these constituent drugs has the potential to cause birth defects and that there have been no adequate and well-controlled studies of the constituent drugs in pregnant women, but that the FDA has determined that the benefits from the use of such drugs in pregnant women may be acceptable despite the potential risks.

Zonisamide, a constituent drug of Empatic, also has a warning that women of childbearing age should be advised to use contraception due to the teratogenicity seen in animal studies. In addition, because of published concerns in academic journals regarding the possible developmental effects of zonisamide in animals as well as reports from Japan in which women receiving zonisamide combined with other anticonvulsants had children with birth defects, it is likely that Empatic, if approved, will receive a "Category X" pregnancy precaution and thus, would be contraindicated for use by pregnant or nursing women with warnings about use of Empatic in women of childbearing age. This means that there could be a limitation on the use of Empatic without adequate contraception or perhaps a prohibition on the use of Empatic by all women of childbearing age. Although we have designed our clinical trials to educate women about the necessity of using adequate contraception while taking, and for a period of time after taking, our product candidates, women may not take the necessary precautions to prevent pregnancy and as a result, women taking our product candidates may risk bearing children with birth defects.

Recently the FDA analyzed reports of suicidal behavior or ideation from placebo-controlled clinical studies of eleven anticonvulsants (including zonisamide). In the FDA's analysis, patients receiving anticonvulsants had approximately twice the risk of suicidal behavior or ideation compared to patients receiving placebo. The relative risk for suicidal behavior or ideation was higher in the patients with epilepsy compared to patients who were given one of the anticonvulsants for conditions other than epilepsy. The FDA has indicated that it will be working with manufacturers of marketed anticonvulsants to include this new information in the labeling of these products. It is possible that any changes related to suicidal behavior or ideation that occur to the labels of these anticonvulsants will be required on the labeling for Empatic.

If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning with Contrave or Empatic or a contraindication;

- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we could be asked to formulate a risk evaluation mitigation strategy that could include a program of post-marketing surveillance or restricted distribution for patients receiving our products;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

Delays in the commencement or completion of clinical testing could result in increased costs to us and delay or limit our ability to generate revenues.

Delays in the commencement or completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- manufacturing sufficient quantities of a product candidate for use in clinical trials;
- obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of obesity or similar indications; and
- retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; and
- lack of adequate funding to continue the clinical trial.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. For instance, the FDA issued draft guidance on developing products for weight management in February 2007, after we had established the design of our first Phase III clinical trial for Contrave. In addition, the Endocrinologic and Metabolic Drugs Advisory Committee convened by the FDA recently reviewed another company's obesity product candidate, known as rimonabant, and determined not to recommend its approval to the FDA. In connection with its review of rimonabant, the committee discussed various aspects of the rimonabant development program, and these discussions provided further insight on the FDA's view of what is and is not acceptable in connection with a clinical trial protocol for obesity product candidates. While we believe the

designs of our ongoing and planned pivotal clinical trials for Contrave are consistent with the current recommendations made by the FDA in the draft guidance and the advisory committee's recent discussions, we cannot guarantee that the FDA will ultimately deem the design of one or more of our clinical trials to be sufficient to support regulatory approval, and that we will not be required to modify our ongoing clinical trials or to conduct additional clinical trials in order to obtain approval. Amendments in response to changes in regulatory requirements or guidance may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

Our product candidates are combinations of generically-available pharmaceutical products, and our success is dependent on our ability to compete against off-label generic substitutes and demonstrate the advantages of our proprietary combination products.

The patents we have in-licensed and our pending patent applications do not prevent physicians from prescribing the generic constituents of our product candidates. We believe that a practitioner seeking safe and effective therapy is not likely to prescribe such off-label generics in place of Contrave or Empatic because the dosage strengths, pharmacokinetic profiles and titration regimens recommended for our Contrave and Empatic product candidates are not available using existing generic preparations of immediate release, or IR, naltrexone, zonisamide IR and bupropion SR, and there are no oral generic SR formulations of naltrexone or zonisamide. However, a physician could seek to prescribe off-label generics in place of Contrave or Empatic. Off-label use occurs when physicians prescribe a drug that is approved by the FDA for one indication for a different, unapproved indication.

With regard to off-label substitution at the pharmacy level, we expect to rely on the novel dose ratios and novel pharmacokinetic properties of our product candidates, as well as the differences in their approved indications, to provide sufficient distinction such that generic preparations are not considered therapeutic equivalents by the FDA. State pharmacy laws in many instances only permit pharmacists to substitute generic products for branded products if the products are therapeutic equivalents. Therefore, the lack of therapeutic equivalency limits generic substitution by pharmacies and/or pharmacy benefit managers. However, we cannot be certain that pharmacists and/or pharmacy benefit managers will not seek prescriber authorization to substitute generics in place of Contrave and Empatic, which could significantly diminish their market potential.

In addition, although we believe the current market prices for the generic forms of naltrexone and zonisamide make generic substitution by physicians, pharmacists or pharmacy benefit managers unlikely, should the prices of the generic forms decline, the motivation for generic substitution may become stronger. Wide scale generic substitution by physicians and at the pharmacy level could have substantial negative consequences to our business.

We rely primarily on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates within our expected timeframes or at all.

We currently rely primarily on Metropolitan Research Associates, or MRA, a CRO, to conduct our clinical trials for Contrave and Empatic, and we may depend on other CROs and independent clinical investigators to conduct our clinical trials in the future. We utilize the services of HHI Clinical & Statistical Services to conduct our data management. The third parties with which we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. CROs and investigators are not our employees, and we have limited ability to control the amount or timing of resources that they devote to our programs. If MRA, other CROs, consultants or independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, it will delay the potential approval of our regulatory applications and the commercialization of our product candidates. In addition, the execution of clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. If these third parties are unable to coordinate and communicate with

one another, our clinical trials may be delayed or the completion and analysis of the data may be delayed or compromised. Moreover, these independent investigators and CROs may also have relationships with other commercial entities, some of which may compete with us. If independent investigators and CROs also contract to provide services for our competitors, it could adversely affect our business.

We expect intense competition in the obesity marketplace for Contrave and Empatic, and new products may emerge that provide different or better therapeutic alternatives for obesity and weight loss.

If approved and commercialized, both Contrave and Empatic will compete with well established prescription drugs for the treatment of obesity, including Xenical (orlistat), marketed by Roche Laboratories Inc., and Meridia (sibutramine), marketed by Abbott Laboratories. Orlistat has also been launched by GlaxoSmithKline in over-the-counter form under the brand name alli, which represents additional competition and potential negative pricing pressure. Both orlistat and sibutramine are marketed by pharmaceutical companies with substantially greater resources than we have. In addition, a number of generic pharmaceutical products are prescribed for obesity, including phentermine, phendimetrazine, benzphetamine and diethylpropion. Some of these generic drugs, and others, are prescribed in combinations that have shown anecdotal evidence of efficacy. These products are sold at much lower prices than we intend to charge for our product candidates, if approved. The availability of a large number of branded prescription products, generic products and over-the-counter products could limit the demand for, and the price we are able to charge for, our product candidates.

Currently there are a number of products in development for obesity which could become competitors against our product candidates. These include products being developed by Arena Pharmaceuticals, Inc., Amgen Inc., Amylin Pharmaceuticals, Inc., Alizyme plc, Merck & Co., Inc., Nastech Pharmaceutical Co., Inc., Neurosearch A/S, Peptimmune, Inc., Sanofi-Aventis, and Vivus, Inc., among others. Based on reports from these companies, it appears that some of these product candidates are entering into later stage clinical trials.

Rimonabant, the Sanofi-Aventis compound, has been approved in certain countries outside of the United States. On June 13, 2007, the Endocrinologic and Metabolic Drugs Advisory Committee convened by the FDA recommended unanimously against approval of rimonabant for use in obese patients. Although such recommendations are not binding on the FDA, on June 29, 2007, Sanofi-Aventis announced its decision to withdraw the rimonabant NDA in the United States. Sanofi-Aventis could, however, resubmit an amended NDA at some point in the future.

New developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our product candidates less competitive. Some of our potential competitors are large pharmaceutical or device firms and have substantially greater resources than we have. These resources could be directed toward the obesity market and include:

- research and development resources, including personnel and technology;
- regulatory experience;
- drug development and clinical trial experience;
- experience and expertise in exploitation of intellectual property rights; and
- capital resources.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more useful and less costly than ours and may also be more successful in manufacturing and marketing their products. We currently outsource our manufacturing and therefore rely on third parties for that competitive expertise. There can be no assurance that we will be able to develop or contract for these capabilities on acceptable economic terms, or at all.

In addition, should both Contrave and Empatic be approved to treat obesity, these product candidates may compete with one another. We are developing Contrave to treat mild to moderate obesity, especially in women with food craving. We are developing Empatic to treat more severe obesity, especially in men and in women beyond the childbearing years. While we intend to direct each product candidate to specific segments of the obesity marketplace, the FDA does not distinguish between these types of obesity and, if approved, any potential label for Contrave and Empatic would be expected to refer to obesity generally. There is no guarantee that we will be successful in marketing Contrave and Empatic to their respective target markets or minimizing competition between them.

We have limited sales and marketing experience or resources, and we may not be able to effectively market and sell our products.

We are developing our obesity product candidates for large markets traditionally served by general and family practitioners and internists. Generalist physicians number in the several hundred thousand in the United States. Traditional pharmaceutical companies employ groups of sales representatives numbering in the thousands to call on this large generalist physician population. In order to adequately address these physician groups, we must either establish sales and marketing collaborations or co-promotion arrangements or expend significant resources to develop our own sales and marketing presence. We currently possess limited resources and may not be successful in establishing collaborations or co-promotion arrangements on acceptable terms, if at all. We also face competition in our search for collaborators, co-promoters and sales force personnel. By entering into strategic collaborations or similar arrangements, we may rely on third parties for financial resources and for development, commercialization, sales and marketing and regulatory expertise. Our collaborators may fail to develop or effectively commercialize our product candidates because they cannot obtain the necessary regulatory approvals or decide to pursue a competitive potential product that may be developed outside of the collaboration. Even if we are able to identify suitable collaborators to assist in the commercialization of our product candidates, they may fail to devote the resources necessary to realize the full commercial potential of our product candidates.

Our development and commercialization strategy depends upon access to findings of safety and effectiveness based on data not developed by us but which the FDA may reference in reviewing our U.S. marketing applications. In territories outside the United States, we must either negotiate access to these safety and effectiveness findings or develop them ourselves.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug, and Cosmetic Act. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. This statutory provision expressly allows the FDA to rely, for purposes of approving an NDA, on findings of safety and effectiveness based on data not developed by the filer of the NDA. Under these guidelines, we were able to move directly into Phase II clinical trials for each of our drug combinations, because our planned NDAs will rely, in part, upon the FDA's findings of safety and effectiveness for the previously-approved products that are incorporated into Contrave and Empatic. Analogous legislation does not exist in other countries. In territories where data are not freely available, we may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds to generate our own data. We may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety and manufacturing dossiers. In addition, even though we can take advantage of Section 505(b)(2) to support potential U.S. approval for our Contrave and Empatic product candidates, the FDA may also require us to perform additional studies or measurements to support changes from the previously-approved products incorporated into our product candidates.

To the extent that a Section 505(b)(2) application relies on the FDA's finding of safety and effectiveness of a previously-approved drug, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's publication called "Approved Drug Products with Therapeutic Equivalence Evaluations," otherwise known as the "Orange Book." Specifically, the applicant must certify when the application is submitted that: (1) there is no patent information listed; (2) the listed patent has expired; (3) the listed patent has

not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid or will not be infringed by the manufacture, use, or sale of the new product. A certification that the new product will not infringe the already approved product's Orange Book listed patents or that such patents are invalid is called a paragraph IV certification. If the applicant has provided a paragraph IV certification to the FDA, the applicant must also send notice of the paragraph IV certification to the NDA holder and patent owner. When we file our NDAs for Contrave and Empatic, we intend to make paragraph IV certifications that our products do not infringe the bupropion SR formulation patents listed in the Orange Book, and send the appropriate notice to the patent holder and NDA holder. In the event that the patent holder or NDA holder files a patent infringement lawsuit against us within 45 days of its receipt of our paragraph IV certification, such lawsuit would automatically prevent the FDA from approving our Section 505(b)(2) NDA until the earliest of 30 months, expiration of the patent (2013), settlement of the lawsuit or a decision in the infringement case that is favorable to us. Any such patent infringement lawsuit could be costly, take a substantial amount of time to resolve and divert management resources. If we obtain FDA approval for either Contrave or Empatic, we could obtain three years of Hatch-Waxman marketing exclusivity for such product, assuming we obtain the first approval for either product candidate for the indication supported by the clinical studies we conducted. Under this form of exclusivity, the FDA would be precluded from approving a marketing application for a duplicate drug product (for example, a product that incorporates the change or innovation represented by our product) for a period of three years, although the FDA may accept and commence review of such applications. However, this form of exclusivity might not prevent the FDA from approving an NDA that relies on its own clinical data to support the change or innovation. Further, if another company obtains approval for either product candidate for the same indication we are studying before we do, our approval could be blocked until the other company's Hatch-Waxman marketing exclusivity expires.

Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. For example, the label ultimately approved for Contrave or Empatic, if any, may include restrictions on use, including restrictions based on pregnancy status, level of obesity and duration of treatment or a "black box" warning related to general concerns regarding antidepressants or otherwise. The FDA may also require the distribution of a Medication Guide to patients outlining the increased risk of suicidal thinking or behavior in children and adolescents or other populations. The FDA could also require a registry to track the patients utilizing the product. Our product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;
- suspend regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

Even if our product candidates receive regulatory approval in the United States, we may never receive approval or commercialize our products outside of the United States.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the United States. As described above, such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on their commercial potential or require costly, post-marketing follow-up studies.

If the suppliers upon whom we rely for active pharmaceutical ingredients, or API, fail to produce such ingredients in the volumes that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the conduct of our clinical trials.

We do not manufacture any of our API nor do we plan to develop any capacity to do so. Instead, we rely on suppliers of API to provide component materials to our other contract manufacturers, who produce finished pharmaceutical products incorporating the API for use in our clinical trials. Currently, we have only one supplier for zonisamide API, a component in our Empatic product candidate, one supplier of naltrexone API, a component in our Contrave product candidate, and one supplier of bupropion API, a component in each of our Empatic and Contrave product candidates.

While a number of manufacturers are FDA-qualified to produce zonisamide and bupropion, and we have already entered into negotiations with other suppliers to act as secondary or supplemental suppliers of these ingredients, we may not be successful in securing these additional supply arrangements on a timely or commercially reasonable basis or at all. The failure or inability of our API suppliers to satisfy our API requirements on a timely basis could cause a disruption of our trials and delay our development program.

Although naltrexone itself is not addictive, synthesis of naltrexone is a multi-step process with a natural opiate starting material that has the potential for abuse and is therefore regulated as a controlled substance under the Federal Controlled Substance Act. As such, manufacturers of naltrexone API must be registered by the Drug Enforcement Administration, or DEA. Manufacturers making naltrexone also must obtain annual quotas from the DEA for the opiate starting material. Because of the DEA-related requirements and modest current demand for naltrexone API, there exist few current manufacturers of this API. Therefore, API costs for naltrexone are greater than for the other constituents of our product candidates. Demand for Contrave may require amounts of naltrexone greater than the currently available worldwide supply. Any lack of sufficient quantities of naltrexone would limit our ability to complete our planned clinical trials and commercially launch Contrave. Although we are evaluating additional possible manufacturers to supplement our current naltrexone manufacturing capacity, including those in the United States, Europe and Asia, we may not be successful in accessing additional manufacturing supply of naltrexone API or other necessary components of our product candidates at the appropriate quantities, quality or price.

To date, all of our purchases of API have been completed by purchase orders. We have no long-term commitments or supply agreements with any of our API suppliers. Although we may seek to establish long-term supply commitments in the future, we may be required to agree to minimum volume requirements, exclusivity arrangements or other restrictions. We may not be able to enter into long-term agreements on commercially reasonable terms, or at all. Consequently, even if and when our product candidates are approved, we may not be able to successfully commercialize these product candidates if we are unable to secure long-term supply commitments for their API components.

If the contract manufacturers upon whom we rely fail to produce our product candidates in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of our product candidates.

We do not currently possess nor do we plan to implement manufacturing processes internally. We currently utilize the services of contract manufacturers to manufacture our clinical supplies. These clinical supplies include the formulations of our product candidates' components using the API from our API suppliers, the tablets combining those components and the Contrave Titration Packs, Empatic Titration Packs and bottles used to package these tablets for use in clinical trials. To date, all of these contract manufacturers have performed services under short-term purchase orders or similar arrangements. We have no long-term commitments or supply agreements with these contract manufacturers. For example, Patheon currently manufactures bupropion SR as well as finished Contrave tablets for our Contrave Phase III clinical trials on a proposal by proposal basis under a master agreement for pharmaceutical development services that we entered into in February 2007. Either party may terminate the agreement upon notice if the other party commits a material breach of its obligations and fails to remedy the breach within 30 days. In addition, we may terminate the agreement immediately for any business reason.

With respect to the manufacturing for our commercial scale product, we intend to eventually pursue long-term agreements with our current manufacturers or transfer the manufacturing to other larger manufacturers. There can be no assurance we will be able to transfer any manufacturing processes to other larger manufacturers. Furthermore, we may be required to agree to minimum volume requirements, exclusivity arrangements or other restrictions. We may not be able to enter into long-term agreements on commercially reasonable terms, or at all. If we change to other manufacturers, the FDA and comparable foreign regulators must approve these manufacturers' facilities and processes prior to use, which would require new testing and compliance inspections, and the new manufacturers would have to be educated in or independently develop the processes necessary for the production of our product candidates.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us, our ability to provide product candidates to patients in our clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of our clinical trials, increase the costs associated with maintaining our clinical trial program and, depending upon the period of delay, require us to commence new trials at significant additional expense or terminate the trials completely.

In addition, all manufacturers of our products must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the generation and maintenance of records and documentation. Manufacturers of our products may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. We have little control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our products. Furthermore, if our manufacturers fail to deliver the required commercial quantities on a timely basis, pursuant to provided specifications and at commercially reasonable prices, we may be unable to meet demand for our products and would lose potential revenues.

Bupropion, which is an API in both Contrave and Empatic, is known to have issues with stability.

Bupropion, which is an API in both Contrave and Empatic, is known to have issues with stability that require manufacturing processes that minimize exposure to moisture and limit oxidation. We are performing stability testing to ensure that our combination tablet of Contrave has sufficient stability to provide the customary two-year stability characteristics and shelf life expected of a conventional pharmaceutical product. Although we are currently conducting stability studies, we cannot be sure that either Contrave or Empatic will be stable, and we may not be able to demonstrate sufficient long-term stability to provide at least two years of shelf life for these product candidates, which could jeopardize our ability to bring such product candidates to market.

We face potential product liability exposure, and, if successful claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for our product candidates;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to commercialize our product candidates.

We have obtained product liability insurance coverage for our clinical trials with a $10.0 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for any of our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

If any of our product candidates for which we receive regulatory approval does not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

The commercial success of our product candidates for which we obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products by both the medical community and patient population. Coverage and reimbursement of our product candidates by third-party payors, including government payors, generally is also necessary for optimal commercial success. The degree of market acceptance of any of our approved products will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;
- the relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;

- limitations or warnings contained in a product's FDA-approved labeling, including, for example, potential "black box" warnings or pregnancy precautions associated with the APIs in Contrave and/or Empatic;
- availability of alternative treatments, including, in the case of Contrave and/or Empatic, a number of competitive products already approved for the treatment of weight loss or expected to be commercially launched in the near future;
- pricing and cost effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain sufficient third-party coverage or reimbursement; and
- the willingness of patients to pay out of pocket in the absence of third-party coverage.

If our product candidates are approved but do not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

We are subject to uncertainty relating to reimbursement policies which, if not favorable to our product candidates, could hinder or prevent our product candidates' commercial success.

Our ability to commercialize our product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other third-party payors establish appropriate coverage and reimbursement levels for our product candidates and related treatments. As a threshold for coverage and reimbursement, third-party payors generally require that drug products have been approved for marketing by the FDA. Third-party payors also are increasingly challenging the effectiveness of and prices charged for medical products and services. We cannot provide any assurances that we will be able to obtain third-party coverage or reimbursement for our product candidates in whole or in part.

The obesity market, in particular, continues to be marked by limited coverage and reimbursement from health insurers and other payors, who have historically viewed obesity as a lifestyle issue. For example, state Medicaid programs, administered by individual states for qualifying low income individuals, are permitted to exclude coverage for weight loss drugs. In addition, weight loss drugs are excluded from coverage under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 designed for eligible seniors and disabled individuals and which went into effect on January 1, 2006.

Currently, our competitors' drug products have limited third-party payor coverage. This means that individuals prescribed such drug products often either have significant out-of-pocket costs or pay for the products entirely by themselves. If our product candidates do not receive adequate coverage or reimbursement, the market acceptance and commercial success of our products may be limited.

Recently, the Medicare program, a federal governmental third-party payor whose policies often are emulated or adopted by other payors, has removed longstanding policy language that obesity itself cannot be considered an illness. This deletion did not alter the statutory prohibition on drug reimbursement by Medicare or result in a change to coverage for particular obesity-related procedures, and treatment for obesity alone remains uncovered. However, the Medicare program has since issued a national policy recognizing coverage for bariatric surgery for co-morbid conditions associated with obesity. Although third-party payor attitudes regarding obesity-related products and services appear to be changing, as exemplified by Medicare changes, we may continue to face a poor coverage and reimbursement environment.

Our failure to successfully acquire, develop and market additional product candidates or approved products would impair our ability to grow.

As part of our growth strategy, we intend to acquire, in-license, develop and/or market additional products and product candidates. Because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising pharmaceutical product candidates and products.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we may acquire will be commercialized profitably or achieve market acceptance.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in health care systems to contain health care costs and improve quality. While reform proposals often involve expanding coverage to more individuals, health care reform may also involve increased government price controls, additional regulatory mandates and other measures designed to lower medical and pharmaceutical costs. Within the United States, the pharmaceutical industry has been a particular focus of both the U.S. Congress, as well as state governments. Proposed reforms include, but are not limited to, increasing regulation of pharmaceutical representatives, restricting direct to consumer advertising and off-label uses, limiting manufacturers' access to marketing data, requiring greater reliance on comparative effectiveness reviews of competing drugs, increasing use of electronic prescribing and authorizing the re-importation of drugs from Canada and other foreign countries to lower pharmaceutical costs to U.S. consumers.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may adversely affect:

- our ability to set a price we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability; and
- the availability of capital.

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of March 14, 2008, we had 25 full-time employees and two part-time employees. We will need to continue to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize our current and any of our future product candidates. Our management and personnel and systems currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- manage our clinical trials effectively, including our ongoing Phase III clinical trials for Contrave which are being conducted at numerous clinical trial sites and our upcoming Phase II clinical trial for Empatic;
- manage the manufacturing and development of Contrave and Empatic;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- attract and retain the breadth and depth of sufficient numbers of talented employees.

We have traditionally utilized the services of outside vendors to perform tasks including clinical trial management, statistics, regulatory affairs, formulation development, pharmacokinetics and other drug development functions. For example, we have engaged part-time individual consultants and the consulting firm PharmaDirections, Inc. to assist us with certain initiatives relating to pharmacology and product development, among others. Our growth strategy may also entail expanding our group of contractors to implement these tasks going forward. Because we rely on a substantial number of consultants, effectively outsourcing many key functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials or other development activities may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Diego, California area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management, particularly Gary D. Tollefson, M.D., Ph.D., our President and Chief Executive Officer. If we lose any members of our senior management team, we may not be able to find suitable replacements, and our business may be harmed as a result. However, we are not aware of any key personnel who have plans to retire or leave our company in the near future. In addition to the competition for personnel, the San Diego area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Although we have employment agreements with each of our executive officers, these agreements are terminable at will at any time with or without notice and, therefore, we may not be able to retain their services as expected. In addition, certain of our executive officers are only required to devote a portion of their full business

time to our business, and therefore may not contribute as much to our growth and development as a full-time member of management could.

In addition, we have scientific and clinical advisors who assist us in formulating our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

We will need to obtain FDA approval of our proposed product names, Contrave and Empatic, and any failure or delay associated with such approval may adversely impact our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or PTO. The FDA typically conducts a rigorous review of proposed product names, including an evaluation of potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims. If the FDA objects to the product names Contrave or Empatic, we may be required to adopt an alternative name for our initial product candidates. If we adopt an alternative name, we would lose the benefit of our existing trademark applications for Contrave and/or Empatic and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

As a manufacturer of pharmaceuticals, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business, without limitation. The regulations that may affect our ability to operate include:

- the federal healthcare program Anti-Kickback Law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail the use of these materials and interrupt our business operations. We do not currently maintain hazardous materials insurance coverage. If we are subject to any liability as a result of our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected. In the future we may seek to establish longer term third-party manufacturing arrangements, pursuant to which we would seek to obtain contractual indemnification protection from such third-party manufacturers potentially limiting this liability exposure.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for Contrave or Empatic could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Risks Related to Intellectual Property

The issued patent rights that we have in-licensed covering Contrave and Empatic are limited to the United States and although we have international patent applications pending, our market opportunity for Contrave and Empatic may be limited by the lack of patent protection in other territories. In addition, although we have additional U.S. and international patent applications pending which seek further protection of all of our product candidates, these applications may not issue on a timely basis or at all.

Contrave is currently protected by U.S. patent number 5,512,593 issued in April 1996 and U.S. patent number 5,817,665 issued in October 1998, which we have licensed on an exclusive basis from Dr. Lee Dante and which we collectively refer to as the Dante patents. Provided maintenance fees are paid, U.S. patent number 5,512,593 is expected to expire in April 2013 and U.S. patent number 5,817,665 is expected to expire in March 2013. The Dante patents do not protect our Contrave product candidate outside of the United States. The Dante patents cover

compositions of certain specified opioid antagonists (including naltrexone) combined with certain specified antidepressants (including bupropion and fluoxetine), and thus provide coverage for both our Contrave and OREX-004 (naltrexone SR/fluoxetine) product candidates.

In addition to the Dante patents, we own a U.S. patent application and related continuation patent applications, which we refer to as the Weber/Cowley patent applications and which are the subject of an agreement with Oregon Health & Science University, or OHSU. The claims currently pending in the Weber/Cowley patent applications are directed to the current composition of our Contrave product candidate and methods for using that composition to effect weight loss. The Weber/Cowley patent applications have not yet issued and we cannot provide assurance that they will issue on a timely basis or at all. We have filed a number of international counterparts to the Weber/Cowley patent applications in foreign countries and also cannot provide assurance that they will issue on a timely basis or at all.

Two of the pending Weber/Cowley patent applications received interim rejections from the PTO, one on the basis that the composition claims were obvious, and the other on the basis that the claimed methods of treatment were disclosed in the prior art. With respect to the Weber/Cowley patent application covering the composition claims, the PTO subsequently issued a Notice of Allowance. If the issue fees for this application are timely paid for, and if the application is not withdrawn from issue by us or by the PTO, we would expect a U.S. patent to issue on this application in due course. If and when a U.S. patent issues as we anticipate based on the Notice of Allowance, we expect to have protection for Contrave extended from 2013 through at least 2024. Although withdrawal from issue is not common, no assurance can be given that this patent application will not be withdrawn from issue, nor can there be any assurance that any patent claims issuing from this application will be sufficiently broad to protect Contrave in the United States. Further, even if this patent ultimately issues, there is no assurance that it will not be successfully opposed or otherwise challenged by third parties. With respect to the Weber/Cowley patent application covering the method of treatment claims, although we believe that we have sufficient arguments, and are working with the PTO to amend the application in such a way as to overcome these interim rejections of claims, there can be no assurance that these rejections and any future rejections will ultimately be overcome or that any claims that may issue will be sufficiently broad to protect our Contrave product candidate in the United States. If these U.S. patent applications and their international counterparts ultimately issue, we expect to have protection extended to at least 2024. However, we cannot be certain that the scope of any issued U.S. or foreign patent will be consistent with the currently pending claims, as there is a significant likelihood that the scope of the currently pending claims will be modified. A European counterpart application to the Weber/Cowley patent applications is currently pending with the European Patent Office, or EPO, and the EPO has issued a Decision to Grant a Patent covering compositions and uses of bupropion and naltrexone for affecting weight loss. However, there is no assurance that the claims in this application, or any other claims, will issue in their currently pending form or at all, or that once issued, they will not be successfully opposed or otherwise challenged by a third party.

We have filed patent applications in the United States and certain foreign countries and under the Patent Cooperation Treaty, or PCT, which is an international treaty providing a unified procedure under which the initial filing of a single patent application can provide an effective filing date in each participating country in which appropriate steps are subsequently taken. These filings seek to protect the formulations and use of SR oral naltrexone, an ingredient in our Contrave and OREX-004 product candidates, but we cannot provide assurance that the claims in these patent applications will issue in their current form or at all. Accordingly, unless the Weber/Cowley patent applications or our other pending patent applications ultimately issue with a scope of protection that protects our Contrave product candidate, a competitor could file an NDA for the development of naltrexone in combination with bupropion, seeking approval as early as 2013, when the Dante patents expire. Alternatively, if a competitor is willing to challenge the scope or validity of the Dante patents, the competitor could file an NDA seeking approval any time before we obtain approval from the FDA of an NDA for Contrave and three years after we obtain such approval. If issued, the Weber/Cowley patent applications and other patent filings have the potential to protect Contrave for an additional 11 years following the expiration of the Dante patents.

Our intellectual property protection for Empatic derives from U.S. patent number 7,109,198, which was issued in September 2006 and which we refer to as the Gadde patent. We in-license this patent on an exclusive basis from Duke University, or Duke, together with several related patent applications. This patent provides composition coverage for the Empatic zonisamide/bupropion combination and also covers methods for using Empatic to treat

obesity and to reduce the risk of hypertension, diabetes or dyslipidemia. Provided maintenance fees are paid, this U.S. patent is expected to expire in May 2023. Duke has received a Notice of Allowance from the PTO for a continuation patent application, which is related to the Gadde patent and also exclusively licensed to us, that covers methods of using zonisamide (including combinations with bupropion) to cause weight loss. If a patent ultimately issues from this allowed continuation application, it will provide additional coverage for methods of using Empatic to treat obesity, until the expected patent expiration in 2023. In addition, Duke has filed international counterparts to the Gadde patent that are currently pending; however, there is no assurance that the claims in these applications will issue in their currently pending form or at all. We have also filed patent applications in the United States, under the PCT and in certain foreign countries with the goal of protecting the formulations and use of zonisamide SR, an ingredient in our Empatic and OREX-003 product candidates, but we cannot provide assurance that the claims in these patent applications will issue in their currently pending form or at all.

We and Duke have filed patent applications in the United States and certain foreign countries with claims directed to compositions and methods for the prevention of drug associated weight gain, with the goal of protecting our Empatic and OREX-003 product candidates and methods of using them. In the United States, this application has received interim rejections from the PTO on the basis that the composition claims were obvious. Although we believe that we have sufficient arguments to, and have amended our application in such a way as to, overcome these interim rejections of claims, there can be no assurance that these rejections and any future rejections will ultimately be overcome or that any claims that may issue will be sufficiently broad to protect the use of our Empatic or OREX-003 product candidates. Likewise, we cannot provide assurance that the claims in the corresponding foreign patent application will issue in their currently pending form or at all.

In addition to the Dante patents and the naltrexone SR patent application mentioned above, we have also filed patent applications in the United States, under the PCT and in certain foreign countries with the goal of protecting the use of our OREX-004 product candidate to treat obsessive-compulsive disorder. Although we have received a favorable preliminary indication of patentability in our PCT application with respect to this indication, we cannot provide assurance that the claims in these patent applications will issue in their currently pending form or at all.

Even if the international patent applications for our product candidates issue or receive approval, we may face additional competition outside of the United States as a result of a lack of patent enforcement in foreign countries and off-label use of other dosage forms of the generic components in our product candidates.

While we have filed patent applications in many countries outside the United States, we do not currently have patent protection for our Contrave, Empatic, OREX-003 or OREX-004 product candidates in any of these foreign jurisdictions. Even if international patents ultimately issue or receive approval, it is likely that the scope of protection provided by such patents will be different from, and possibly less than, the scope provided by our corresponding U.S. patents. The success of our international market opportunity is dependent upon the enforcement of patent rights in various other countries. A number of countries in which we have filed or intend to file patent applications have a history of weak enforcement of intellectual property rights. Even if we have patents issued in these jurisdictions, there can be no assurance that our patent rights will be sufficient to prevent generic competition or unauthorized use.

We may face competition from the off-label use of other dosage forms of the generic components in our product candidates. In addition, others may attempt to commercialize our product candidate combinations in the countries of the European Union, Canada, Mexico, Japan or other markets where we do not have patent protection for our product candidates. Due to the lack of patent protection for these combinations in territories outside the United States and the potential for correspondingly lower prices for the drugs in those markets, it is possible that patients will seek to acquire the generic IR components of our product candidates (naltrexone IR and zonisamide IR), in those other territories. The off-label use of the generic IR components in the United States or the importation of the generic IR components from foreign markets could adversely affect the commercial potential for our product candidates and adversely affect our overall business and financial results.

We have in-licensed all or a portion of the rights to our product candidates from third parties. If we default on any of our material obligations under those licenses, we could lose rights to our product candidates.

We have in-licensed and otherwise contracted for rights to our product candidates, and we expect to enter into similar licenses in the future to supplement our product candidate pipeline. Under the relevant agreements, we are subject to commercialization, development, sublicensing, royalty, insurance and other obligations. If we fail to comply with any of these requirements, or otherwise breach these license agreements, the licensor may have the right to terminate the license in whole or to terminate the exclusive nature of the license. Loss of any of these licenses or the exclusive rights provided therein could harm our financial condition and operating results. For example, our license agreement with Dr. Dante requires us to use commercially reasonable efforts to develop, obtain regulatory approval of and commercialize our Contrave product candidate. To the extent we are unable to comply with these obligations, the license may be terminated.

Restrictions on our patent rights relating to our product candidates may limit our ability to prevent third parties from competing against us.

Our success will depend on our ability to obtain and maintain patent protection for our product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. Composition of matter patents on APIs are generally considered to be the strongest form of intellectual property protection for pharmaceutical products as they apply without regard to any method of use. Entirely new individual chemical compounds, often referred to as new chemical entities, are typically entitled to composition of matter coverage. Current law also allows novel and unobvious combinations of old compounds to receive composition of matter coverage for the combination. However, we cannot be certain that the current law will remain the same, or that our product candidates will be considered novel and unobvious by the PTO and courts.

In addition to composition of matter patents and patent applications, we also have filed method of use patent applications. This type of patent protects the use of the product only for the specified method. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if these competitors do not actively promote their product for our targeted indication, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Although we believe we and our licensors have conducted appropriate prior art searches relating to our method of use patents and patent applications, there is no assurance that all of the potentially relevant prior art has been found. Moreover, because the constituents of our combination product candidates have been on the market as separate monotherapeutic products for many years, it is possible that these monotherapies have previously been used off-label in such a manner that such prior usage would affect the validity of our method of use patents.

Patent applications in the United States and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we and the inventors of the issued patents and applications that we in-licensed were the first to conceive inventions covered by the patents and pending patent applications or that we and those inventors were the first to file patent applications for such inventions.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants, some of whom assist with the development of other obesity drugs. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing products. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates and/or proprietary technologies may give rise to claims of infringement of the patent rights of others. There may be issued patents of third parties of which we are currently unaware that may be infringed by our product candidates or proprietary technologies. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe.

We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. If one of these patents is found to cover our product candidates, proprietary technologies or their uses, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to commercialize our product candidates or use our proprietary technologies unless we or they obtained a license to the patent. A license may not be available to us or our collaborators on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, technologies or methods pending a trial on the merits, which could be years away.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. If a third party claims that we or our collaborators infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party's rights, and if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from selling or licensing the product unless the third party licenses its product rights to us, which it is not required to do;
- if a license is available from a third party, we may have to pay substantial royalties and fees and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our products or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

We will be obtaining our bupropion SR, zonisamide SR, naltrexone SR, our finished Contrave and Empatic tablets combining these components, and our Contrave Titration Packs, Empatic Titration Packs and bottles used to package these tablets from third-party manufacturers. Similarly, it is likely that we will be obtaining the components of our OREX-003 and OREX-004 product candidates from third parties as well. Each aspect of product design, formulation, manufacturing, packaging, and use has the potential to implicate third-party patent rights. For example, we are currently negotiating with potential licensors for rights to new formulations of bupropion SR for commercial purposes that we believe may improve the intellectual property profile of our Contrave and Empatic product candidates and avoid potential infringement of third-party patent rights. In order to secure rights to a new formulation of bupropion SR, we may choose to pay a combination of up-front fees, milestone payments and/or royalties on net sales of products. However, we cannot be certain that we will be able to enter into a definitive license agreement on commercially reasonable terms or at all. Accordingly, we are also developing our own formulation of bupropion SR that we believe will not infringe third-party patent rights. If we do not obtain licensed rights to a bupropion SR formulation or successfully complete the development of our own formulation, we could be exposed

to potential patent infringement liability from third parties who hold patents on various formulations of bupropion. In addition, even if we successfully complete the development of our own formulation, we could still be exposed to potential patent infringement liability from third parties who hold patents on various formulations of bupropion. Because we intend to use a formulation of bupropion SR in our commercial Contrave and Empatic products that is different from the formulation we are currently using in our clinical trials, we will need to demonstrate in clinical trials and/or additional preclinical studies that its bioavailability and bioequivalence is comparable to that of the bupropion SR formulation used in our clinical trials. We expect we will be able to conduct these trials and these studies concurrently with our pivotal trials.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering these or other aspects of our products, technology or methods, as implemented by us or by third-party manufacturers with whom we contract. Because of the large number of patents issued and patent applications filed in our field, we believe there is a risk that third parties may allege they have patent rights encompassing our products, technology or methods. Such third-party patent rights, if relevant, could prevent us from adopting or marketing a particular formulation or product, or could expose us to patent infringement liability.

Although we have entered into a settlement agreement designed to prevent the parties to the agreement from asserting infringement and other specified claims against our Empatic product candidate in the United States, and abroad, disputes with third parties relating to our Empatic product could nevertheless affect our intellectual property rights.

In June 2004, we jointly filed a lawsuit with Duke, against Elan Corporation, plc, Elan Pharma International Ltd. and Elan Pharmaceuticals, Inc., which we refer to collectively as Elan, Eisai, Inc. and Eisai Co., Ltd., which we refer to together as Eisai, and Julianne E. Jennings, a former employee of Elan, in the U.S. District Court for the Middle District of North Carolina, Durham Division, to resolve a dispute over rights in an invention relating to the use of zonisamide to treat obesity. We alleged in this lawsuit that scientists at Duke made the invention, and that Elan improperly used information supplied by the Duke scientists to file a U.S. patent application on the invention, in which Ms. Jennings (then an Elan product manager) is named as the sole inventor. This patent application was later assigned by Elan to Eisai. Duke also filed a U.S. patent application on the invention at issue, which patent application is exclusively licensed to us. This is the Gadde continuation patent application discussed above for which Duke received a Notice of Allowance from the PTO. In December 2006, we, Elan, Eisai, Duke and Ms. Jennings entered into a settlement agreement to settle the lawsuit. Upon execution of the settlement agreement, the lawsuit was dismissed with prejudice.

Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the agreement, released each other from all claims and demands arising under the laws of the United States or any state within the United States existing as of the date of the settlement agreement that arise out of or relate to the lawsuit or the specified Duke and Eisai patents that may issue from certain patent applications claiming the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions. In addition, if Elan, Eisai or Ms. Jennings obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Eisai patent application, Elan, Eisai and Ms. Jennings have each agreed that they will not assert such patent against any of our products containing zonisamide in combination with any other active pharmaceutical agent, including bupropion. Likewise, if Duke obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Duke patent application, we and Duke have agreed that we will not assert any such patent against Elan, Eisai or Ms. Jennings for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai. As discussed above, Duke has received a Notice of Allowance from the PTO for a patent application having such claims.

In September 2007, we and Duke entered into a settlement agreement with Eisai which resolves the foreign aspects of the dispute referenced in the paragraph above. Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the agreement, released each other from all claims and demands arising under the laws of any country outside of the United States existing as of the date of the agreement that arise out of or relate to the lawsuit or certain specified Duke and Eisai foreign patents that may issue from certain patent

applications claiming the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions. In addition, if Eisai obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Eisai foreign patent applications, Eisai has agreed that it will not assert any such patent against any product of ours containing zonisamide in combination with any other active pharmaceutical agent, including bupropion. Likewise, if Duke obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Duke foreign patent applications, we and Duke have agreed that we will not assert any such patent against Eisai for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai.

Although we have resolved the U.S. lawsuit and entered into a settlement agreement containing terms that would prevent Eisai, Elan and Ms. Jennings from asserting specified U.S. patents against our Empatic product and have entered into a settlement agreement containing terms that would prevent Eisai from asserting specified foreign patents against our Empatic product, there is no assurance that the parties will abide by these settlement agreements. There also is no assurance that Eisai, Elan and/or Ms. Jennings do not have, or will not in the future obtain, other patent rights not covered by the settlement agreements that could be asserted against our Empatic product candidate or our other product candidates. Furthermore, Elan and Ms. Jennings are not parties to the settlement agreement which resolves the foreign aspects of the dispute. Although PTO records indicate that Eisai has abandoned its pending patent application, it may take steps to revive the application. In the event that Eisai revives its application and both Duke and Eisai maintain their pending U.S. patent applications for use of zonisamide to treat obesity or other weight-related disorders, such actions may lead to initiation of a patent interference to determine which party invented first. We are not relying on any patent Duke may obtain directed to zonisamide as the sole active ingredient to treat obesity or other weight disorder to protect our Empatic product candidate. The U.S. settlement agreement also contains terms that would not allow Eisai, Elan or Ms. Jennings to use any patent they may obtain by winning an interference to prevent the sale of our Empatic product, if approved. However, if Duke loses the interference or abandons its patent application covering the use of zonisamide as the sole active ingredient to treat obesity or other weight disorder, then the potential additional protection for our Empatic product candidate that could result from such a patent will not be available to us.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on the Gadde patent covering Empatic are due to be paid to the PTO in several stages over the lifetime of the patent. Future maintenance fees will also need to be paid on the Dante patents. We have systems in place to remind us to pay these fees, and we employ an outside firm, Computer Patent Annuities, to pay annuity fees due to foreign patent agencies on our pending foreign patent applications. The PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

The PTO has accepted our statement of use for our trademark application for our corporate logo for use in connection with pharmaceutical preparations and substances for the treatment of obesity, inducement of weight loss and prevention of weight gain and indicated that a registration for such will issue in due course. We have a foreign trademark application pending in Canada for the same mark and have obtained trademark registrations in Europe and Japan for the same mark. In addition, we have a Notice of Allowance from the PTO for the intent-to-use

trademark application for our corporate name OREXIGEN for use in connection with pharmaceutical preparations for the treatment of disorders of the central nervous system. We have a foreign trademark application pending in Canada for the same mark and have obtained trademark registrations in Europe and Japan for the same mark. We have obtained foreign trademark registrations for the corporate name Orexigen Therapeutics, Inc. in Europe and Japan and have a pending trademark application for the same mark in Canada. The application for CONTRAVE in the United States for use in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss has been allowed for registration, and we expect the registration to issue shortly. An application for the CONTRAVE mark remains pending in the United States in connection with certain printed materials and medical information services. We have received a Notice of Allowance from the PTO for the intent-to-use trademark application for the mark EMPATIC for use in connection with pharmaceutical preparations for the treatment of obesity and inducing weight loss, various printed materials, and medical information services. We have also obtained foreign trademark registrations for the mark CONTRAVE in Europe and Japan and an application for this mark is pending in Canada. Applications for the mark EMPATIC are pending in Europe and Canada, and the mark is registered in Japan. However, no assurance can be given that our allowed trademark applications will actually become registered, or that our registered trademarks can be maintained or enforced. During trademark registration proceedings in the various countries, we have received and expect to receive rejections. Although we are given an opportunity to respond to those rejections, there can be no assurance that the rejections can be successfully overcome. In addition, in the PTO and in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to cancel registered trademarks. For example, another pharmaceutical company opposed the registration of Excalia, the prior mark for the product candidate that we now call Empatic. No assurance can be given that opposition or cancellation proceedings will not be filed against our trademarks, nor can there be any assurance that our trademarks would survive such proceedings.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to Our Finances and Capital Requirements

We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a development stage company with a limited operating history. We have focused primarily on developing our first two product candidates, Contrave and Empatic, with the goal of supporting regulatory approval for these product candidates. We have financed our operations almost exclusively through the sale of our preferred and common stock and debt and have incurred losses in each year since our inception in September 2002. Net losses were $57.8 million in 2007, $27.5 million in 2006, $12.1 million in 2005, $7.7 million in 2004 and $1.9 million in 2003. As of December 31, 2007, we had an accumulated deficit of $106.9 million. These losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our development expenses, as well as clinical product manufacturing expenses, to increase in connection with our ongoing and planned clinical trials for our product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we may incur significant sales, marketing and outsourced manufacturing expenses as well as continued development expenses. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

We have not generated any revenue from our product candidates and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our development-stage product candidates, and we do not know when, or if, we will generate any revenue. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our ongoing and planned clinical trials for Contrave and Empatic;
- obtain regulatory approval for Contrave and Empatic;
- manufacture commercial quantities of our product candidates at acceptable cost levels if regulatory approvals are received; and
- identify and enter into one or more strategic collaborations to effectively market and sell our product candidates.

Even if one or more of our product candidates is approved for commercial sale, which we do not expect to occur for several years (we do not expect to file our first NDA until late 2009 at the earliest), we anticipate incurring significant costs associated with commercializing any approved product. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenues, we will not become profitable and may be unable to continue operations without continued funding.

Our short operating history makes it difficult to evaluate our business and prospects.

We were incorporated in September 2002. Our operations to date have been limited to organizing and staffing our company and conducting product development activities primarily for our first two product candidates, Contrave and Empatic. We have not yet demonstrated an ability to obtain regulatory approval for or commercialize a product candidate. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

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

Developing products for the obesity market, conducting clinical trials, establishing outsourced manufacturing relationships and successfully manufacturing and marketing drugs that we may develop is expensive. We believe that our existing cash and cash equivalents, which includes the net proceeds from our public offering completed in January 2008, will be sufficient to fund the completion of our Phase III clinical trials for Contrave, the initiation and completion of our second Phase IIb clinical trial for Empatic and the initiation of our Phase II proof-of-concept clinical trials for OREX-003 and OREX-004. However, we have based these estimates on assumptions that may prove to be wrong, and we could spend our available financial resources much faster than we currently expect. Further, we will need to raise additional capital to:

- fund our operations and continue to conduct clinical trials to support potential regulatory approval of marketing applications;
- qualify and outsource the commercial-scale manufacturing of our products under cGMPs; and
- commercialize Contrave, Empatic or any other product candidates that we may develop, in-license or acquire, if any of these product candidates receive regulatory approval.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and cost of our clinical trials and other product development programs for Contrave, Empatic and any other product candidates that we may develop, in-license or acquire;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates;

- the costs and timing of completion of outsourced commercial manufacturing supply arrangements for each product candidate;
- the timing of regulatory approval of our product candidates, if at all;
- the costs of establishing sales, marketing and distribution capabilities, should we elect to do so;
- the effect of competing technological and market developments; and
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. We currently have no commitments or agreements relating to any of these types of transactions.

Until we can generate a sufficient amount of product revenue and achieve profitability, we expect to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our two existing product candidates or future development programs;
- addition or termination of clinical trials or funding support;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting our product candidates or those of our competitors;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements; and
- if any of our product candidates receives regulatory approval, the level of underlying demand for our product candidates and wholesalers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted. Debt financing typically contains covenants that restrict operating activities. Our credit and security agreement, as amended, with Merrill Lynch Capital is secured by a pledge of all of our assets other than, subject to certain limited exceptions, intellectual property, and contains a variety of operational covenants, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions, among other restrictions. Any future debt financing we enter into may involve similar or more onerous covenants that restrict our operations. Any borrowings under the credit and security agreement, as amended, with Merrill Lynch Capital or any future debt

financing will need to be repaid, which creates additional financial risk for our company, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations.

If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our current product candidates, potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. If adequate funds are not available, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the development of one or more of our product candidates.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to public company compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or the SEC, and the Nasdaq Stock Market, Inc., have imposed various new requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure. In particular, commencing in this fiscal year 2008, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management and our independent registered public accounting firm to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404. We currently do not have an internal audit function, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources.

Risks Relating to Securities Markets and Investment in Our Stock

The market price of our common stock has fluctuated and is likely to continue to fluctuate, which could reduce the market price of our common stock.

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Since the commencement of trading in connection with our initial public offering, or IPO, through March 14, 2008, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During this approximately eleven-month period, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $10.20 to a high sale price of $19.15. This market volatility is likely to continue and could reduce the market price of

our common stock, regardless of our operating performance. In addition, the trading price of our common stock could change significantly over short periods of time in response to many factors, including:

- the results from our clinical trials, including our current Phase III clinical trials for Contrave and our upcoming Phase II clinical trial for Empatic;
- FDA or international regulatory actions, including failure to receive regulatory approval for any of our product candidates;
- announcements regarding manufacturing or supply developments for Contrave or Empatic;
- failure of any of our product candidates, if approved, to achieve commercial success;
- announcements of the introduction of new products by us or our competitors;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements concerning product development results or intellectual property rights of others;
- litigation or public concern about the safety of our potential products;
- actual and anticipated fluctuations in our quarterly operating results;
- deviations in our operating results from the estimates of securities analysts or other analyst comments;
- additions or departures of key personnel;
- third-party coverage and reimbursement policies;
- developments concerning current or future strategic collaborations; and
- discussion of us or our stock price by the financial and scientific press and in online investor communities.

The realization of any of the risks described in these "Risk Factors" could also have a dramatic and material adverse impact on the market price of our common stock.

Future sales of our common stock may depress our stock price.

Persons who were our stockholders prior to the sale of shares in our IPO continue to hold a substantial number of shares of our common stock that they will be able to sell in the public market in the near future. Significant portions of these shares are held by a small number of stockholders. Sales by our current stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. For example, certain of our executive officers have established selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for the purpose of effecting specified sales of our common stock over a specified period of time. Moreover, the holders of a substantial number of shares of common stock may have rights, subject to certain conditions, to require us to file registration statements to permit the resale of their shares in the public market or to include their shares in registration statements that we may file for ourselves or other stockholders.

We have also registered all common stock that we may issue under our employee benefits plans. As a result, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws. In addition, our directors and executive officers may in the future establish programmed selling plans under Rule 10b5-1 of the Exchange Act for the purpose of effecting sales of our common stock, in addition to the already established plans. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Our executive officers and directors and their affiliates will exercise significant influence over stockholder voting matters in a manner that may not be in the best interests of all of our stockholders.

As of March 14, 2008, our executive officers and directors and their affiliates will together control approximately 36.7% of our outstanding common stock. As a result, these stockholders will collectively be able to significantly influence all matters requiring approval of our stockholders, including the election of directors and

approval of significant corporate transactions. The concentration of ownership may delay, prevent or deter a change in control of our company even when such a change may be in the best interests of some stockholders, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations;
- a requirement of approval of not less than 66⅔% of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors, including to delay or impede a merger, tender offer or proxy contest involving our company. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

We have never paid dividends on our capital stock, and because we do not anticipate paying any cash dividends in the foreseeable future, capital appreciation, if any, of our common stock will be your sole source of gain on an investment in our stock.

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Furthermore, our credit and security agreement, as amended, with Merrill Lynch Capital restricts our ability to pay dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may become involved in securities class action litigation that could divert management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

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

None.

Item 2. ***Properties.***

In December 2007, we entered into a lease agreement covering approximately 22,229 square feet of office space which we intend to use as our corporate headquarters in La Jolla, California. The term of the lease will begin on the day of substantial completion of the tenant improvements, which date is not anticipated to be sooner than April 1, 2008. In addition, we lease approximately 4,369 square feet of space in our current headquarters in San Diego, California under a lease that expires in October 2011. We intend to sublease these premises. We have no laboratory, research or manufacturing facilities. We believe that our current facilities are adequate for our needs for the immediate future and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations on commercially reasonable terms.

Item 3. ***Legal Proceedings.***

In June 2004, we jointly filed a lawsuit with Duke against Elan Corporation, plc, Elan Pharma International Ltd. and Elan Pharmaceuticals, Inc., which we refer to collectively as Elan, Eisai, Inc. and Eisai Co., Ltd., which we refer to together as Eisai, and Julianne E. Jennings, a former employee of Elan, in the U.S. District Court for the Middle District of North Carolina, Durham Division, to resolve a dispute over rights in an invention relating to the use of zonisamide to treat obesity. We alleged in this lawsuit that scientists at Duke made the invention, and that Elan improperly used information supplied by the Duke scientists to file a U.S. patent application on the invention, in which Ms. Jennings (then an Elan product manager) is named as the sole inventor. This patent application was later assigned by Elan to Eisai. Duke also filed a U.S. patent application on the invention at issue, which patent application has been exclusively licensed to us. In December 2006, we, Elan, Eisai, Duke and Ms. Jennings entered into a settlement agreement to settle the lawsuit. Upon execution of the settlement agreement, the lawsuit was dismissed with prejudice.

Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the agreement, released each other from all claims and demands arising under the laws of the United States or any state within the United States existing as of the date of the settlement agreement that arise out of or relate to the lawsuit or the specified Duke and Eisai patents that may issue from certain patent applications claiming the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions. In addition, each of Elan and Ms. Jennings have represented that they are not currently seeking and do not currently possess any patent rights in the United States relating to the use of zonisamide for the treatment of obesity or other weight-related disorders or conditions. In addition, if Elan, Eisai or Ms. Jennings obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Eisai patent application, Elan, Eisai and Ms. Jennings have each agreed that they will not assert such patent against any of our products containing zonisamide in combination with any other active pharmaceutical agent, including bupropion. Likewise, if Duke obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Duke patent application, we and Duke have agreed that we will not assert any such patent against Elan, Eisai or Ms. Jennings for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai.

In September 2007, we and Duke entered into a settlement agreement with Eisai which resolves the foreign aspects of the above dispute. Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the agreement, released each other from all claims and demands arising under the laws of any country outside of the United States existing as of the date of the agreement that arise out of or relate to the lawsuit or certain specified Duke and Eisai foreign patents that may issue from certain patent applications claiming the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions. In addition, if Eisai obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Eisai foreign patent applications, Eisai has agreed that it will not assert any such patent against any

product of ours containing zonisamide in combination with any other active pharmaceutical agent, including bupropion. Likewise, if Duke obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Duke foreign patent applications, we and Duke have agreed that we will not assert any such patent against Eisai for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai.

Although we have resolved the U.S. lawsuit and entered into a settlement agreement containing terms that would prevent Eisai, Elan and Ms. Jennings from asserting specified U.S. patents against our Empatic product, and have entered into a settlement agreement containing terms that would prevent Eisai from asserting specified foreign patents against our Empatic product, there is no assurance that the parties will abide by these settlement agreements. There also is no assurance that Eisai, Elan and/or Ms. Jennings do not have, or will not in the future obtain, other patent rights not covered by the settlement agreements that could be asserted against our Empatic product candidate or our other product candidates. Furthermore, Elan and Ms. Jennings are not parties to the settlement agreement which resolves the foreign aspects of the dispute. In addition, both Duke and Eisai have thus far maintained their pending U.S. patent applications for use of zonisamide to treat obesity or other weight-related disorders, which may lead to initiation of a patent interference to determine which party invented first. We are not relying on any patent Duke may obtain directed to zonisamide as the sole active ingredient to treat obesity or other weight disorder to protect our Empatic product candidate. The U.S. settlement agreement also contains terms that would not allow Eisai, Elan or Ms. Jennings to use any patent they may obtain by winning an interference to prevent the sale of our Empatic product, if approved. However, if Duke loses the interference or abandons its patent application covering the use of zonisamide as the sole active ingredient to treat obesity or other weight disorder, then the potential additional protection for our Empatic product candidate that could result from such a patent will not be available to us.

We believe that there are currently no other claims that would have a material adverse impact on our financial position, operations or potential performance.

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

None.

PART II

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

Market Information

Our common stock has been traded on the Nasdaq Global Market under the symbol "OREX" since April 26, 2007. Prior to that time, there was no public market for our common stock.

The following table sets forth the high and low sales price of our common stock, as reported by the Nasdaq Global Market for the period indicated.

	High	Low
Year Ended December 31, 2007:		
Fourth Quarter	$18.45	$12.83
Third Quarter	17.86	12.83
Second Quarter (beginning April 26, 2007)	19.15	12.50
First Quarter	N/A	N/A

On March 14, 2008, the last reported sale price of our common stock on the Nasdaq Global Market was $10.81. As of March 14, 2008, there were 35 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock and we do not currently intend to pay any cash dividends on our common stock. We expect to retain future earnings, if any, to fund the development and growth of our business. The payment of dividends by us on our common stock is limited by our credit and security agreement, as amended, with Merrill Lynch Capital. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements and contractual restrictions.

Use of Proceeds

Our initial public offering of common stock was effected through a Registration Statement on Form S-1 (File No. 333-139496) which was declared effective by the Securities and Exchange Commission on April 25, 2007. On April 26, 2007, additional shares of our common stock were registered through a Registration Statement filed pursuant to Rule 462(b) (File No. 333-142375). On May 1, 2007, a total of 7,000,000 shares of common stock were sold on our behalf at an initial public offering price of $12.00 per share, for aggregate gross offering proceeds of $84.0 million, managed by Merrill Lynch & Co., JMP Securities, JPMorgan and Leerink Swann & Company. In addition, on May 1, 2007, in connection with the exercise of the underwriters' over-allotment option, 1,050,000 additional shares of common stock were sold on our behalf at the initial public offering price of $12.00 per share, for aggregate gross offering proceeds of $12.6 million.

We paid to the underwriters underwriting discounts totaling approximately $6.8 million in connection with the offering. In addition, we incurred additional costs of approximately $2.0 million in connection with the offering, which when added to the underwriting discounts paid by us, amounts to total costs of approximately $8.8 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and offering expenses, were approximately $87.9 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of December 31, 2007, we had used approximately $2.5 million of the net proceeds from the offering to fund clinical trials for our two product candidates, Contrave™ and Empatic™, and other research and development activities, and we invested the remainder of the proceeds in investment-grade, interest bearing instruments, pending their use to fund ongoing research and development activities. The amount and timing of our expenditures will depend on several factors, including the progress of our clinical trials and commercialization efforts as well as the amount of cash used in our operations.

Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2007.

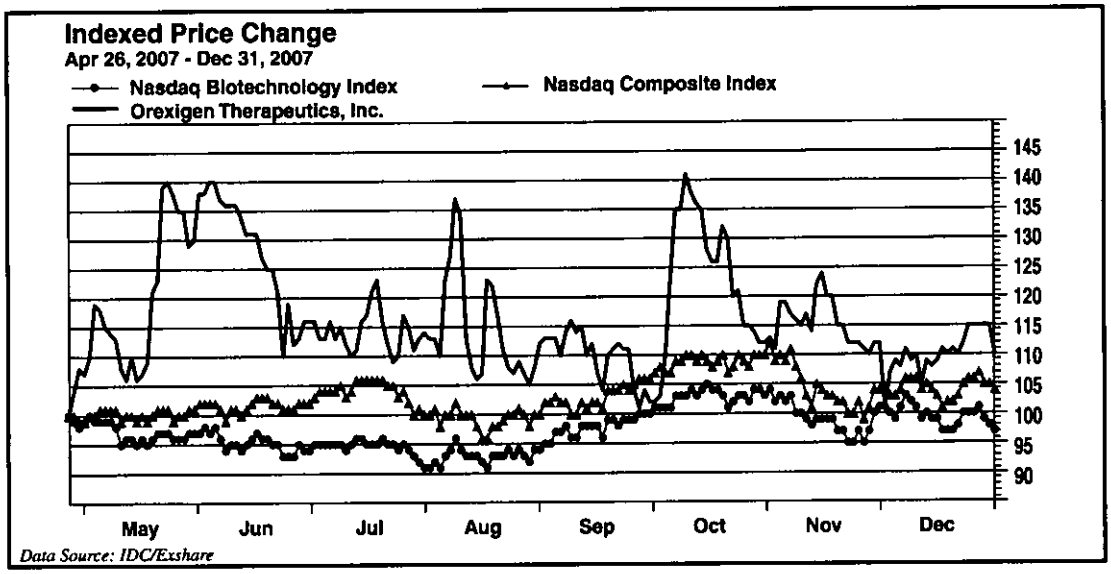
	Shares Issuable Upon Exercise of Outstanding Awards	Weighted Average Exercise Price	Number of Securities Available for Future Issuance
Equity compensation plans approved by security holders:			
2004 Stock Plan	2,279,730	$ 1.48	—
2007 Equity Incentive Award Plan	593,632	$14.63	3,634,608

The 2007 Equity Incentive Award Plan was adopted at the time of our initial public offering which coincided with our discontinuation of granting awards under the 2004 Stock Plan. Stock options under the 2007 Equity Incentive Award Plan have an exercise price equal to the fair market value of the underlying common stock at the date of grant, generally vest over a period of four years, and have a ten-year life. The 2007 Equity Incentive Award Plan contains an "evergreen" provision which allows for annual increases in the number of shares available for future issuance on January 1 of each year during the ten-year term of the plan, beginning on January 1, 2008. The annual increase in the number of shares shall be equal to the lesser of (i) 5% of our outstanding common stock on the applicable January 1, (ii) 2,000,000 shares of common stock, or (iii) a lesser amount determined by our board of directors.

Comparative Stock Performance Graph

The information contained in this Stock Performance Graph section shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to the liabilities of section 18 of the Exchange Act unless we specifically incorporate it by reference into a document filed under the Securities Act or the Exchange Act.

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since April 26, 2007, which is the date our common stock first began trading on the Nasdaq Global Market, to two indices: the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of $100 on April 26, 2007. The comparisons in the graph are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance of our common stock.



	April 26, 2007	December 31, 2007
Orexigen Therapeutics, Inc.	$100	$109.6
Nasdaq Composite Index	$100	$103.8
Nasdaq Biotechnology Index	$100	$ 97.3

Sales of Unregistered Securities

None.

Repurchases of Equity Securities

None.

Item 6. *Selected Financial Data*

The following selected financial data should be read together with our financial statements and related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this annual report.

	Years Ended December 31,					Period From September 12, 2002 (Inception) to December 31, 2007
	2007	2006	2005	2004	2003	
	(In thousands, except per share amounts)					
Statement of Operations Data:						
Revenues:						
Collaborative agreement	$ —	$ —	$ 174	$ —	$ —	$ 174
License revenue	88	88	88	—	—	265
Total revenues	88	88	262	—	—	439
Operating expenses:						
Research and development	50,253	22,586	9,709	6,145	1,164	89,857
General and administrative	10,657	5,870	3,386	1,590	667	22,171
Total operating expenses	60,910	28,456	13,095	7,735	1,831	112,028
Loss from operations	(60,822)	(28,368)	(12,833)	(7,735)	(1,831)	(111,589)
Other income (expense):						
Interest income	3,901	872	744	47	—	5,564
Interest expense	(846)	(8)	—	(5)	(50)	(910)
Total other income (expense)	3,055	864	744	42	(50)	4,654
Net loss	(57,767)	(27,504)	(12,089)	(7,693)	(1,881)	(106,935)
Accretion to redemption value of redeemable convertible preferred stock	(10)	(31)	(24)	(13)	—	(78)
Deemed dividend of beneficial conversion for Series C preferred stock	—	(13,860)	—	—	—	(13,860)
Net loss attributable to common stockholders	$(57,777)	$(41,395)	$(12,113)	$(7,706)	$(1,881)	$(120,873)
Basic and diluted net loss per share(1)	$ (3.08)	$ (18.87)	$ (6.12)	$ (5.01)	$ (2.31)	
Shares used to calculate net loss per share(1)	18,757	2,193	$ 1,980	1,539	814	

(1) See Note 2 of Notes to Financial Statements for an explanation of the method used to calculate the net loss per share and the number of shares used in the computation of the per share amounts.

	As of December 31,				
	2007	2006	2005	2004	2003
	(In thousands)				
Balance Sheet Data:					
Cash and cash equivalents and investment securities, available-for-sale	$ 85,454	$ 34,413	$ 27,647	$ 1,674	$ 19
Working capital (deficit)	74,648	29,644	26,412	1,318	(188)
Total assets	91,320	36,810	28,114	1,750	46
Long-term debt, less current portion	11,072	—	—	—	—
Redeemable convertible preferred stock	—	45,897	45,866	10,928	—
Deficit accumulated during the development stage	(106,935)	(49,168)	(21,664)	(9,576)	(1,882)
Total stockholders' equity (deficit)	64,883	(15,847)	(20,576)	(9,537)	(1,877)

Item 7. *Management's Discussion And Analysis Of Financial Condition And Results Of Operations*

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with "Item 6 — Selected Financial Data" and our financial statements and related notes appearing elsewhere in this annual report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under "Item 1A — Risk Factors" and elsewhere in this annual report.

Overview

Background

We are a biopharmaceutical company focused on the development of pharmaceutical product candidates for the treatment of central nervous system, or CNS, disorders, including obesity. Our lead product candidates targeted for obesity are Contrave, which is in Phase III clinical trials, and Empatic, which is in the later stages of Phase II clinical development. Each of these product candidates is a combination of generic drugs, which we have systematically screened for synergistic CNS activity. We seek to combine chemical entities that, individually, have already received regulatory approval and have been commercialized previously, into new product candidates that we believe address unmet medical needs and are patentable. We are testing these combinations in an effort to demonstrate adequate efficacy and safety for potential regulatory approval. We have not yet received regulatory approval for any product candidate. In addition, we plan to continue to screen drugs for synergistic CNS activity and, based on the results, we may advance other potential combination product candidates into clinical trials.

In addition, we have begun developing two additional product candidates: OREX-003 for the mitigation of weight gain associated with antipsychotic therapy and OREX-004 for the treatment of obsessive-compulsive disorder.

We are a development stage company. We have incurred significant net losses since our inception in September 2002. As of December 31, 2007, we had an accumulated deficit of $106.9 million. These losses have resulted principally from costs incurred in connection with research and development activities, primarily costs of clinical trial activities associated with our current product candidates, and general and administrative expenses. We expect to continue to incur operating losses for the next several years as we pursue the clinical development and market launch of our product candidates and acquire or in-license additional products and technologies, and add the necessary infrastructure to support our growth.

In May 2007, we completed our initial public offering, or IPO, of 7,000,000 shares of common stock at a public offering price of $12.00 per share. Net cash proceeds from the IPO were approximately $76.2 million, after deducting underwriting discounts, commissions and estimated offering expenses payable by us. In connection with the closing of the IPO, all of our shares of convertible preferred stock outstanding at the time of the offering were automatically converted into 16,462,231 shares of common stock. Also in May 2007, the underwriters exercised their overallotment option and purchased an additional 1,050,000 shares of our common stock, from which we received cash proceeds, net of underwriting discounts, of approximately $11.7 million.

In January 2008, we completed a public offering of 7,000,000 shares of common stock at a public offering price of $11.00 per share. Net cash proceeds from the public offering are estimated to be approximately $72.4 million, after deducting underwriting discounts, commissions and estimated offering expenses payable by us. In February 2008, the underwriters exercised a portion of their overallotment option and purchased an additional 326,435 shares of our common stock, from which we received cash proceeds, net of underwriting discounts, of approximately $3.4 million.

Revenues

We have generated approximately $439,000 in revenue from inception through December 31, 2007, resulting from the sublicensing of technology and amounts earned under a collaborative agreement. During 2005, we sublicensed technology to Cypress Bioscience, Inc., or Cypress, for an upfront payment of $1.5 million, and this amount is being recognized ratably over the estimated life of the sublicensed patent. In addition, we recognized

revenue of approximately $174,000 during the year ended December 31, 2005 related to a collaborative agreement with Eli Lilly and Company, or Eli Lilly, the term of which has since expired. We do not expect to generate any significant revenues from licensing, achievement of milestones or product sales unless and until we are able to obtain regulatory approval of, and commercialize, our product candidates either ourselves or with a collaborator. However, we may never generate revenues from our product candidates as we may never succeed in obtaining regulatory approval or commercializing our product candidates.

Research and Development Expenses

The majority of our operating expenses to date have been incurred in research and development activities. Our research and development expenses consist primarily of costs associated with clinical trials managed by our contract research organizations, or CROs, product development efforts and manufacturing costs. License fees, salaries and related employee benefits for certain personnel, and costs associated with certain non-clinical activities such as regulatory expenses, are also included in this amount. Our most significant costs to date are expenses incurred in connection with the clinical trials for Contrave and Empatic. The clinical trial expenses include payments to vendors such as CROs, investigators, suppliers of clinical drug materials and related consultants. We charge all research and development expenses to operations as incurred because the underlying technology associated with these expenditures relates to our research and development efforts and has no alternative future uses.

At any time, we have several ongoing research projects. Our internal research and development resources are not directly tied to any individual research project and are primarily deployed across our Contrave and Empatic programs, both of which target the obesity market. We are developing our two obesity product candidates in parallel and, due to the fact that we use shared resources across projects, we do not maintain information regarding our internal costs incurred for our research and development programs on a program-specific basis. We use external service providers to manage our clinical trials, to manufacture the product supplies used in these trials and for formulations development, consulting and other activities. Prior to 2007, our external service providers did not generally bill us on a program-specific basis.

The following table summarizes our research and development expenses for the year ended December 31, 2007. Costs that are not attributable to a specific research program are included in the "Other" category (in thousands):

Costs of external service providers:	
Obesity	$44,514
Non-Obesity	554
Other	737
Subtotal	45,805
Internal costs	2,734
Stock-based compensation	1,714
Total research and development costs	$50,253

At this time, due to the risks inherent in the clinical trial process and given the early stage of our product development programs, we are unable to estimate with any certainty the costs we will incur in the continued development of our product candidates for potential commercialization. Clinical development timelines, the probability of success and development costs can differ materially from expectations. While we are currently focused on advancing each of our product development programs, our future research and development expenses will depend on the clinical success of each product candidate, as well as ongoing assessments as to each product candidate's commercial potential. In addition, we cannot forecast with any degree of certainty which product candidates will be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

We expect our development expenses to grow over the next few years as we continue the advancement of our product development programs. We initiated our Phase IIb clinical trial for Contrave in July 2005 and our Phase IIb

clinical trial for Empatic in July 2006. In the second quarter of 2007, we initiated our first two Phase III clinical trials for Contrave and in the fourth quarter of 2007, we initiated our last two Phase III clinical trials for Contrave. The lengthy process of completing our clinical trials and seeking regulatory approval for our product candidates requires the expenditure of substantial resources. Any failure by us or delay in completing our clinical trials, or in obtaining regulatory approvals, could cause a delay in the commencement of product revenues and cause our research and development expenses to increase and, in turn, have a material adverse effect on our results of operations. We do not expect any of our current product candidates to be commercially available in major markets before 2010, if at all.

General and Administrative

Our general and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, accounting and internal support functions. In addition, general and administrative expenses include professional fees for legal, consulting and accounting services. We anticipate increases in general and administrative expenses as we add personnel, comply with the reporting obligations applicable to publicly-held companies, and continue to build our corporate infrastructure in support of our continued development and preparation for the potential commercialization of our product candidates.

Other Income (Expense)

Other income consists of interest earned on our cash, cash equivalents and investment securities. Interest expense consists of interest incurred in connection with the $25.0 million credit and security agreement, as amended, with Merrill Lynch Capital.

Income Taxes

As of December 31, 2007, we had federal and state net operating loss carryforwards of approximately $91.0 million and $92.4 million, respectively. If not utilized, the net operating loss carryforwards will begin expiring in 2022 for federal purposes and 2012 for state purposes. As of December 31, 2007, we had federal and state research and development tax credit carryforwards of approximately $5.3 million and $4.1 million, respectively. The federal tax credits will begin expiring in 2023 unless previously utilized and the state tax credits carry forward indefinitely. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset taxable income. An analysis was performed which indicated that multiple ownership changes have occurred in previous years which created annual limitations on the Company's ability to utilize its net operating loss and tax credit carryovers. Such limitations will result in approximately $900,000 of tax benefits related to net operating loss and tax credit carryforwards that will expire unused. Accordingly, the related net operating loss and research and development tax credit carryforwards have been removed from deferred tax assets accompanied by a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, limitations created by future ownership changes, if any, will not impact our effective tax rate.

Beneficial Conversion Feature

During November 2006, we completed the sale of 8,771,930 shares of Series C convertible preferred stock for net proceeds of approximately $29.9 million. The Series C convertible preferred stock was sold at a price per share below the anticipated IPO price. Accordingly, pursuant to EITF Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, we recorded a deemed dividend on the Series C convertible preferred stock of $13,859,649, which is equal to the number of shares of Series C convertible preferred stock sold multiplied by the difference between the estimated fair value of the underlying common stock and the Series C conversion price per share.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in conformity with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that

affect the reported amounts of assets, liabilities, expenses and related disclosures. Actual results could differ from those estimates.

We believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Expenses

A substantial portion of our ongoing research and development activities are performed under agreements we enter into with external service providers, including CROs, which conduct many of our research and development activities. We accrue for costs incurred under these contracts based on factors such as estimates of work performed, patient enrollment, progress of patient studies and other events. However, the level of estimates can be significant. To date, we have not made any material adjustments to our estimates of clinical trial expenses. We make good faith estimates that we believe to be accurate, but the actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

Stock-Based Compensation

Effective January 1, 2006, we adopted Statement of Financial Accounting Standards, or SFAS, No. 123(R), *Share-Based Payment*, which is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation*, and supersedes Accounting Principles Board, or APB, Opinion No. 25, *Accounting for Stock Issued to Employees*, using the prospective transition method. SFAS No. 123(R) requires that share-based payment transactions with employees be recognized in the financial statements based on their fair value and recognized as compensation expense over the vesting period. We calculate the fair value of stock option grants using the Black-Scholes option-pricing model.

The adoption of SFAS 123(R) for the year ended December 31, 2006 resulted in the recognition of additional stock-based compensation expense of $834,500. Of this amount, $372,000 is included in research and development expense and $462,500 is included in general and administrative expense for the year ended December 31, 2006.

At December 31, 2006, total unrecognized share-based compensation costs related to non-vested option awards was $11.0 million, of which $8.4 million arose from the adoption of SFAS No. 123(R). This $8.4 million is expected to be recognized over a weighted average period of approximately 3.6 years. The remaining $2.6 million relates to stock awards granted prior to the adoption of SFAS No. 123(R) and is expected to be recognized over a weighted average period of 2.2 years.

Prior to January 1, 2006, we applied the intrinsic-value-based method of accounting prescribed by APB Opinion No. 25 and related interpretations. Under this method, if the exercise price of the award equaled or exceeded the fair value of the underlying stock on the measurement date, no compensation expense was recognized. The measurement date was the date on which the final number of shares and exercise price were known and was generally the grant date for awards to employees and directors. If the exercise price of the award was below the fair value of the underlying stock on the measurement date, then compensation cost was recorded, using the intrinsic-value method, and was generally recognized in the statements of operations over the vesting period of the award.

During the period from April 1, 2005 to December 31, 2005, we granted options to employees to purchase a total of 1,113,396 shares of common stock at an exercise price of $0.60 per share. During the year ended December 31, 2006, we granted options to employees to purchase a total of 1,235,444 shares of common stock at exercise prices ranging from $0.70 to $6.00 per share. These fair market values of our common stock were established by our board of directors. We did not use a contemporaneous valuation from an unrelated valuation specialist because, at the time these stock options were issued, we believed our estimates of the fair value of the common stock to be reasonable and consistent with our understanding of how similarly situated companies in our industry were valued. In connection with our IPO, we reassessed the fair values of our common stock and the reassessed fair value of our common stock starting April 2005 was $4.24 per share. The reassessed fair value of our common stock was increased from $4.24 per share in April 2005 to $10.00 per share in September 2006.

We granted options in May 2005 at $0.60 per share, in May 2006 at $0.70 per share, in September 2006 at $2.00 per share and in November 2006 at $6.00 per share. Based upon the reassessment discussed above, we determined that the reassessed fair value of the options to purchase 1,113,396 shares of common stock granted to employees during

May 2005 was $6.00 per share and the 262,944 options granted in May 2006 and 972,500 options granted to employees in September and November 2006 were at $7.00 and $10.00 per share, respectively. In February 2007, based on additional clinical information, we increased the grant price for options granted in February 2007 to $10.72.

Since the closing of our IPO in May 2007, the exercise price for all option grants have been consistent with the corresponding closing price of our common stock on the Nasdaq Global Market on the date of grant, as required by the terms of our 2007 equity incentive award plan.

Equity instruments issued to non-employees are recorded at their fair value as determined in accordance with SFAS No. 123(R) and Emerging Issues Task Force 96-18, *Accounting for Equity Instruments That are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods and Services*, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

Income Taxes

In July 2006, the Financial Accounting Standards Board, or FASB, issued Financial Interpretation No. 48, or FIN 48, *Accounting for Uncertainty in Income Taxes — An Interpretation of FASB Statement No. 109*. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an entity's financial statements in accordance with SFAS 109, *Accounting for Income Taxes,* and prescribes a recognition threshold and measurement attributes for financial statement disclosure of tax positions taken or expected to be taken on a tax return. Under FIN 48, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. Additionally, FIN 48 provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006 and was adopted by us on January 1, 2007. The adoption of FIN 48 did not impact our financial condition, results of operations or cash flows. We do not anticipate that the adoption of FIN 48 will have a material effect on our effective tax rate in future periods.

Results of Operations

Comparison of year ended December 31, 2007 to year ended December 31, 2006

Revenues. Revenues for the years ended December 31, 2007 and 2006 were $88,000 and $88,000, respectively, and were related to our sublicensed technology to Cypress.

Research and Development Expenses. Research and development expenses increased to $50.3 million for the year ended December 31, 2007 from $22.6 million for the comparable period during 2006. This increase of $27.7 million was due primarily to increased expenses in connection with our Contrave Phase III clinical trials, related proprietary product formulation work and consulting activities totaling approximately $24.3 million. The remaining increase is primarily the result of increases in salaries and personnel related costs totaling approximately $1.6 million and stock-based compensation costs totaling approximately $1.1 million.

General and Administrative Expenses. General and administrative expenses increased to $10.7 million for the year ended December 31, 2007 from $5.9 million for the comparable period during 2006. This increase of $4.8 million was principally due to increases in salaries and personnel related costs totaling approximately $1.4 million, increases in stock-based compensation costs totaling approximately $1.1 million, increases in other professional fees totaling approximately $725,000 and increases in legal fees totaling approximately $462,000.

Interest and Other Income. Interest income increased to $3.9 million for the year ended December 31, 2007 from $872,000 for the comparable period during 2006. This increase of $3.0 million was due to the increase in average cash and investment balances as a result of our IPO in May 2007 and our Series C preferred stock financing in November 2006.

Interest Expense. Interest expense increased to $846,000 for the year ended December 31, 2007 primarily due to the amortization of debt issuance costs incurred in connection with the $25.0 million credit and security agreement, as amended, with Merrill Lynch Capital and interest expense on the $10.0 million and $8.0 million borrowed under the credit and security agreement in March 2007 and December 2007, respectively.

Comparison of year ended December 31, 2006 to year ended December 31, 2005

Revenues. Revenues for the year ended December 31, 2006 were $88,000 and were related to our sublicensed technology to Cypress. Revenues decreased $174,000 as a result of the completion of the collaborative agreement with Eli Lilly as of December 31, 2005. Cypress accounted for 34% and 100% of our revenue for the year ended December 31, 2005 and the year ended December 31, 2006, respectively. Eli Lilly accounted for 66% of our revenue for the year ended December 31, 2005.

Research and Development Expenses. Research and development expenses increased to $22.6 million for the year ended December 31, 2006 from $9.7 million for the comparable period during 2005. This increase of $12.9 million was due primarily to increased expenses in connection with clinical trials and consulting expenses totaling approximately $12.5 million. The remaining increase is the result of increases in salaries and personnel related costs and stock-based compensation costs totaling approximately $1.1 million, offset by a decrease in licensing fees of approximately $560,000.

General and Administrative Expenses. General and administrative expenses increased to $5.9 million for the year ended December 31, 2006 from $3.4 million for the comparable period during 2005. This increase of $2.5 million was primarily due to an increase in stock-based compensation costs of $751,000, and an increase in legal fees, salaries and personnel related costs, other professional fees, travel, and consulting fees totaling $1.3 million.

Interest and Other Income. Interest income increased to $872,000 for the year ended December 2006 from $744,000 for the year ended December 31, 2005. This increase of $128,000 was due to the increase in average cash and investment balances as a result of investing the proceeds received from the sale of Series B preferred stock in May 2005 and higher interest rates in 2006.

Interest Expense. Interest expense increased to $8,000 for the year ended December 31, 2006 primarily due to the amortization of debt issuance costs incurred in connection with the $25.0 million credit and security agreement, as amended, with Merrill Lynch Capital.

Comparison of year ended December 31, 2005 to year ended December 31, 2004

Revenues. Revenues for the year ended December 31, 2005 consisted of $88,000 resulting from a sublicensing of technology and $174,000 from amounts earned under a collaborative agreement. We received no revenues in prior years. During 2005, we sublicensed technology to Cypress for an upfront payment of $1.5 million and this amount is being recognized ratably over the estimated life of the patent. In addition, we recognized revenue of approximately $174,000 during the year ended December 31, 2005 related to a collaborative agreement with Eli Lilly. Cypress accounted for 34% and Eli Lilly accounted for 66% of our revenue for the year ended December 31, 2005.

Research and Development Expenses. Research and development expenses increased to $9.7 million for the year ended December 31, 2005 from $6.1 million for the year ended December 31, 2004. This increase of $3.6 million was due primarily to increased expenses in connection with clinical trials and consulting expenses totaling approximately $2.9 million. In addition, salaries and related personnel costs increased by approximately $229,000 and stock-based compensation costs increased by approximately $214,000.

General and Administrative Expenses. General and administrative expenses increased to $3.4 million for the year ended December 31, 2005 from $1.6 million for year ended December 31, 2004. This increase of $1.8 million was primarily due to an increase of approximately $900,000 related to stock-based compensation charges and $600,000 for salaries and related personnel costs as we expanded our general and administrative functions to support our operations.

Interest and Other Income. Interest income increased to $744,000 for the year ended December 31, 2005 from $47,000 for the year ended December 31, 2004. This increase of $697,000 was due to the increase in average cash and investment balances as a result investing the proceeds received from the sale of Series B Preferred stock in May 2005.

Liquidity and Capital Resources

Since inception, our operations have been financed primarily through the sale of equity securities. Through December 31, 2007, we received net proceeds of approximately $163.7 million from the sale of shares of our preferred and common stock as follows:

- from September 12, 2002 to December 31, 2006, we issued and sold a total of 1,053,572 shares of common stock for aggregate net proceeds of $14,801;
- in March 2004, we issued and sold a total of 9,322,035 shares of Series A redeemable convertible preferred stock for aggregate net proceeds of $9.2 million and the conversion of promissory notes and interest thereon totaling $1.7 million;
- from April 2005 to May 2005, we issued and sold 14,830,509 shares of Series B redeemable convertible preferred stock for aggregate net proceeds of $34.9 million;
- in November 2006, we issued and sold a total of 8,771,930 shares of Series C convertible preferred stock for aggregate net proceeds of $29.9 million; and
- in May 2007, we issued and sold a total of 8,050,000 shares of common stock for aggregate net proceeds of $87.9 million.

As of December 31, 2007, we had $29.0 million in cash and cash equivalents and an additional $56.5 million in investment securities, available-for-sale. In addition, in January and February of 2008, we raised additional cash totaling approximately $75.8 million from the sale of shares of our common stock in a public offering. We have invested a substantial portion of our available cash in money market funds placed with reputable financial institutions for which credit loss is not anticipated and in corporate debt obligations. In addition, we have established guidelines relating to diversification and maturities of our investments to preserve principal and maintain liquidity.

Net cash used in operating activities was $54.4 million and $21.8 million for the years ended December 31, 2007 and 2006, respectively. Net cash used in each of these periods was primarily a result of external research and development expenses, clinical trial costs, personnel-related costs, third-party supplier expenses and professional fees.

Net cash used by investing activities was $40.3 million for the year ended December 31, 2007 compared to net cash provided by investing activities of $3.4 million for the year ended December 31, 2006. These amounts are primarily the result of the net purchases, sales and maturities of investment securities.

Net cash provided by financing activities was $104.2 million for the year ended December 31, 2007 as a result of the sale of common stock in our IPO in May 2007 for aggregate net proceeds of $88.0 million and $10.0 and $8.0 million draws against the credit and security agreement, as amended, with Merrill Lynch Capital in March 2007 and December 2007, respectively.

We cannot be certain if, when or to what extent we will receive cash inflows from the commercialization of our product candidates. We expect our development expenses to be substantial and to increase over the next few years as we continue the advancement of our product development programs.

As a biopharmaceutical company focused on in-licensing and developing proprietary pharmaceutical product candidates, we have entered into license agreements to acquire the rights to develop and commercialize our Contrave and Empatic product candidates. Pursuant to these agreements, we obtained exclusive licenses to the patent rights and know-how for selected indications and territories. Under our license agreement with Duke University, we issued 442,624 shares of our common stock in March 2004 and may be required to make future milestone payments totaling up to $1.7 million upon the achievement of various milestones related to regulatory or commercial events. Under our license agreement with Lee Dante, M.D., we issued an option to purchase 73,448 shares of our common stock in April 2004 at an exercise price of $0.10 per share, which expires in April 2014. In April 2006, Dr. Dante exercised options with respect to 35,000 of these shares. We also paid Dr. Dante an upfront fee of $100,000 and may be required to make future milestone payments totaling up to $1.0 million upon the achievement of a milestone related to a regulatory event. Under our license agreement with Oregon Health &

Science University, we issued 76,315 shares of our common stock in December 2003 and paid an upfront fee of $65,000. Under these three agreements, we are also obligated to pay royalties on any net sales of the licensed products.

Our future capital uses and requirements depend on numerous factors. These factors include but are not limited to the following:

- the progress of our clinical trials, including expenses to support the trials and milestone payments that may become payable;
- our ability to establish and maintain strategic collaborations, including licensing and other arrangements;
- the costs involved in enforcing or defending patent claims or other intellectual property rights;
- the costs and timing of regulatory approvals;
- the costs of establishing sales or distribution capabilities;
- the successful commercialization of our products; and
- the extent to which we in-license, acquire or invest in other indications, products, technologies and businesses.

In December 2006, we entered into a credit and security agreement with Merrill Lynch Capital providing for potential borrowing until June 30, 2007 of up to $17.0 million. In July 2007, we entered into a first amendment to the credit and security agreement with Merrill Lynch Capital. The first amendment provides for, among other things, the extension of the period during which Merrill Lynch Capital is obligated to make advances under the credit and security agreement to us from June 30, 2007 to December 31, 2007. In November 2007, we entered into a second amendment to the credit and security agreement with Merrill Lynch Capital. The second amendment provides for, among other things, the increase of the total amount available for advances under the credit and security agreement from $17.0 million to $25.0 million, our obligation to request an advance of $8.0 million on or before December 31, 2007, and the extension of the period during which Merrill Lynch Capital is obligated to make advances to us under the credit and security agreement from December 31, 2007 to December 31, 2008.

In March 2007, we drew down $10.0 million under the credit and security agreement, and in December 2007, we drew down $8.0 million. Under the credit and security agreement, we are required to make monthly payments of principal and interest and all amounts then outstanding will become due and payable upon the earlier to occur of July 1, 2011 or three years from the funding of any amounts under the agreement. Interest accrues on amounts outstanding under the agreement at a base rate set forth in the agreement plus an applicable margin, which ranges from 3.75% to 4.25% based on the date of borrowing. Amounts outstanding under the credit and security agreement at December 31, 2007 bear interest at an average rate of 9.2%. The loan is collateralized by substantially all of our assets other than, subject to certain limited exceptions, intellectual property. Subject to certain limited exceptions, amounts prepaid under the credit and security agreement are subject to a prepayment fee equal to 3% of the amount prepaid. In addition, upon repayment of the amounts borrowed for any reason, we will be required to pay an exit fee equal to the greater of $900,000 or 5% of the total amounts borrowed under the credit facility. Under the terms of the agreement, we are subject to operational covenants, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make specified investments and engage in merger, consolidation or asset sale transactions, among other restrictions.

We believe that our existing cash and cash equivalents, along with the borrowing capacity under our credit and security agreement, as amended, with Merrill Lynch Capital, will be sufficient to meet our projected operating requirements through at least the next 12 months.

Until we can generate significant cash from our operations, we expect to continue to fund our operations with existing cash resources, proceeds of potential offerings of our equity securities, potential borrowings and potential corporate collaborations. In addition, we may finance future cash needs through the sale of additional equity securities, strategic collaboration agreements and other debt financing. In addition, we cannot be sure that our existing cash and investment resources will be adequate, that additional financing will be available when needed or that, if available, financing will be obtained on terms favorable to us or our stockholders. Having insufficient funds

may require us to delay, scale back or eliminate some or all of our development programs, relinquish some or even all rights to product candidates or renegotiate less favorable terms than we would otherwise choose. Failure to obtain adequate financing also may adversely affect our ability to operate as a going concern. If we raise additional funds by issuing equity securities, substantial dilution to existing stockholders would likely result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial requirements that may restrict our ability to operate our business.

Contractual Obligations and Commitments

The following table describes our long-term contractual obligations and commitments as of December 31, 2007 (in thousands):

	Payments Due by Periods				
	Total	Less Than 1 Year	1-3 Years	4-5 Years	After
Long-term debt obligations(1)	$15,807	$4,735	$10,072	$1,000	$ —
Long-term liabilities(2)	941	—	920	21	—
Operating lease obligations	6,476	572	2,640	2,544	720
License obligations(3)	—	—	—	—	—
Total	$23,224	$5,307	$13,632	$3,565	$720

(1) In December 2006, we entered into a credit and security agreement with Merrill Lynch Capital providing for the potential borrowing of up to $17.0 million. In November 2007, the amount available for borrowing under the credit and security agreement was increased to $25.0 million. In March and December 2007, we drew down $10.0 million and $8.0 million, respectively, under the credit and security agreement.

(2) Primarily represents fees due to the lender incurred in connection with our credit and security agreement with Merrill Lynch Capital due on the earlier of the repayment of total amounts borrowed or termination of the agreement.

(3) License obligations do not include additional payments of up to $2.7 million due upon the occurrence of certain milestones related to regulatory or commercial events or potential payments of up to $5.7 million to Duke University should we receive milestone payments from Cypress under our agreement with Cypress (up to $3.7 million excluding milestone payments unrelated to sleep apnea). We may also be required to pay royalties on any net sales of the licensed products. License payments may be increased based on the timing of various milestones and the extent to which the licensed technologies are pursued for other indications. These milestone payments and royalty payments under our license agreements are not included in the table above because we cannot, at this time, determine when or if the related milestones will be achieved or the events triggering the commencement of payment obligations will occur.

We also enter into agreements with third parties to manufacture our product candidates, conduct our clinical trials and perform data collection and analysis. Our payment obligations under these agreements depend upon the progress of our development programs. Therefore, we are unable at this time to estimate with certainty the future costs we will incur under these agreements.

Recent Accounting Pronouncements

In July 2006, the Financial Accounting Standards Board, or FASB, issued FASB Interpretation No. 48, *Accounting for the Uncertainty in Income Taxes — an Interpretation of FASB Statement No. 109*, or FIN 48, which clarifies the accounting uncertainty in tax positions. This interpretation requires that we recognize in our consolidated financial statements the impact of a tax position if that position is more likely than not to be sustained on audit, based on the technical merits of the position. The provisions of FIN 48 are effective as of the beginning of 2007. The adoption of FIN 48 did not affect our financial position, results of operations or cash flows.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*, or SFAS 157. This statement defines fair value as used in numerous accounting pronouncements, establishes a framework for measuring fair

value in accounting principles generally accepted in the United States, or GAAP, and expands disclosure related to the use of fair value measures in financial statements. SFAS 157 does not expand the use of fair value measures in financial statements, but standardizes its definition and guidance in GAAP. The standard emphasizes that fair value is a market-based measurement and not an entity-specific measurement based on an exchange transaction in which the entity sells an asset or transfers a liability (exit price). SFAS 157 establishes a fair value hierarchy from observable market data at the highest level, to fair value based on an entity's own fair value assumptions, at the lowest level. SFAS 157 will be effective for us beginning in 2008. We are currently evaluating the impact, if any, that the adoption of SFAS 157 will have on our financial position, results of operations and our cash flows.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities — including an Amendment of FASB Statement No. 115*, or SFAS 159, which permits, but does not require, entities to measure certain financial instruments and other assets and liabilities at fair value on an instrument-by-instrument basis. Unrealized gains and losses on items for which the fair value option has been elected should be recognized in earnings at each subsequent reporting date. SFAS 159 is effective for us as of January 1, 2008 and cannot be adopted early unless SFAS 157 is also adopted. We are currently evaluating the impact, if any, the adoption of SFAS 159 may have on our financial position, results of operations and our cash flows.

In June 2007, the FASB issued EITF 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities*, or EITF 07-3. The scope of this issue is limited to nonrefundable advance payments for goods and services related to research and development activities. EITF 07-3 addresses whether such advanced payments should be expensed as incurred or capitalized. We are required to adopt EITF 07-3 effective January 1, 2008. We do not expect the adoption of EITF 07-3 to have a material impact on our results of operations or financial position.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet activities.

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

Our cash and cash equivalents as of December 31, 2007 consisted primarily of money market funds and corporate debt obligations. We do not have any auction rate securities on our balance sheet, as they are not permitted by our investment policy. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term marketable debt securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of our investment will probably decline. To minimize this risk, we intend to continue to maintain our portfolio of cash equivalents and short-term investments in a variety of securities including commercial paper, money market funds and government and non-government debt securities, all with various maturities. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate.

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

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited the accompanying balance sheets of Orexigen Therapeutics, Inc. (a development stage company) as of December 31, 2007 and 2006 and the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years ended December 31, 2007, 2006 and 2005 and for the period from September 12, 2002 (inception) to December 31, 2007. 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Orexigen Therapeutics, Inc. (a development stage company) at December 31, 2007 and 2006 and the results of its operations and its cash flows for the years ended December 31, 2007, 2006 and 2005 and for the period from September 12, 2002 (inception) to December 31, 2007, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the financial statements, Orexigen Therapeutics, Inc. changed its method of accounting for share-based payments as required by Statement of Financial Accounting Standards No. 123 (revised in 2004), *Share-Based Payment*, on January 1, 2006.

/s/ Ernst & Young LLP

San Diego, California
March 24, 2008

OREXIGEN THERAPEUTICS, INC.
(a development stage company)

BALANCE SHEETS
(In thousands, except share and par value amounts)

	December 31, 2007	December 31, 2006
ASSETS		
Current assets:		
Cash and cash equivalents	$ 28,967	$ 19,425
Investment securities, available-for-sale	56,487	14,988
Prepaid expenses and other current assets	2,471	222
Total current assets	87,925	34,635
Property and equipment, net	924	528
Restricted cash	1,125	155
Other assets	1,346	1,492
Total assets	$ 91,320	$ 36,810
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 4,114	$ 1,699
Accrued expenses	4,340	3,204
Deferred revenue, current portion	88	88
Long-term debt, current portion	4,735	—
Total current liabilities	13,277	4,991
Deferred revenue, less current portion	1,147	1,235
Long-term debt, less current portion	11,072	—
Other long-term liabilities	941	534
Commitments and contingencies		
Series A and B redeemable convertible preferred stock, $.001 par value, no shares authorized, issued and outstanding at December 31, 2007 and 24,152,544 shares authorized, issued and outstanding at December 31, 2006; aggregate liquidation preference of $46,000 at December 31, 2006	—	45,897
Stockholders' equity (deficit):		
Preferred stock,$.001 par value, 10,000,000 shares authorized at December 31, 2007 and no shares authorized at December 31, 2006; no shares issued and outstanding at December 31, 2007	—	—
Series C convertible stock, $.001 par value, no shares authorized, issued or outstanding at December 31, 2007 and 8,771,930 shares authorized, issued and outstanding at December 31, 2006; aggregate liquidation preference of $30,000 at December 31, 2006	—	9
Common stock, $.001 par value, 100,000,000 shares authorized at December 31, 2007 and 50,000,000 shares authorized at December 31, 2006; 26,982,601 and 2,398,039 shares issued and outstanding at December 31, 2007 and 2006, respectively	27	2
Additional paid-in capital	171,571	33,299
Accumulated other comprehensive income	220	11
Deficit accumulated during the development stage	(106,935)	(49,168)
Total stockholders' equity (deficit)	64,883	(15,847)
Total liabilities and stockholders' equity (deficit)	$ 91,320	$ 36,810

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.
(a development stage company)

STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

	Years Ended December 31,			Period from September 12, 2002 (Inception) to December 31, 2007
	2007	2006	2005	
Revenues:				
Collaborative agreement	$ —	$ —	$ 174	$ 174
License revenue	88	88	88	265
Total revenues	88	88	262	439
Operating expenses:				
Research and development	50,253	22,586	9,709	89,857
General and administrative	10,657	5,870	3,386	22,171
Total operating expenses	60,910	28,456	13,095	112,028
Loss from operations	(60,822)	(28,368)	(12,833)	(111,589)
Other income (expense):				
Interest income	3,901	872	744	5,564
Interest expense	(846)	(8)	—	(910)
Total other income (expense)	3,055	864	744	4,654
Net loss	(57,767)	(27,504)	(12,089)	(106,935)
Accretion to redemption value of redeemable convertible preferred stock	(10)	(31)	(24)	(78)
Deemed dividend of beneficial conversion for Series C preferred stock	—	(13,860)	—	(13,860)
Net loss attributable to common stockholders	$(57,777)	$(41,395)	$(12,113)	$(120,873)
Net loss per share attributable to common stockholders — basic and diluted(1)	$ (3.08)	$ (18.87)	$ (6.12)	
Shares used to compute basic and diluted net loss per share attributable to common stockholders(1)	18,757	2,193	1,980	

(1) As a result of the issuance of 8,050,000 shares of common stock in the Company's initial public offering in May 2007 and the conversion of the Company's preferred stock into 16,462,231 shares of common stock upon completion of the Company's initial public offering, there is a lack of comparability in the basic and diluted net loss per share amounts for the periods presented. See Note 2 for further discussion.

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.
(a development stage company)

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
PERIOD FROM SEPTEMBER 12, 2002 (INCEPTION) TO DECEMBER 31, 2007
(In thousands, except per share amounts)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Series C Convertible Preferred Stock		Additional Paid-In Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at September 12, 2002 (inception)	—	$ —	—	$ —	—	$—	—	$—	$ —	$ —	$—	$ —	$ —
Issuance of common stock to founder at $0.002 per share in exchange for services in September	—	—	—	—	650	1	—	—	—	—	—	—	1
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(1)	(1)
Balance at December 31, 2002	—	—	—	—	650	1	—	—	—	—	—	(1)	—
Issuance of common stock at $0.002 per share for cash in June, November and December	—	—	—	—	949	1	—	—	1	—	—	—	2
Issuance of common stock at $0.002 per share in exchange for services in December	—	—	—	—	443	—	—	—	1	—	—	—	1
Issuance of common stock at $0.002 per share in exchange for technology in December	—	—	—	—	76	—	—	—	—	—	—	—	—
Issuance of common stock options to consultant in exchange for services	—	—	—	—	—	—	—	—	1	—	—	—	1
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(1,881)	(1,881)
Balance at December 31, 2003	—	—	—	—	2,118	2	—	—	3	—	—	(1,882)	(1,877)
Issuance of Series A redeemable convertible preferred stock at $1.18 per share for cash in January, net of issuance costs	7,864	9,194	—	—	—	—	—	—	—	—	—	—	—
Issuance of Series A redeemable convertible preferred stock for conversion of notes payable and accrued interest in January	1,458	1,721	—	—	—	—	—	—	—	—	—	—	—
Issuance of common stock at $0.002 per share in exchange for technology in March	—	—	—	—	443	—	—	—	44	—	—	—	44
Issuance of common stock options to consultants in exchange for services in March	—	—	—	—	—	—	—	—	2	—	—	—	2
Accretion of redeemable convertible preferred stock to redemption value	—	13	—	—	—	—	—	—	(13)	—	—	—	(13)
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(7,693)	(7,693)
Balance at December 31, 2004	9,322	10,928	—	—	2,561	2	—	—	36	—	—	(9,575)	(9,537)
Deferred employee stock based compensation related to issuance of stock options to employees	—	—	—	—	—	—	—	—	5,029	(5,029)	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	—	1,113	—	—	1,113
Stock-based compensation for common stock issued to consultants in exchange for services	—	—	—	—	—	—	—	—	2	—	—	—	2
Repurchase of common stock at $0.002 per share for cash in January	—	—	—	—	(267)	—	—	—	—	—	—	—	—
Exercise of common stock options at $0.10 per share for cash	—	—	—	—	59	—	—	—	6	—	—	—	6
Issuance of Series B redeemable convertible preferred stock for cash at $2.36 per share in April and May, net of issuance costs	—	—	14,831	34,915	—	—	—	—	—	—	—	—	—

OREXIGEN THERAPEUTICS, INC.
(a development stage company)

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)— (Continued)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Series C Convertible Preferred Stock		Additional Paid-In Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount					
Accretion of redeemable convertible preferred stock to redemption value	—	13	—	10	—	—	—	—	(24)	—	—	—	(24)
Comprehensive loss:													
Unrealized loss on securities, available-for-sale	—	—	—	—	—	—	—	—	—	—	(47)	—	(47)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(12,089)	(12,089)
Total comprehensive loss													(12,136)
Balance at December 31, 2005	9,322	10,941	14,831	34,925	2,353	2	—	—	5,049	(3,916)	(47)	(21,664)	(20,576)
Reversal of deferred compensation upon adoption of FAS 123(R)	—	—	—	—	—	—	—	—	(3,916)	3,916	—	—	—
Exercise of common stock options at $0.10 and $0.60 per share for cash	—	—	—	—	45	—	—	—	7	—	—	—	7
Stock-based compensation expense	—	—	—	—	—	—	—	—	2,258	—	—	—	2,258
Accretion of redeemable convertible preferred stock to redemption value	—	14	—	17	—	—	—	—	(31)	—	—	—	(31)
Issuance of Series C convertible preferred stock for cash at $3.42 per share in November, net of issuance costs	—	—	—	—	—	—	8,772	9	29,932	—	—	—	29,941
Beneficial conversion feature — deemed dividend on issuance of Series C convertible preferred stock	—	—	—	—	—	—	—	—	13,860	—	—	—	13,860
Beneficial conversion feature — deemed dividend of beneficial conversion feature for Series C convertible preferred stock	—	—	—	—	—	—	—	—	(13,860)	—	—	—	(13,860)
Comprehensive loss:													
Unrealized loss on securities, available-for-sale	—	—	—	—	—	—	—	—	—	—	58	—	58
Net loss	—	—	—	—	—	—	—	—	—	—	—	(27,504)	(27,504)
Total comprehensive loss													(27,446)
Balance at December 31, 2006	9,322	10,955	14,831	34,942	2,398	2	8,772	9	33,299	—	11	(49,168)	(15,847)
Accretion of redeemable convertible preferred stock to redemption value	—	4	—	6	—	—	—	—	(10)	—	—	—	(10)
Issuance of common stock in initial public offering at $12.00 per share, net of issuance costs	—	—	—	—	8,050	8	—	—	87,883	—	—	—	87,891
Conversion of preferred stock in connection with initial public offering	(9,322)	(10,959)	(14,831)	(34,948)	16,462	17	(8,772)	(9)	45,899	—	—	—	45,907
Exercise of common stock options at $0.10, $0.60, $0.70 and $2.00 per share for cash	—	—	—	—	73	—	—	—	77	—	—	—	77
Stock-based compensation expense	—	—	—	—	—	—	—	—	4,423	—	—	—	4,423
Comprehensive loss:													
Unrealized loss on securities, available-for-sale	—	—	—	—	—	—	—	—	—	—	209	—	209
Net loss	—	—	—	—	—	—	—	—	—	—	—	(57,767)	(57,767)
Total comprehensive loss													(57,558)
Balance at December 31, 2007	—	$ —	—	$ —	26,983	$27	—	$—	$171,571	$ —	$220	$(106,935)	$ 64,883

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.
(a development stage company)

STATEMENTS OF CASH FLOWS
(In thousands)

	Years Ended December 31,			Period from September 12, 2002 (Inception) to December 31, 2007
	2007	2006	2005	
Operating activities				
Net loss	$ (57,767)	$(27,504)	$(12,089)	$(106,935)
Adjustments to reconcile net loss to net cash used in operating activities:				
Amortization of premium (discount) on investment securities, available-for-sale	(2,476)	74	33	(2,368)
Amortization of debt issuance costs	203	8	—	211
Depreciation	138	44	9	195
Loss on disposal of fixed assets	—	—	4	4
Issuance of common stock in exchange for technology and services	—	—	—	47
Stock-based compensation	4,423	2,258	1,115	7,799
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(2,249)	43	(262)	(2,471)
Accounts payable and accrued expenses	3,551	3,490	1,053	8,509
Other assets	(130)	(167)	9	(324)
Deferred rent	7	34	—	41
Deferred revenue	(88)	(88)	1,412	1,235
Net cash used in operating activities	(54,388)	(21,808)	(8,716)	(94,057)
Investing activities				
Purchases of investment securities, available-for-sale	(134,814)	(21,447)	(34,687)	(190,949)
Maturities and sales of investment securities, available-for-sale	96,000	25,351	15,700	137,051
Purchases of property and equipment	(534)	(427)	(151)	(1,123)
Restricted cash	(970)	(125)	—	(1,125)
Net cash provided by (used in) investing activities	(40,318)	3,352	(19,138)	(56,146)
Financing activities				
Proceeds from borrowings of long-term debt	18,000	—	—	18,000
Payments on borrowings on long-term debt	(2,193)	—	—	(2,193)
Proceeds from issuance of redeemable convertible preferred stock for cash, net of issuance costs	—	—	34,915	44,109
Proceeds from issuance of convertible preferred stock for cash, net of issuance costs	—	29,940	—	29,940
Proceeds from promissory notes	—	—	—	1,665
Costs paid in connection with loan agreement	(43)	(183)	—	(226)
Costs paid in connection with initial public offering	623	(623)	—	—
Proceeds from issuance of common stock, net of repurchases	87,968	7	5	87,982
Costs paid in connection with public offering	(107)	—	—	(107)
Net cash provided by financing activities	104,248	29,141	34,920	179,170
Increase (decrease) in cash and cash equivalents	9,542	10,685	7,066	28,967
Cash and cash equivalents at beginning of period	19,425	8,740	1,674	—
Cash and cash equivalents at end of period	$ 28,967	$ 19,425	$ 8,740	$ 28,967
Supplemental Disclosure				
Interest paid	$ 581	$ —	$ —	$ 581
Unrealized gain (loss) on investment securities, available-for-sale	$ 209	$ 58	$ (47)	$ 220
Non-cash financing activities				
Conversion of notes payable and accrued interest to redeemable convertible preferred stock	$ —	$ —	$ —	$ 1,721
Accretion to redemption value of redeemable convertible preferred stock	$ 10	$ 31	$ 24	$ 78

See accompanying notes.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Orexigen Therapeutics, Inc. (the "Company"), a Delaware corporation, is a biopharmaceutical company focused on the development and commercialization of pharmaceutical products for the treatment of central nervous system disorders, with an initial focus on obesity. The Company was incorporated in September 2002 and commenced operations in 2003.

The Company's primary activities since incorporation have been organizational activities, including recruiting personnel, conducting research and development, including clinical trials, and raising capital. Since the Company has not yet begun principal operations of commercializing a product candidate, the Company is considered to be in the development stage. In addition, the Company has experienced losses since its inception, and as of December 31, 2007, had an accumulated deficit of $106.9 million. The Company expects to continue to incur losses for at least the next several years. Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support the Company's cost structure, and until that time, the Company will continue to raise additional equity or debt financing. Management believes that it has sufficient capital to fund operations through at least the next 12 months.

2. Summary of Significant Accounting Policies

Initial Public Offering

In May 2007, the Company completed its initial public offering of 7,000,000 shares of its common stock at a public offering price of $12.00 per share. Net cash proceeds from the initial public offering were approximately $76.2 million, after deducting underwriting discounts, commissions and estimated offering costs payable by the Company. In connection with the closing of the initial public offering, all of the Company's shares of convertible preferred stock outstanding at the time of the offering were automatically converted into 16,462,231 shares of common stock. In May 2007, the underwriters exercised their overallotment option and purchased an additional 1,050,000 shares of the Company's common stock, from which the Company received cash proceeds, net of underwriting discounts and commissions, of approximately $11.7 million.

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 disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents.

Investment Securities, Available-for-Sale

The Company classifies all investment securities as available-for-sale, as the sale of such securities may be required prior to maturity to implement management strategies. These investment securities are carried at fair value, with unrealized gains and losses reported as accumulated other comprehensive income (loss) until realized. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion, as well as interest and dividends, are included in interest income. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis and are also included in interest income.

Restricted Cash

Restricted cash represents certificates of deposit pledged as collateral for letters of credit issued by the Company in connection with the execution of operating leases in September 2006 ($125,000) and December 2007 ($1.0 million).

Fair Value of Financial Instruments

The carrying amount of cash and cash equivalents, accounts payable and accrued expenses are considered to be representative of their respective fair value because of the short-term nature of these items. Investment securities, available-for-sale, are carried at fair value.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents and investment securities, available-for-sale. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. However, management believes the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which these deposits are held. Additionally, the Company has established guidelines regarding the diversification of its investments and their maturities, which are designed to maintain safety and liquidity.

Concentration of Revenue

Cypress Bioscience, Inc. ("Cypress") accounted for 100%, 100%, 34% and 60% of revenue for the years ended December 31, 2007, 2006 and 2005, and for the period from September 12, 2002 (inception) to December 31, 2007, respectively. Eli Lilly and Company ("Eli Lilly") accounted for 0%, 0%, 66% and 40% of revenue for the years ended December 31, 2007, 2006 and 2005, and for the period from September 12, 2002 (inception) to December 31, 2007, respectively.

Property and Equipment

Property and equipment is stated at cost and depreciated over the estimated useful lives of the assets (three to five years) using the straight-line method. Leasehold improvements are stated at cost and amortized over the shorter of their useful lives or the lease term.

Impairment of Long-Lived Assets

In accordance with Statement of Financial Accounting Standards ("SFAS") No. 144, *Accounting for the Impairment of Disposable Long-Lived Assets*, the Company will record impairment losses on long-lived assets 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. While the Company's current and historical operating losses and cash flows 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, 2007.

Research and Development Costs

All research and development costs are charged to expense as incurred and consist principally of costs related to clinical trials managed by the Company's contract research organizations, license fees and salaries and related benefits. Clinical trial costs are a significant component of research and development expenses. These costs are accrued based on estimates of work performed, and requires estimates of total costs incurred based on patients

enrolled, progress of patient studies and other events. Clinical trial costs are subject to revision as the trials progress and revisions are charged to expense in the period in which they become known.

Patent Costs

All costs related to filing and pursuing patent applications are expensed as incurred as recoverability of such expenditures is uncertain.

Income Taxes

The Company accounts for income taxes in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes* ("SFAS No. 109"). Under SFAS No. 109, deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax basis of assets and liabilities using enacted tax rates which will be in effect when the differences reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax asset will be realized.

Revenue Recognition

The Company has entered into an agreement with Cypress which contains multiple elements, including non-refundable upfront fees, payments for reimbursement of research costs, payments associated with achieving specific development milestones and royalties based on specified percentages of net product sales, if any. The Company applies the revenue recognition criteria outlined in Staff Accounting Bulletin ("SAB") No. 104, *Revenue Recognition* and Emerging Issues Task Force ("EITF") Issue 00-21, *Revenue Arrangements with Multiple Deliverables*. In applying these revenue recognition criteria, the Company considers a variety of factors in determining the appropriate method of revenue recognition under these arrangements, such as whether the elements are separable, whether there are determinable fair values and whether there is a unique earnings process associated with each element of a contract. If the required ongoing obligations involve minimal or no cost effort, nonrefundable up front fees would be recognized upon receipt. Otherwise, non-refundable upfront fees are recognized over the period the related services are provided or over the period the Company has significant involvement. Revenue from milestones is recognized as agreed upon scientific events are achieved, as long as the event is substantial and was not readily assured at the beginning of the collaboration.

During 2005, the Company entered into a collaborative research and development contract with Eli Lilly and Company. The agreement was to provide research and development over a term of one year on a best efforts basis at which time the agreement terminated. Amounts received were recognized over the term of the agreement.

Advance payments received in excess of amounts earned are classified as deferred revenue until earned.

Stock-Based Compensation

Prior to January 1, 2006, the Company applied the intrinsic-value-based method of accounting prescribed by APB Opinion No. 25, *Accounting for Stock issued to Employees* ("APB Opinion No. 25"), and its related interpretations, to account for its equity-based awards to employees and directors. Under this method, if the exercise price of the award equaled or exceeded the fair value of the underlying stock on the measurement date, no compensation expense was recognized. The measurement date was the date on which the final number of shares and exercise price were known and was generally the grant date for awards to employees and directors. If the exercise price of the award was below the fair value of the underlying stock on the measurement date, then compensation cost was recorded, using the intrinsic-value method, and was generally recognized in the statements of operations over the vesting period of the award.

SFAS No. 123, *Accounting for Stock-Based Compensation* ("SFAS No. 123") required disclosures as if the fair-value-based method had been applied to all outstanding and unvested awards in each period. For purposes of disclosures required by SFAS No. 123, the estimated fair value of the options is amortized on a straight-line basis over the vesting period. The fair value of these awards was estimated at the date of grant using the Minimum Value option pricing model with the following weighted average assumptions for all periods: risk free interest rate of 4.40%; dividend yield of 0%; and a weighted average expected life of the options of six years. The effect of using the Minimum Value option pricing model on these grants did not result in pro forma results that were materially different from the reported net loss for the year ended December 31, 2005.

Effective January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards No. 123(R), *Share-Based Payment* ("SFAS No. 123(R)") using the prospective transition method and therefore, prior period results have not been restated. SFAS No. 123(R) supersedes APB Opinion No. 25, and its related interpretations, and revises guidance in SFAS No. 123. Under this transition method, the compensation cost related to all equity instruments granted prior to, but not yet vested as of, the adoption date is recognized based on the grant-date fair value which is estimated in accordance with the original provisions of SFAS No. 123; however, those options issued prior to but unvested on January 1, 2006 and valued using the minimum value method are excluded from the options subject to SFAS 123(R). Compensation costs related to all equity instruments granted after January 1, 2006 is recognized at the grant-date fair value of the awards in accordance with the provisions of SFAS No. 123(R). Additionally, under the provisions of SFAS No. 123(R), the Company is required to include an estimate of the number of awards that will be forfeited in calculating compensation costs, which is recognized over the requisite service period of the awards on a straight-line basis. No related tax benefits of the share-based compensation costs have been recognized since the Company's inception.

During the year ended December 31, 2006, the Company recorded share-based compensation costs of approximately $834,500, or $0.38 per share, as a result of the adoption of SFAS No. 123(R). Of this amount, $372,000 is included in research and development expenses and $462,500 is included in general and administrative expense. No related tax benefits of the share-based compensation costs have been recognized since the Company's inception.

The fair value of each option award is estimated on the date of grant using the Black-Scholes option valuation model. The following weighted-average assumptions were utilized for the calculations during each period:

	Years Ended December 31,	
	2007	2006
Expected life (in years)	6.1	6.2
Expected volatility	70.0%	70.0%
Risk-free interest rate	4.1%	4.7%
Expected dividend yield	—	—

The risk-free interest rate assumption was based on the United States Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued. The assumed dividend yield was based on the Company's expectation of not paying dividends in the foreseeable future. The weighted average expected life of options was calculated using the simplified method as prescribed by the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 107 ("SAB No. 107"). This decision was based on the lack of relevant historical data due to the Company's limited historical experience. In addition, due to the Company's limited historical data, the estimated volatility also reflects the application of SAB No. 107, incorporating the historical volatility of comparable companies whose share prices are publicly available.

The weighted average grant-date fair values of stock options granted during the years ended December 31, 2007 and 2006 was $9.46 and $8.34 per share, respectively.

Total stock-based compensation expense recognized during the year ended December 31, 2007 and 2006 and the period from September 12, 2002 (inception) to December 31, 2007 was comprised of the following (in thousands):

	Years Ended December 31,		Period from September 12, 2002 (Inception) to December 31, 2007
	2007	2006	
General and administrative	$2,709	$1,649	$5,263
Research and development	1,714	609	2,536
	$4,423	$2,258	$7,799

At December 31, 2007, total unrecognized share-based compensation costs related to non-vested stock options granted during the year ended December 31, 2007 was approximately $11.3 million which related to 1.9 million shares. This unrecognized cost is expected to be recognized over a weighted-average period of approximately 3.5 years. Unrecognized share-based compensation related to non-vested stock option awards granted prior to January 1, 2006 was approximately $1.5 million and is expected to be recognized over a weighted average period of 1.2 years.

In addition, prior to the adoption of SFAS No. 123(R), the Company presented deferred compensation as a separate component of stockholders' equity. In accordance with the provisions of SFAS No. 123(R), on January 1, 2006, the Company offset deferred compensation against additional paid-in-capital.

Equity instruments issued to non-employees are recorded at their fair value as determined in accordance with SFAS No. 123 and Emerging Issues Task Force Issue No. 96-18, *Accounting for Equity Instruments That are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods and Services*, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period. In connection with the issuance of options to purchase shares of common stock to non-employees, the Company recorded total stock-based compensation within stockholders' equity totaling $264,000, $151,000 and $2,000 for the years ended December 31, 2007, 2006 and 2005, respectively.

Comprehensive Income (Loss)

The Company has applied Statement of Financial Accounting Standards No. 130, *Reporting Comprehensive Income*, which requires that all components of comprehensive income, including net income, be reported in the financial statements in the period in which they are recognized. Comprehensive income (loss) consists of net loss and certain changes in stockholders' equity that are excluded from net loss. Comprehensive income (loss) for the years ended December 31, 2007, 2006 and 2005 has been reflected in the Statement of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit). Accumulated other comprehensive income (loss), which is included in Stockholders' Equity (Deficit), represents unrealized gains and losses on investment securities, available-for-sale.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period less the weighted average number of shares subject to repurchase. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common stock equivalents

outstanding during the period determined using the treasury stock method. Stock options and shares to be issued upon conversion of the redeemable convertible preferred stock are considered to be common stock equivalents and were not included in the net loss per share calculation for the years ended December 31, 2007, 2006 and 2005 because the inclusion of such shares would have had an anti-dilutive effect.

	Years Ended December 31,		
	2007	2006	2005
	(In thousands, except per share amounts)		
Historical			
Numerator:			
Net loss attributable to common stockholders	$(57,777)	$(41,395)	$(12,113)
Denominator:			
Weighted average common shares outstanding	18,789	2,379	2,330
Weighted average unvested common shares subject to repurchase	(32)	(186)	(350)
Denominator for basic and diluted net loss attributable to common stockholders	18,757	2,193	1,980
Net loss attributable to common stockholders per share — basic and diluted	$ (3.08)	$ (18.87)	$ (6.12)

Historical outstanding anti-dilutive securities not included in the diluted net loss per share calculation include the following (in thousands):

	As of December 31,		
	2007	2006	2005
Common stock options	2,873	2,297	1,339
Common shares subject to repurchase	—	110	275
Redeemable convertible preferred stock (as converted)	—	16,462	12,076
	2,873	18,869	13,690

Pro Forma Net Loss per Share

The pro forma disclosure below shows what net loss per share would have been if the conversion of our shares of redeemable convertible preferred stock had occurred at the beginning of the respective periods being reported using the as-if-converted method. All shares of convertible preferred stock were automatically converted to 16,462,231 shares of common stock upon the completion of our initial public offering in May 2007. This pro forma information provides supplemental information that helps investors compare the results of prior periods after giving effect to the change in capitalization resulting from the conversion of preferred stock. The pro forma basic net loss per share is computed as follows (in thousands, except per share amounts):

	Years Ended December 31,		
	2007	2006	2005
Numerator:			
Net loss attributable to common stockholders	$(57,777)	$(41,395)	$(12,113)
Adjustment to eliminate accretion on preferred stock and beneficial conversion of series C preferred stock	10	13,891	24
Pro forma net loss	$(57,767)	$(27,504)	$(12,089)
Denominator:			
Weighted average shares of common stock outstanding	18,757	2,193	1,980
Pro forma adjustment to reflect assumed conversion of preferred stock, as-if-converted	5,457	12,545	9,768
Denominator for pro forma basic and diluted net loss per share	24,214	14,738	11,748
Pro forma basic and diluted net loss per share	$ (2.39)	$ (1.87)	$ (1.03)

New Accounting Standards Not Yet Adopted

In September 2006, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 157, *Fair Value Measurements* ("SFAS No. 157"), which defines fair value, establishes a framework for measuring fair value under GAAP, and expands disclosures about fair value measurements. SFAS No. 157 will be effective for fiscal years beginning after November 15, 2007, which is the Company's fiscal year 2008. The Company has not yet evaluated the potential impact of adopting SFAS No. 157 on its financial statements.

In February 2007, the FASB issued Statement of Financial Accounting Standards No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities* ("SFAS No. 159"), which allows an entity to voluntarily choose to measure certain financial assets and liabilities at fair value. SFAS No. 159 will be effective for fiscal years beginning after November 15, 2007, which is the Company's fiscal year 2008. The Company has not yet evaluated the potential impact of adopting SFAS No. 159 on its financial statements.

In June 2007, the FASB issued EITF 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* (EITF 07-3). The scope of this issue is limited to nonrefundable advance payments for goods and services related to research and development activities. EITF 07-3 addresses whether such advanced payments should be expensed as incurred or capitalized. The Company is required to adopt EITF 07-3 effective January 1, 2008. The Company does not expect the adoption of EITF 07-3 to have a material impact on its results of operations or financial position.

3. Commitments and Contingencies

Credit and Security Agreement

In December 2006, the Company entered into a Credit and Security Agreement with Merrill Lynch Capital (the "Credit Agreement") providing for potential borrowing until June 30, 2007 of up to $17.0 million. In March 2007, the Company drew down $10.0 million on the Credit Agreement. In July 2007, the Company entered into a First Amendment to Credit and Security Agreement with Merrill Lynch Capital (the "First Amendment"). The First Amendment provides for, among other things, the extension of the period during which Merrill Lynch Capital is obligated to make advances under the Credit Agreement to the Company from June 30, 2007 to December 31, 2007. In November 2007, the Company entered into a Second Amendment to Credit and Security Agreement with Merrill Lynch Capital (the "Second Amendment"). The Second Amendment amends and restates certain provisions of the Credit Agreement as amended by the First Amendment. The Second Amendment provides for, among other things, the increase of the total amount available for advances under the Credit Agreement from $17.0 million to $25.0 million, the obligation of the Company to request an advance of $8.0 million on or before December 31, 2007, and the extension of the period during which Merrill Lynch Capital is obligated to make advances to the Company under the Credit Agreement from December 31, 2007 to December 31, 2008. In December 2007, the Company drew down an additional $8.0 million under the Credit Agreement, as amended.

The Company is required to make monthly payments of principal and interest and all amounts outstanding under the Credit Agreement will become due and payable on the earlier of July 1, 2011 or three years after the funding of any amounts under the Credit Agreement. Interest accrues on amounts outstanding at a base rate set forth in the agreement plus an applicable margin, which ranges from 3.75% to 4.25% based on the date of borrowing. The loan is collateralized by substantially all of the Company's assets other than, subject to certain limited exceptions, intellectual property. Subject to certain limited exceptions, amounts prepaid under the Credit Agreement are subject to a prepayment fee equal to 3% of the amount prepaid. In addition, upon repayment of the total amounts borrowed for any reason, the Company will be required to pay an exit fee equal to the greater of $900,000 or 5% of the total amounts borrowed under the Credit Agreement. Under the terms of the agreement, the Company is subject to operational covenants, including limitations on the Company's ability to incur liens or additional debt, pay dividends, redeem stock, make specified investments and engage in merger, consolidation or asset sale transactions, among other restrictions. As of December 31, 2007, $18.0 million has been drawn under this agreement. The average rate of interest on the amounts outstanding at December 31, 2007, which is fixed through maturity, is 9.2%.

At December 31, 2007, future minimum principal payments under the Credit Agreement, as amended, are as follows (in thousands):

Due in:	
2008	$ 4,735
2009	6,026
2010	4,046
2011	1,000
	15,807
Less current portion	(4,735)
	$11,072

Included in other assets at December 31, 2007 and 2006 is approximately $1,126,000 and $683,000, respectively, related to costs incurred in connection with the Credit Agreement, as amended. At December 31, 2007 and 2006, this amount includes $900,000 and $500,000, respectively, which was earned by the lender upon the closing of the loan agreement and can be used to offset up to $900,000 of the exit fee, which is payable upon the

earlier of repayment of amounts borrowed or termination of the agreement. These costs are being amortized to interest expense over the term of the Credit Agreement, as amended, and such amortization totaled approximately $203,000, $8,000 and $211,000 for the year ended December 31, 2007 and 2006, and for the period from September 12, 2002 (inception) to December 31, 2007, respectively.

Operating Lease

In September 2006, the Company entered into a five-year operating lease for office facilities commencing on November 1, 2006. Monthly rental payments are adjusted on an annual basis and the lease expires in October 2011, with one option to renew for a three-year term on the same terms and conditions. As security for the lease, the landlord required a letter of credit for $125,000 through April 2009, at which time the security can be reduced to $70,000. The letter of credit is collateralized by a certificate of deposit in the same amount, which is included in restricted cash in the accompanying balance sheet at December 31, 2007 and 2006. The Company cannot withdraw from the certificate of deposit until all obligations have been paid and the bank's obligation to provide the letter of credit terminates. Rent expense is being recorded on a straight-line basis over the life of the lease.

In December 2007, the Company entered into an operating lease agreement for office facilities in San Diego, California. The term of the lease will begin on the day of substantial completion of the tenant improvement, which date is not anticipated to be sooner than April 1, 2008 and is for an initial term of 64 months. The monthly rental payments are adjusted on an annual basis. As security for the lease, the landlord required a letter of credit for $1.0 million. The letter of credit is collateralized by a certificate of deposit in the same amount, which is included in restricted cash in the accompanying balance sheet at December 31, 2007. The amount of security required will be reduced every 12 months until the 61st month of the lease term, at which time the amount of security required is zero. Rent expense is being recorded on a straight-line basis over the life of the lease.

Future minimum payments under the operating leases and a small equipment lease as of December 31, 2007 are as follows (in thousands):

Years Ending December 31,	
2008	$ 572
2009	1,298
2010	1,342
2011	1,346
2012	1,198
Thereafter	720
	$6,476

Total rent expense for the years ended December 31, 2007, 2006 and 2005, and for the period from September 12, 2002 (inception) to December 31, 2007 was approximately $215,000, $60,0000, $2,000, and $307,000, respectively.

Technology and License Agreements

Oregon Health & Science University

In June 2003, the Company entered into a license agreement with Oregon Health & Science University ("OHSU") whereby the Company acquired an assignment of any rights OHSU may have to a U.S. provisional patent application and OHSU licensed to the Company, on a co-exclusive basis, an issued patent. As consideration for this license agreement, the Company paid an upfront fee of $65,000 and issued 76,315 shares of the Company's common stock to OHSU. In addition, pursuant to the agreement, the Company was required to make a payment of

$20,000 upon receipt of a pair of mice, a payment of an additional $20,000 upon receipt of any additional pair of mice and a payment of 50% of expenses incurred in the maintenance and prosecution of the licensed issued patent. In December 2007, the license agreement between the Company and OHSU was amended. The amendment provides for, among other things, the change from a co-exclusive license to the patent rights underlying the *in vitro* model that the Company has used for screening combination therapies for impact on neuronal activity to an exclusive license to such patent rights, and the agreement on the part of the Company to pay 100% of the costs associated with such patent rights. In addition, the Company agreed to reimburse OHSU approximately $42,000, which represents patent costs incurred by OHSU to date with respect to such rights. The amendment also gives OHSU the right to not file any patent application or to abandon any patent or patent application included in the patent rights, in which case it must provide 60 days prior written notice to the Company and, in response, the Company may elect at its sole cost to pursue these actions.

As of December 31, 2007, the Company has paid a total of approximately $36,000 in connection with the maintenance and prosecution of the patent. The Company is also required to pay a royalty on net sales for each licensed product covered by one of the licensed patents. At December 31, 2007, no royalty payments have been made or are payable under this agreement as the product has not been launched and sales have not commenced.

The term of the agreement generally extends until the last of the subject patent rights expire, which is expected to occur in 2024 assuming patents issue with respect to the Company's pending Weber/Cowley patent applications. The Company may unilaterally terminate the agreement and/or any licenses in any country upon specified written notice to OHSU. OHSU may terminate the agreement upon delivery of written notice if the Company commits a material breach of its obligations and fails to remedy the breach within a specified period or may immediately terminate the agreement upon the delivery of written notice concerning the occurrence of specified bankruptcy proceedings. In addition, upon written notice and the Company's failure to remedy any of the following breaches within a specified period, OHSU may terminate or modify the agreement: if the Company cannot demonstrate to OHSU's satisfaction that it has taken, or can be expected to take within a reasonable time, effective steps to achieve practical application of the licensed products and/or licensed processes; or if the Company has willfully made a false statement of, or willfully omitted, a material fact in any report required by the agreement; or if the Company commits a substantial breach of a covenant or agreement contained in the license.

Duke University

In March 2004, the Company entered into a patent license agreement (the "Duke Agreement") with Duke University ("Duke") whereby the Company acquired, among other things, an exclusive worldwide license to a U.S. patent. As consideration for this license, the Company issued 442,624 shares of its common stock to Duke and may be required to make future milestone payments totaling $1.7 million upon the achievement of various milestones related to regulatory or commercial events. The Company is also obligated to pay a royalty on net sales of products covered by the license. The Company has the right to grant sublicenses to third parties, subject to an obligation to pay Duke a royalty on any revenue it receives under such sublicensing arrangements. At December 31, 2007, no such payments have been made or are payable under the Duke Agreement as the product has not been launched and sales have not commenced. In January 2005, the Company sublicensed the technology to Cypress for a non-refundable upfront payment of $1.5 million.

As a result of the Company's sublicensing of the Duke technology to Cypress for specified uses, the Company may be required to make future payments to Duke of up to $5.7 million ($3.7 million excluding milestone payments related to sleep apnea, see further discussion following) upon Cypress's achievement of various regulatory milestones. The term of the agreement generally extends until the last licensed patent right expires, which is expected to occur in 2023. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful misconduct, or illegal conduct of the other party with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other

party commits a material breach of its obligations and fails to remedy the breach within a specified period. The Company may also voluntarily terminate the agreement upon delivery of written notice within a specified time period. Duke may terminate the agreement upon delivery of written notice if the Company fails to meet certain specified milestones of the agreement and fail to remedy such a breach within the specified period. In addition, Duke may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Lee Dante, M.D.

In June 2004, the Company entered into a patent license agreement with Lee G. Dante, M.D. whereby the Company acquired an exclusive worldwide license to two U.S. patents. As consideration for this license, the Company paid upfront fees totaling $100,000 and granted Dr. Dante an option to purchase 73,448 shares of its common stock. The Company is also obligated to pay a royalty on net sales of products covered by the license. The Company will be required to make a one-time milestone payment to Dr. Dante in the amount of $1.0 million upon the occurrence of a specified regulatory event. The Company has the right to grant sublicenses of the patented technology to third parties, subject to its obligation to pay Dr. Dante a royalty on any revenue it receives from such arrangements. At December 31, 2007, no such payments have been made or are payable under this agreement as the technology has not been sublicensed, the product has not been launched and sales have not commenced.

The term of the agreement generally extends until the last licensed patent right expires, which is expected to occur in 2013. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful misconduct, or illegal conduct of the other party with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period. The Company may also voluntarily terminate the agreement upon delivery of written notice within a specified time period. In addition, Dr. Dante may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Cypress Bioscience, Inc.

In January 2005, the Company entered into a license agreement with Cypress whereby the Company sublicensed certain of its rights under a patent license agreement with Duke University ("Duke") to Cypress for specified uses. As consideration for this license, Cypress paid the Company non-refundable upfront fees of $1.5 million. The term of the license agreement generally extends until the licensed patent expires, which is expected to occur in 2023. Cypress can require the Company to provide clinical support for any of the specified uses over the term of the agreement. Accordingly, this $1.5 million is being recognized over 17 years, the estimated term of the agreement. In addition, Cypress is obligated to pay the Company a royalty on net sales of any products covered by the sublicensed technology. Cypress may also be required to make future milestone payments to the Company of up to $57.0 million upon its achievement of various regulatory milestones. In June 2006, Cypress announced that the results of a completed Phase IIa trial did not support continuing its development program for obstructive sleep apnea, one of the specified uses under the agreement. Therefore, the Company's receipt of $20.0 million of milestone payments related to sleep apnea is unlikely at this time.

For each of the years in the three year period ended December 31, 2007 and for the period September 12, 2002 (inception) to December 31, 2007, the Company recognized revenues under this agreement of $88,000 and $265,000, respectively. At December 31, 2007 and December 31, 2006, deferred revenue under this agreement totaled $1,235,000 and $1,323,000, respectively.

As a result of the Company's sublicensing of the Duke technology to Cypress for specified uses, the Company may be required to make future payments to Duke of up to $5.7 million ($3.7 million excluding milestone payments related to sleep apnea) upon Cypress's achievement of various regulatory milestones. The term of the Cypress agreement generally extends until the last licensed patent right expires, which is expected to occur in 2023. Either party may terminate the agreement upon delivery of written notice if the other party commits fraud, willful

misconduct, or illegal conduct of the other party with respect to the subject matter of the agreement. In addition, either party may terminate the agreement upon delivery of written notice if the other party commits a material breach of its obligations and fails to remedy the breach within a specified period. Cypress may terminate the agreement for any reason upon delivery of written notice within the specified period. Cypress may also terminate with no notice if an unfavorable judgment is entered against the Company or any other party relating to the patents we have sublicensed to Cypress. In addition, Cypress may terminate the agreement upon specified bankruptcy, liquidation or receivership proceedings.

Eli Lilly and Company

In December 2004, the Company entered into a Drug Study Agreement with Eli Lilly whereby the Company and Eli Lilly would enter into a joint Drug Study program. Eli Lilly was required to make a payment of $87,000 upon execution of the agreement and $87,000 upon the completion of the pre-clinical study, which was completed in December 2005. For the year ended December 31, 2005 and for the period from September 12, 2002 (inception) to December 31, 2007, the Company recognized revenue totaling $174,000 under this agreement.

4. Investment Securities, Available-for-Sale

The Company invests its excess cash in investment securities, principally debt instruments of financial institutions and corporations with strong credit ratings. A summary of the estimated fair value of investment securities, available-for-sale, is as follows at December 31, 2007 and 2006 (in thousands):

			Unrealized		
December 31, 2007	**Maturity in Years**	**Amortized Cost**	**Gains**	**Losses**	**Fair Value**
Corporate debt obligations	Less than 1	$49,194	$218	$(2)	$49,410
Corporate debt obligations	2-3	7,073	4	—	7,077
Total investment securities		$56,267	$222	$(2)	$56,487

			Unrealized		
December 31, 2006	**Maturity in Years**	**Amortized Cost**	**Gains**	**Losses**	**Fair Value**
Corporate debt obligations	Less than 1	$ 31,820	$11	$—	$ 31,831
Corporate debt obligations	2-3	1,249	—	—	1,249
		33,069	11	—	33,080
Less cash equivalents		(18,092)			(18,092)
Amounts classified as investments		$ 14,977	$11	$—	$ 14,988

5. Property and Equipment

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

	Useful Life in Years	December 31, 2007	December 31, 2006
Furniture and fixtures	5	$ 311	$311
Computer equipment	3 to 5	111	105
Leasehold improvements	5	42	36
Laboratory equipment		648	126
		1,112	578
Accumulated depreciation		(188)	(50)
Property and equipment, net		$ 924	$528

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2007	December 31, 2006
Accrued preclinical and clinical trial expenses	$2,079	$2,269
Accrued compensation related expenses	1,760	762
Accrued legal and professional expenses	87	104
Other accrued expenses	414	69
	$4,340	$3,204

7. Redeemable Convertible Preferred Stock and Stockholders' Equity

Redeemable Convertible Preferred Stock

During January 2004, the Company entered into agreements with several investors who collectively purchased 7,863,776 shares of Series A redeemable convertible preferred stock ("Series A Preferred Stock") at $1.18 per share for cash proceeds of $9,193,866, net of issuance costs of $85,387. In addition, notes payable and accrued interest totaling $1,720,747 were converted into 1,458,259 shares of Series A Preferred Stock.

During April and May 2005, the Company entered into agreements with several investors who collectively purchased 14,830,509 shares of Series B redeemable convertible preferred stock ("Series B Preferred Stock" and, together with the Series A Preferred Stock, the "Preferred Stock") at $2.36 per share for cash proceeds totaling $34,914,721, net of issuance costs of $85,279.

Each share of Preferred Stock was automatically convertible into common stock upon (i) the affirmative election of the holders of two-thirds of the outstanding shares of Preferred Stock, or (ii) the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which the per share price is at least $12.16 (as may be adjusted), and the gross cash proceeds are at least $30.0 million. Upon the closing of the initial public offering of 8,050,000 shares of the Company's common stock in May 2007, all shares of the Company's outstanding redeemable preferred stock were converted into an aggregate of 12,076,269 shares of common stock.

The holders (collectively, the "Preferred Holders") of Preferred Stock were entitled to receive non-cumulative dividends at a rate of 8% per annum. These dividends were payable when and if declared by the Board of Directors. At December 31, 2006, and at the time of the initial public offering, the Board of Directors had not declared any dividends. The preferred dividends were payable in preference and in priority to any dividends on the Company's common stock.

The holders of the Series A Preferred Stock and Series B Preferred Stock were entitled to receive liquidation preferences at the rate of $1.18 and $2.36 per share, respectively. Liquidation payments to the holders of Preferred Stock have priority and are made in preference to any payments to the holders of common stock.

The holders of Series A Preferred Stock were entitled to elect three members of the Company's Board of Directors, and the holders of Series B Preferred Stock were entitled to elect two members of the Company's Board of Directors.

In addition, at any time after April 22, 2010 and upon the election of the holders of at least two-thirds of the outstanding shares of Preferred Stock, and only after all outstanding shares of the Series B Preferred Stock have been redeemed, the Company was required to redeem in three annual installments, the outstanding shares of Preferred Stock by a cash payment equal to the original issue price ($1.18 for Series A Preferred Stock and $2.36 for Series B Preferred Stock) plus any declared but unpaid dividends, as adjusted for stock dividends, combinations or splits.

The Company accreted the carrying value of these securities to the Liquidation Preference and Redemption Value as of April 23, 2010, the earliest date on which the Preferred Holders could require the redemption of the outstanding shares. The difference between the Carrying Value and the Liquidation Preference and Redemption Value of the Preferred Stock represented the amount of issuance costs remaining to be accreted.

At December 31, 2006, redeemable convertible Preferred Stock consisted of the following (in thousands):

Series	Shares Authorized, Issued and Outstanding	Liquidation Preference and Redemption Value	Carrying Value
Series A	9,322	$11,000	$10,955
Series B	14,831	35,000	34,942
	24,153	$46,000	$45,897

Convertible Preferred Stock

During November 2006, the Company sold 8,771,930 shares of Series C convertible Preferred Stock at $3.42 per share, resulting in net proceeds of approximately $29.9 million. The Series C convertible Preferred Stock was sold at a price per share below the anticipated IPO price. Accordingly, pursuant to Emerging Issues Task Force Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, the Company recorded a deemed dividend on the Series C convertible Preferred Stock of approximately $13.9 million which is equal to the number of shares of Series C convertible Preferred Stock sold multiplied by the difference between the estimated fair value of the underlying preferred stock and the Series C conversion price per share. The deemed dividend increases the net loss applicable to common stockholders in the calculation of basic and diluted net loss per common share for the year ended December 31 2006 and is reported as a charge to additional paid-in capital.

Each share of Series C convertible Preferred Stock was automatically convertible into common stock upon (i) the affirmative election of the holders of two-thirds of the outstanding shares of Preferred Stock, or (ii) the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which the per share price is at least $12.16 (as may be adjusted), and the gross cash proceeds are at least $30.0 million. Upon

the closing of the initial public offering of 8,050,000 shares of the Company's common stock in May 2007, all shares of the Company's outstanding convertible preferred stock were converted into an aggregate of 4,385,962 shares of common stock.

The holders of Series C convertible Preferred Stock were entitled to receive liquidation preferences at the rate of $3.42 per share. Liquidation payments to the holders of Series C convertible Preferred Stock had priority and were to be made in preference to any payments to the holders of common stock.

Common Stock

During 2002 and 2003, and in connection with the founding of the Company, the Company issued 1,599,600 shares of common stock at $0.002 per share in exchange for cash and services. In addition, during 2003, in exchange for consulting services rendered to the Company, the Company issued two individuals a total of 442,624 shares of the Company's common stock at $0.002 per share.

During May 2006, the Board of Directors approved an amendment to the Company's Certificate of Incorporation to increase the number of authorized common shares by 3,000,000, resulting in the total number of authorized common shares of 38,000,000. In addition, during November 2006, the Board of Directors approved an amendment to the Company's Certificate of Incorporation to increase the number of authorized shares of common stock to 50,000,000.

In February 2007, the Company's Board of Directors and stockholders approved a one-for-two reverse stock split of the Company's outstanding common stock. A Certificate of Amendment to the Company's Amended and Restated Certificate of Incorporation was filed on April 9, 2007 effecting the one-for-two reverse stock split. All common and per-share data included in these financial statements have been retroactively restated to reflect the one-for-two reverse stock split.

Stock Options

During 2004, the Company adopted the 2004 Stock Plan (the "2004 Plan") under which, as amended, 1,659,275 shares of common stock are reserved for issuance to employees, directors and consultants of the Company at December 31, 2005. During May 2006, the Board of Directors approved an increase to the number of common shares available for issuance under the 2004 Plan by 1,500,000, resulting in the total number of shares available under the 2004 Plan of 3,159,275 at December 31, 2006. The 2004 Plan provides for the grant of incentive stock options, non-statutory stock options and rights to purchase restricted stock to eligible recipients. Recipients of incentive stock options shall be eligible to purchase shares of the Company's common stock at an exercise price equal to no less than the estimated fair market value of such stock on the date of grant. The maximum term of options granted under the 2004 Plan is ten years. The options generally vest over four years, and some are immediately exercisable. At December 31, 2007, 2,279,730 shares of our common stock were reserved for future issuance upon the exercise of outstanding options under the 2004 Plan.

In February 2007, the Company's stockholders approved the 2007 Equity Incentive Award Plan (the "2007 Plan"), which became effective in April 2007, under which 3,525,000 shares of common stock were initially reserved for future issuance to employees, directors and consultants of the Company. The 2007 Plan provides for the issuance of stock options, stock appreciation rights, restricted stock units, performance stock units, and other stock-based awards. The 2007 Plan has an initial term of ten years. As of the effectiveness of the 2007 Plan, no additional shares will be granted under the 2004 Plan. At December 31, 2007, options to purchase 593,632 shares have been granted and are outstanding under the 2007 Plan.

The following table summarizes stock option transactions for the 2004 and 2007 Plans since inception:

	Number of Options	Weighted Average Exercise Price
Outstanding at December 31, 2002 and 2003	—	$ —
Granted	223,624	$ 0.10
Outstanding at December 31, 2004	223,624	$ 0.10
Granted	1,260,683	$ 0.54
Exercised	(58,973)	$ 0.10
Cancelled	(86,203)	$ 0.10
Outstanding at December 31, 2005	1,339,131	$ 0.52
Granted	1,240,444	$ 1.86
Exercised	(45,000)	$ 0.16
Cancelled	(237,513)	$ 0.60
Outstanding at December 31, 2006	2,297,062	$ 1.24
Granted	648,632	$14.29
Exercised	(72,332)	$ 1.06
Outstanding at December 31, 2007	2,873,362	$ 4.19

The following table summarizes information about stock options outstanding under the 2004 and 2007 Plans at December 31, 2007:

	Outstanding Options		Exercisable Options		
Exercise Price	Number of Outstanding Options	Weighted Average Remaining Contractual Life (In Years)	Number of Exercisable Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (In Years)
$0.10	177,403	7.0	177,403	$ 0.10	7.0
$0.60	840,883	7.4	674,216	$ 0.60	7.4
$0.70	254,944	8.5	254,944	$ 0.70	8.5
$2.00	909,000	8.8	272,177	$ 2.00	8.8
$6.00	42,500	8.9	11,510	$ 6.00	8.9
$10.72	55,000	9.1	—	$10.72	—
$14.25	46,632	10.0	—	$14.25	—
$14.26	272,000	10.0	—	$14.26	—
$14.46	5,000	9.8	—	$14.46	—
$14.59	72,000	9.6	1,302	$14.59	9.6
$14.82	68,000	9.9	—	$14.82	—
$15.45	130,000	9.6	—	$15.45	—
	2,873,362	8.5	1,391,552	$ 0.89	7.8

In connection with the preparation of a registration statement for the Company to sell shares of its common stock in an initial public offering, the Company reassessed the estimated fair value of the common stock in light of the expected completion of the offering. The Company did not use a contemporaneous valuation from an unrelated

valuation specialist. The Company has not historically obtained contemporaneous valuations by an unrelated valuation specialist because, at the time of the issuances of stock options, the Company believed its estimates of the fair value of its common stock to be reasonable and consistent with its understanding of how similarly situated companies in its industry were valued. Based upon the reassessment, the Company determined that the reassessed fair value of the options granted to employees from April 2005 to December 2006 was greater than the exercise price of those options. Prior to April 1, 2005, the exercise price of the Company's employee stock options equaled the estimated fair value of the common stock on the date of grant. Information on employee stock options granted from April 1, 2005 through December 30, 2006 is summarized as follows:

Date of Issuance	Number of Options Granted	Exercise Price	Fair Value Estimate per Common Share	Intrinsic Value per Option Share
May 2005	1,113,396	$0.60	$ 6.00	$5.40
May 2006	262,944	$0.70	$ 7.00	$6.30
September 2006	935,000	$2.00	$10.00	$8.00
November 2006	37,500	$6.00	$10.00	$4.00

The 1,113,396 options granted in 2005 included in the above table were accounted for using the options' intrinsic value, or the difference between the reassessed fair value as per the above table and the exercise price of the options. This amount is being amortized over the vesting period, generally four years on a straight-line basis. For the years ended December 31, 2005 and 2006, the amount included in stock-based compensation expense totals approximately $1,112,800 and $1,271,800, respectively.

The aggregate intrinsic value of options outstanding and exercisable at December 31, 2007 was approximately $29,000,000 and $19,000,000, respectively. The aggregate intrinsic value of options exercised during the year ended December 31, 2007 was approximately $1,000,000.

A summary of the status of our non vested options as of December 31, 2007, and changes during the year ended December 31, 2007, is presented below:

	Shares	Weighted Average Grant-Date Fair Value
Non vested outstanding at December 31, 2006	1,793,171	$3.53
Granted	648,632	9.16
Vested	(666,766)	3.26
Non vested outstanding at December 31, 2007	1,775,037	$5.69

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consists of the following at December 31, 2007:

Stock options issued and outstanding	2,873,362
Authorized for future option grants	3,634,608
	6,507,970

8. Income Taxes

Significant components of the Company's deferred tax assets are summarized at December 31, 2007 and 2006 are shown below. A valuation allowance has been established as realization of such assets has not met the more likely than not threshold requirement under SFAS 109.

	December 31,	
	2007	2006
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 36,841	$ 17,154
Research and development credits	6,376	3,326
Deferred revenue	503	539
Other, net	461	245
Total deferred tax assets	44,181	21,264
Less valuation allowance	(44,181)	(21,264)
	$ —	$ —

At December 31, 2007, the Company has federal and state net operating loss carryforwards of approximately $91.0 million and $92.4 million, respectively. The federal and state loss carryforwards begin to expire in 2022 and 2012, respectively, unless previously utilized. At December 31, 2007, the Company has federal and state research and development tax credit carryforwards of $5.3 million and $4.1 million, respectively. The federal research and development tax credits begin to expire in 2023 unless previously utilized and the state tax credits carry forward indefinitely.

Additionally, the utilization of the net operating loss and research and development tax credit carryforwards is subject to an annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, and similar state provisions due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes limit the amount of net operating loss and research and development tax credit carryforwards and other deferred tax assets that can be utilized to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Sections 382 and 383, results from transactions increasing ownership of certain stockholders or public groups in the stock of the corporation by more than 50 percentage points over a three-year period. An analysis was performed which indicated that multiple ownership changes have occurred in previous years which created annual limitations on the Company's ability to utilize its net operating loss and research and development tax carryovers. Such limitations will result in approximately $900,000 of tax benefits related to net operating loss and research and development tax carryforwards that will expire unused. Accordingly, the related net operating loss and research and development tax carryforwards have been removed from deferred tax assets accompanied by a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, limitations created by future ownership changes, if any, will not impact our effective tax rate.

In July 2006, the FASB issued Financial Interpretation No. 48, or FIN 48, *Accounting for Uncertainty in Income Taxes — An Interpretation of FASB Statement No. 109*, which clarifies the accounting for uncertainty in income taxes recognized in a company's financial statements in accordance with Statement of Financial Accounting Standards No. 109, "Accounting for Income Taxes." FIN 48 prescribes a recognition threshold and measurement process for recording in the financial statements uncertain tax positions taken or expected to be taken in a tax return. Additionally, FIN 48 provides guidance on the de-recognition, classification, interest and penalties, accounting in interim periods, and disclosure requirements for uncertain tax positions. The Company adopted FIN 48 as of January 1, 2007. Due to the valuation allowance, the adoption of FIN 48 did not impact the Company's financial condition, results of operations or cash flows. As a result of the adoption, the Company recorded a net decrease to deferred tax assets of approximately $651,000 and a corresponding reduction to valuation allowance. The following table summarizes the activity related to the Company's gross unrecognized tax benefits (in thousands):

Balance at January 1, 2007	$ 768
Increases related to current year tax positions	1,110
Balance at December 31, 2007	$1,878

Due to the valuation allowance, none of the unrecognized tax benefits as of December 31, 2007, would reduce the Company's annual effective tax rate.

The Company files income tax returns in the United States and in various state jurisdictions with varying statutes of limitations. Due to net operating losses incurred, the Company's tax returns from inception to date are subject to examination by taxing authorities. The Company's policy is to recognize interest expense and penalties related to income tax matters as a component of income tax expense. As of December 31, 2007, the Company had no interest or penalties accrued for uncertain tax positions.

9. Litigation

On June 14, 2004, the Company and Duke jointly filed a lawsuit against Elan Corporation, plc, Elan Pharma International Ltd., Elan Pharmaceuticals, Inc. (collectively, "Elan"), Eisai, Inc., Eisai Co., Ltd. (together, "Eisai") and a former employee of Elan to resolve a dispute over rights in an invention relating to the use of zonisamide to treat obesity. The Company and Duke allege that scientists at Duke made the invention, and that Elan improperly used information supplied by the scientists to file a patent application on the invention. The Company and Duke sought a declaratory judgment of correct inventorship and ownership of the Elan patent application, as well as damages and injunctive relief for copyright infringement, fraud, conversion, unjust enrichment, unfair and deceptive trade practices, and unfair competition. Duke also has filed a patent application on the invention at issue, which has been exclusively licensed to the Company. On January 30, 2006, without addressing the merits of the lawsuit, the court decided on jurisdictional grounds that it could not decide the inventorship issue and, therefore, dismissed the request for a declaratory judgment. The court stayed all other claims against Elan until the U.S. Patent and Trademark Office ("PTO") resolves Duke's request for interference between the Duke and Elan patent applications. The Company expects the PTO to decide the inventorship issue if an interference is declared.

On December 14, 2006, the Company, Elan, Eisai and the former Elan employee entered into a settlement agreement to settle the lawsuit. Upon execution of the settlement agreement, the lawsuit was dismissed with prejudice. Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the settlement agreement, released each other from all claims and demands arising under the laws of the United States or any state within the United States existing as of the date of the settlement agreement that arise out of or relate to the lawsuit or the specified Duke and Eisai patent applications. The releases do not apply to the parties' rights with respect to claims and demands outside the United States (see following paragraph). In addition, each of Elan, Eisai and the former Elan employee have represented that they are not currently seeking and do not currently possess any

patent rights in the United States relating to the use of zonisamide for the treatment of obesity or other weight-related disorders or conditions. In addition, Elan and the former Elan employee have agreed not to assert any such U.S. patent against the Company's Empatic (formerly Excalia) product, which contains zonisamide and bupropion to treat obesity, even if Eisai later obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Eisai patent application. Likewise, if Duke obtains a U.S. patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the Duke patent application, the Company and Duke have agreed that the Company will not assert any such patent against Elan, Eisai or the former Elan employee for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai.

In September 2007, the Company and Duke entered into a settlement agreement with Eisai, which resolves the foreign aspects of the dispute over rights in an invention relating to the use of zonisamide to treat obesity. Under the terms of the settlement agreement, the parties have, subject to limitations set forth in the agreement, released each other from all claims and demands arising under the laws of any country outside of the United States existing as of the date of the agreement that arise out of or relate to the lawsuit or certain specified Duke and Eisai foreign patents that may issue from certain patent applications claiming the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions. In addition, if Eisai obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Eisai foreign patent applications, Eisai has agreed that it will not assert any such patent against the Company relating to our Empatic product candidate, which contains zonisamide and bupropion and is being developed to treat obesity. Likewise, if Duke obtains a foreign patent containing a claim that encompasses the use of zonisamide as the sole active ingredient to treat obesity or other weight-related disorders or conditions that issues from or is based upon the specified Duke foreign patent applications, the Company and Duke have agreed that the Company will not assert any such patent against Eisai for any conduct relating to Zonegran, which is a zonisamide product currently marketed by Eisai.

The Company is not currently a party to any other material legal proceedings.

10. Related Party Transactions

During the year ended December 31, 2003 and 2004, two of the Company's stockholders, which are affiliated venture funds, loaned the Company $1,650,000 and $15,000, respectively. The notes were interest bearing at an annual rate of 6.25% and were due in January 2004. During January 2004, the notes, and accrued interest totaling $55,747, were converted into 1,458,259 shares of Series A Preferred Stock.

During the years ended December 31, 2006 and 2005 and for the period September 12, 2002 (inception) to December 31, 2007, the Company reimbursed a company, which is the general partner of the two stockholders venture funds, for expenses incurred on the Company's behalf. These expenses, which included amounts for rent, totaled $28,000, $10,000 and $194,000 for the years ended December 31, 2006, 2005 and for the period September 12, 2002 (inception) to December 31, 2007, respectively. Rent expense paid under a month-to-month rental agreement to this founding stockholder totaled $23,500, $1,900 and $54,926 for the years ended December 31, 2006 and 2005 and for the period September 12, 2002 (inception) to December 31, 2007, respectively.

During August 2006, the Company entered into a sponsored research agreement with OHSU, one of the Company's stockholders, for work conducted by the laboratory of Dr. Michael Cowley, an officer and employee of the Company. The agreement, which was terminated in February 2008, provided for payment by the Company to OHSU of up to approximately $847,500 over the 30 month term of the agreement, was primarily for the continuation of research underlying the license agreement entered into between the Company and OHSU in June 2003 (Note 3). As of December 31, 2007, approximately $556,000 was paid to OHSU under the terms of this agreement.

11. Employee Benefit Plan

During 2007, the Company adopted a 401(k) Plan which allows employees to contribute up to 100% of their annual compensation up to the maximum annual amount prescribed by the Internal Revenue Service. The Company may elect to make a discretionary contribution or match a discretionary percentage of employee contributions. During the year ended December 31, 2007, the Company's matching contributions to the plan were approximately $29,000.

12. Selected 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. Selected quarterly financial data for years ended December 31, 2007 and 2006 are as follows (in thousands):

	Year Ended December 31, 2007			
	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
Selected quarterly financial data:				
Revenues	$ 22	$ 22	$ 22	$ 22
Total operating expenses	12,489	12,496	15,632	20,293
Net loss	(12,169)	(11,630)	(14,548)	(19,420)
Net loss attributable to common stockholders	(12,177)	(11,633)	(14,548)	(19,419)
Net loss per common stockholder — basic and diluted(1)	(5.26)	(0.63)	(0.54)	(0.72)

	Year Ended December 31, 2006			
	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
Selected quarterly financial data:				
Revenues	$ 21	$ 21	$ 21	$ 25
Total operating expenses	5,503	5,631	7,619	9,703
Net loss	(5,234)	(5,384)	(7,424)	(9,462)
Net loss attributable to common stockholders	(5,242)	(5,391)	(7,431)	(23,331)
Net loss per common stockholder — basic and diluted(1)	(2.49)	(2.48)	(3.34)	(10.28)

(1) Net loss per common stockholder is computed independently for each of the quarters presented. Therefore the sum of the quarterly net loss per share will no necessarily equal the total for the year.

13. Subsequent Events

Public Offering of Common Stock

In January 2008, the Company completed a public offering of 7,000,000 shares of its common stock at a public offering price of $11.00 per share. Net cash proceeds from the public offering are estimated to be approximately $72.4 million, after deducting underwriting discounts, commissions and estimated offering expenses payable by the Company. In February 2008, the underwriters exercised a portion of their overallotment option and purchased an additional 326,435 shares of the Company's common stock, from which the Company received cash proceeds, net of underwriting discounts and commissions, of approximately $3.4 million.

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

None.

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

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

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

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

None.

PART III

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

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

Information regarding Directors, Executive Officers and Corporate Governance is hereby incorporated by reference to the our definitive proxy statement, which will be filed with the SEC within 120 days after December 31, 2007.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our internet website at www.orexigen.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a "code of ethics" within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. ***Executive Compensation.***

Information regarding Executive Compensation is hereby incorporated by reference to our definitive proxy statement.

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

Information regarding Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters is hereby incorporated by reference to our definitive proxy statement.

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

Information regarding Certain Relationships and Related Transactions, and Director Independence is hereby incorporated by reference to our definitive proxy statement.

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

Information regarding the Principal Accounting Fees and Services is hereby incorporated by reference to our definitive proxy statement.

PART IV

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

(a) Documents filed as part of this report:

1. The following financial statements of Orexigen Therapeutics, Inc. are filed as part of this report under Item 8 — Financial Statements and Supplementary Data:

	Page Number
Balance Sheets — December 31, 2007 and 2006	83
Statements of Operations — Years Ended December 31, 2007, 2006 and 2005 and Period from Inception (September 12, 2002) to December 31, 2007	84
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity — Period from Inception (September 12, 2002) to December 31, 2007	85
Statements of Cash Flows — Years Ended December 31, 2007, 2006 and 2005 and Period from Inception (September 12, 2002) to December 31, 2007	87
Notes to Financial Statements	88

2. List of financial statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. List of Exhibits required by Item 601 of Regulation S-K. See paragraph (b) below.

(b) The following exhibits are filed as part of this report:

Exhibit Number	Description
3.1(1)	Amended and Restated Certificate of Incorporation of the Registrant
3.2(1)	Amended and Restated Bylaws of the Registrant
4.1(1)	Form of the Registrant's Common Stock Certificate
4.2(1)	Second Amended and Restated Investors' Rights Agreement dated November 20, 2006
4.3(2)	Registration Rights Waiver and Amendment dated January 6, 2008
10.1(1)	Form of Director and Executive Officer Indemnification Agreement
10.2(#)	Form of Executive Officer Employment Agreement
10.3#(1)	2004 Stock Plan and forms of option agreements thereunder
10.4#(1)	Independent Director Compensation Policy
10.5#(1)	2007 Equity Incentive Award Plan and forms of option and restricted stock agreements thereunder
10.6(1)	Lease dated September 22, 2006 by and between the Registrant and Prentiss/Collins Del Mar Heights LLC
10.7†(1)	License Agreement dated June 27, 2003 by and between the Registrant and Oregon Health & Science University
10.8†(1)	Amendment to License Agreement dated June 27, 2003 by and between the Registrant and Oregon Health & Science University
10.9†(1)	Letter Agreement Amendment to License Agreement dated June 27, 2003 by and between the Registrant and Oregon Health & Science University
10.10†(1)	License Agreement dated March 31, 2004 by and between the Registrant and Duke University
10.11†(1)	Amendment No. 1 to License Agreement dated March 31, 2004 by and between the Registrant and Duke University
10.12†(1)	Amendment No. 2 to License Agreement dated March 31, 2004 by and between the Registrant and Duke University
10.13†(1)	License Agreement dated June 1, 2004 by and between the Registrant and Lee G. Dante, M.D.
10.14†(1)	License Agreement dated January 3, 2005 by and between the Registrant and Cypress Bioscience, Inc.
10.15(1)	Credit and Security Agreement dated December 15, 2006 by and between the Registrant and Merrill Lynch Capital
10.16(1)	Settlement Agreement dated December 14, 2006 by and among the Registrant, Duke University, Elan Corporation, plc, Elan Pharma International Ltd., Elan Pharmaceuticals, Inc., Eisai, Inc., Eisai Co., Ltd. and Julianne E. Jennings
10.17(1)	Master Agreement for Pharmaceutical Development Services dated February 16, 2007 by and between Registrant and Patheon Pharmaceuticals Inc.
10.18†(3)	Consulting Agreement dated June 15, 2007 by and between the Registrant and PharmaDirections, Inc
10.19(4)	First Amendment to Credit and Security Agreement dated July 2, 2007 by and between the Registrant and Merrill Lynch Capital
1020#(5)	Amendment No. 1 to Employment Agreement dated August 22, 2007 by and between the Registrant and Gary D. Tollefson
10.21(6)	Settlement Agreement dated September 12, 2007 by and among the Registrant, Duke University, Eisai, Inc. and Eisai Co. Ltd.
10.22(7)	Second Amendment to Credit and Security Agreement dated November 6, 2007 by and between the Registrant and Merrill Lynch Capital
10.23(8)	Amendment No. 3 to License Agreement dated December 10, 2007 by and between the Registrant and Oregon Health & Science University
10.24(8)	Office Lease dated December 11, 2007 by and between the Registrant and Mullrock 3 Torrey Pines, LLC
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm

Exhibit Number	Description
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14 and Rule 15d-14 of the Securities Exchange Act of 1934, as amended
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14 and Rule 15d-14 of the Securities Exchange Act of 1934, as amended
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(1) Filed with the Registrant's Registration Statement on Form S-1 on December 19, 2006, as amended (File No. 333-139496).

(2) Filed with the Registrant's Current Report on Form 8-K on January 7, 2008.

(3) Filed with the Registrant's Current Report on Form 8-K on June 20, 2007.

(4) Filed with the Registrant's Current Report on Form 8-K on July 3, 2007.

(5) Filed with the Registrant's Current Report on Form 8-K on August 28, 2007.

(6) Filed with the Registrant's Current Report on Form 8-K on September 18, 2007.

(7) Filed with the Registrant's Current Report on Form 8-K on November 8, 2007.

(8) Filed with the Registrant's Current Report on Form 8-K on December 14, 2007.

† Confidential treatment has been granted for portions of this exhibit. These portions have been omitted from the Registration Statement and filed separately with the Securities and Exchange Commission.

# Indicates management contract or compensatory plan.

* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of Orexigen Therapeutics, Inc., whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

OREXIGEN THERAPEUTICS, INC.

By: /s/ Gary D. Tollefson
Gary D. Tollefson
President and Chief Executive Officer

Dated: March 27, 2008

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

Signature	Title	Date
/s/ Gary D. Tollefson, M.D., Ph.D. Gary D. Tollefson, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 27, 2008
/s/ Graham K. Cooper Graham K. Cooper	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 27, 2008
/s/ Eckard Weber, M.D. Eckard Weber, M.D.	Chairman of the Board of Directors	March 27, 2008
/s/ Louis C. Bock Louis C. Bock	Director	March 27, 2008
/s/ Brian H. Dovey Brian H. Dovey	Director	March 27, 2008
/s/ Joseph S. Lacob Joseph S. Lacob	Director	March 27, 2008
/s/ Michael F. Powell, Ph.D. Michael F. Powell, Ph.D.	Director	March 27, 2008
/s/ Daniel K. Turner III Daniel K. Turner III	Director	March 27, 2008

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Corporate Information

Management

Gary D. Tollefson, M.D., Ph.D.
President and Chief Executive Officer

Anthony A. McKinney
Chief Operating Officer

Graham K. Cooper
Chief Financial Officer and Treasurer

Michael A. Cowley, Ph.D.
Chief Scientific Officer

Eduardo Dunayevich, M.D.
Chief Medical Officer

Carol A. Baum
Vice President of Commercialization

Franklin P. Bymaster
Vice President of Neuroscience

Ronald P. Landbloom, M.D.
Vice President of Medical and Regulatory Affairs

Walter Piskorski
Vice President of Technical Operations

Heather D. Turner
Vice President, General Counsel and Secretary

Board of Directors

Eckard Weber, M.D.
Chairman of the Board of Directors

Louis C. Bock
Managing Director,
Scale Venture Partners

Brian H. Dovey
Managing Member,
Domain Associates LLC

Joseph S. Lacob
Partner, Kleiner Perkins
Caufield & Byers

Michael F. Powell, Ph.D.
Managing Director,
Sofinnova Ventures

Gary D. Tollefson, M.D., Ph.D.
President and Chief Executive Officer,
Orexigen Therapeutics, Inc.

Daniel K. Turner III
General Partner,
Montreux Equity Partners

Transfer Agent

American Stock Transfer & Trust Co.
59 Maiden Lane
New York, NY 10038
800-937-5449
www.amstock.com

2008 Annual Meeting

June 10, 2008

Independent Auditors

Ernst & Young LLP
4370 La Jolla Village Drive
Suite 500
San Diego, CA 92122

Legal Counsel

Latham & Watkins LLP
12636 High Bluff Drive
Suite 400
San Diego, CA 92130

Investor Information

Exchange: Nasdaq National Market
Symbol: OREX
Website: www.orexigen.com

Designed by Curran & Connors, Inc. / www.curran-connors.com

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(858) 875-8600
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END