Table of Contents

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, 2014

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.)*
3344 N. Torrey Pines Ct., Suite 200 La Jolla, California	**92037**
(Address of Principal Executive Offices)	*(Zip Code)*

(858) 875-8600
(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, $0.001 par value	**The NASDAQ Global Market**

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 whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☑ 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 ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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

As of June 30, 2014, the aggregate market value of common stock held by nonaffiliates of the registrant was approximately $711.0 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 February 23, 2015, the Registrant had 123,727,546 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 2015 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, 2014.

OREXIGEN THERAPEUTICS, INC.

FORM 10-K FOR THE FISCAL YEAR ENDED DECEMBER 31, 2014
TABLE OF CONTENTS

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, or Exchange Act, and is subject to the safe harbor provisions created by that statute. Forward-looking statements are based on our management's current beliefs, expectations 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," "probability" or other similar expressions that are intended to identify forward-looking statements.

These statements include but are not limited to statements regarding: the potential for Contrave®/Mysimba™ to achieve commercial success globally; the potential for and timing of the receipt of marketing authorization by the European Commission; the potential to obtain marketing authorizations or commercialization partner(s) for Contrave in territories outside of North America; the benefit risk profile for Contrave; the potential for past Contrave clinical trials to predict the outcome of future Contrave clinical trials; and the potential to demonstrate the real world weight loss potential of Contrave with a commercially available comprehensive lifestyle intervention program. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Actual results may differ materially from those expressed or implied in this report by the forward-looking statements due to the risk and uncertainties inherent in our business, including the ability for Mysimba to obtain marketing authorization in Europe; the ability to obtain partnerships and marketing authorizations globally; competition in the global obesity market, particularly from existing therapies; the possibility that the public announcement of the results of the interim analysis would later be deemed to jeopardize the integrity of the Light Study potentially resulting in the requirement to conduct additional, costly studies; additional analysis of the interim results or new data from the continuing Light Study, including safety-related data, and the additional cardiovascular outcomes trial, may produce negative or inconclusive results, or may be inconsistent with the conclusion that the interim analysis was successful; the results from the interim analysis may not be sufficient to satisfy or respond to the data requirements of the EMA in connection with the review of our community marketing authorization application for Mysimba; our dependence on Takeda to carry out the commercial launch of Contrave in North America; our ability to obtain and maintain global intellectual property protection for Contrave and Mysimba; the potential that the interim analysis of the Light Study may not be predictive of future results in the Light Study or other clinical trials; the potential for early termination of our collaboration agreement with Takeda; the therapeutic and commercial value of Contrave and Mysimba; our ability to maintain sufficient capital to fund our operations for the foreseeable future; estimates of the capacity of manufacturing and other facilities to support Contrave; and the other risks and uncertainties discussed under the heading "Item 1A—Risk Factors," and elsewhere in this in this Annual Report on Form 10K.

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. Except as required by law, 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 treatment of obesity. Our product, Contrave®, was approved in the United States by the U.S. Food and Drug Administration, or FDA, in September 2014 as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index, or BMI, of 30 kg/m^2 or greater (obese), or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

In October 2013, we submitted an application for marketing authorization with the European Medicines Agency, or EMA, for Contrave under the name Mysimba™. In December 2014, the Committee for Medicinal Products For Human Use, or CHMP, of the EMA adopted a positive opinion recommending the European Commission, or EC, grant a centralized marketing authorization, or CMA, for Mysimba. The CHMP recently released minutes from their December meeting stating that the positive opinion for Mysimba was adopted by a majority vote with 31 members in favor and two opposed. Procedurally, a positive opinion and recommendation of the CHMP is then referred to the EC's Standing Committee for Medicinal Products, or Standing Committee, which is composed of representatives from each member state of the European Union, or E.U. The EC recently informed us that at the request of one member state, the draft EC decision granting marketing authorization for Mysimba will be reviewed during a meeting of the Standing Committee being held in March 2015. A positive decision issued by the EC in favor of granting a CMA would allow Mysimba to be placed on the market in all 28 E.U. member states, as well as Iceland, Liechtenstein and Norway.

The obesity epidemic is one of the largest public health challenges the world is currently facing. Approximately 500 million adults worldwide have a BMI equal or greater than 30 and are considered obese. Approximately 3.4 million deaths annually are attributed directly to individuals being obese or overweight. In light of this epidemic, we are developing Contrave and Mysimba for large markets traditionally served by primary care physicians. In September 2010, we entered into a collaboration agreement with Takeda Pharmaceutical Company Limited, or Takeda, to develop and commercialize Contrave in the United States, Canada and Mexico. Subject to certain terms and conditions, the collaboration agreement allows us to co-promote Contrave in the United States. We currently retain marketing rights for Contrave outside the United States, Canada and Mexico.

We believe in the long-term value of our product in the United States, the E.U. and elsewhere and our strategy for Contrave is to pursue marketing authorizations worldwide and pharmaceutical partnerships for global commercialization. We endeavor to find high-performing partners that share our vision for Contrave and will allow us to address the obesity epidemic in a meaningful way for the entire potential patent life of our drug. With Contrave approved for marketing in the United States, we believe this positions us for regulatory approvals in many other countries, with the goal of establishing a global brand in many territories worldwide. In addition to establishing partnerships for the potential commercialization of Contrave outside the United States, Canada and Mexico, we are also exploring development opportunities to enhance the clinical profile of Contrave by seeking to maximize its utility in its targeted population, as well as studying Contrave in additional indications and populations, new formulations and in combination with other products to assess its potential to treat other conditions, including a common comorbidity to obesity, type 2 diabetes.

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. Upon FDA approval of Contrave, we received three years of exclusivity under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch Waxman Act. Moreover, we hold patents in the United States and Europe that cover the composition of Contrave (bupropion HCl ER/naltrexone HCl ER), as well as the use of Contrave for the treatment of obesity. These U.S. patents expire in 2025 and 2024, respectively. 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.

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 2010, the obesity rate had more than doubled to approximately 36% of the U.S. population of adults over 20 years of age, according to the United States Centers for Disease Control and Prevention, or the CDC. According to a November 2009 report from the United Health Foundation, the American Public Health Association and Partnership for Prevention, it is estimated that by 2018, 43% of the U.S. adult population will be obese. In addition, obesity rates are projected to exceed 50% in 39 U.S. states by 2030, according to an October 2012 article in the Journal of the American Medical Association.

The growing prevalence of obesity has increasingly been recognized as a significant public health problem. The CDC has identified obesity as a chronic disease that is one of the leading causes of preventable deaths 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 1.4 billion people worldwide considered to be overweight, of which at least 500 million are estimated to be obese. As a result, private and governmental entities worldwide are beginning to take steps to fight against obesity. The American Medical Association recently recognized obesity as a disease and a European court recently ruled obesity may be considered a disability. The Patient Protection and Affordable Care Act, or PPACA, allows corporate wellness programs to address obesity with economic incentives and the Treat and Reduce Obesity Act has strong support and a reintroduction to the U.S. Congress is currently being planned. In 2013, the American Association of Clinical Endocrinologists, or AACE, published treatment guidelines for obese or overweight patients with type 2 diabetes or pre-diabetes that include anti-obesity pharmacotherapy in conjunction with lifestyle modification for certain patients and the European Association for the Study of Obesity calls for use of pharmacotherapy as part of a comprehensive strategy for disease (obesity) management.

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 Obesity Society. Beyond these consequences, a number of co-morbidities involving the central nervous system, or CNS, may be complicated by obesity. These co-morbidities include anxiety, depression, substance abuse, chronic pain and insomnia. According to our market research, physicians in the United States report that approximately 63% of their obese patients have been diagnosed with depression or display signs and symptoms of untreated depression. As seen in the 2013 AACE guidelines, we believe there is a growing recognition within the medical community that obesity significantly exacerbates these conditions and other co-morbidities. We expect that more effective pharmacological treatment of obesity may also be a cornerstone in managing its co-morbidities.

Obesity and its co-morbidities are believed to cause significant added cost to the health care system. According to a January 2012 article in the Journal of Health Economics, annual U.S. obesity-related medical costs amount to an estimated $209.7 billion, which means that approximately 20.6% of U.S. national health expenditures are spent treating obesity-related illness. A 2009 study examining the future impact of obesity on direct health care expenses projected these expenditures to increase to approximately $344 billion per year by 2018. Obesity has been linked to a more than one-quarter increase in health spending since the mid-1980s. Despite the obesity rate, increasing public interest in the obesity epidemic and significant medical repercussions and economic costs associated with obesity, we believe there continues to be a need for more effective pharmacological interventions.

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. By 2008, the number of total U.S. prescriptions for obesity products had increased to only approximately 6.8 million. In 2012, we conducted quantitative market research with 1,000 physicians, that suggest the U.S. market for obesity therapeutics could grow three to four fold within five years from a 2012 base of approximately 8 million prescriptions. While there has been a broad recognition of obesity as a public health crisis, we believe that the obesity epidemic will continue to be a major cause of morbidity, mortality and excess health care costs in the United States. The history of this obesity epidemic, combined with the substantial economic cost associated with obesity, we believe underscores the unmet need and the potential for novel therapeutics to continue to dramatically grow the market for obesity therapies.

The Orexigen Solution for Obesity

Contrave regulates appetite and energy expenditure through CNS activity. We believe, and our research suggests that the CNS plays an important role in the 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 contains numerous redundant circuits and compensatory mechanisms to maintain body weight, which 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). 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 weight loss products that do not work by acting on the CNS 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 weight loss plateau typically seen after several months or a year of therapy. In addition, they generally do not address the behavioral elements that contribute to unhealthy eating behaviors and, ultimately, obesity. We believe Contrave sustains weight loss by preventing the body's natural tendency to counteract efforts to lose weight. In addition, we are attempting to target the underlying behavioral mechanisms of craving and reward that drive excess consumption.

Contrave (Mysimba)

Contrave is a fixed dose combination of bupropion HCl extended release, or ER, and naltrexone HCl ER. We chose these constituents based on 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 patents in the United States that cover the composition of Contrave (bupropion HCl/naltrexone HCl ER), as well as the use of Contrave for the treatment of obesity. We have also filed additional U.S. patents covering various aspects of Contrave. In addition, we own or have exclusive rights to numerous patent applications currently pending in various jurisdictions outside of the United States with respect to compositions, methods of use and formulations relating to Contrave.

Naltrexone was approved in the United States in 1984 for the treatment of opioid addiction and in 1994 for the treatment of alcoholism. It is marketed under the brand names ReVia®, and in an injectable extended release formulation, Vivitrol®, which was approved in 2006 for the treatment of alcohol dependence and expanded in 2010 to include prevention of relapse to opioid dependence. Naltrexone immediate release formulation 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. Nausea is a well-known side effect associated with naltrexone immediate release that affects its tolerability. In our Contrave Phase II clinical trials, we used the generic immediate release formulation of naltrexone. In our Phase III clinical trials, naltrexone was delivered in our proprietary ER 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 immediate release 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. In the 12-month period ending in August 2012, prescriptions of bupropion in the United States totaled approximately 26.6 million, 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 in clinical trials for the treatment of depression was modest weight loss. Subsequently, bupropion has been studied for weight loss; results have shown approximately 3% placebo-corrected 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 proopiomelanocortin, or POMC, neurons within an area in the hypothalamus known as the arcuate nucleus. Increased firing of POMC neurons appears to lead to a reduction of appetite and an increase in energy expenditure. This is a major pathway by which naturally occurring peptides regulate body weight. Bupropion-induced stimulation of POMC activates this weight loss pathway.

Stimulation of POMC also produces beta-endorphin, an opioid occurring naturally in the body. Our early research identified a receptor on the POMC neuron that recognizes beta-endorphin. We 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 as a likely compensatory mechanism to preserve body mass. Based on this discovery, we chose naltrexone as the second component in Contrave because it is a potent opioid receptor antagonist which competes with beta-endorphin, thus limiting its access at the 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. We expect this to translate into a greater weight loss that should be sustainable over an extended time period.

As a second attribute, 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. 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 anticipate that Contrave may have an additional therapeutic attribute for patients who report food craving or obsession, helping them manage their eating behavior.

The COR Program

We conducted controlled Phase II and Phase IIb clinical trials for Contrave in a total of 657 patients. Based on the results of these trials, we concluded that Contrave showed sufficient efficacy as compared to each individual monotherapy and placebo and an acceptable safety and tolerability profile to warrant continued development in pivotal Phase III clinical trials.

Our Phase III program for Contrave was comprised of four distinct clinical trials that evaluated more than 4,500 patients. Based on our Phase II and Phase IIb trial results and feedback from the FDA, these four Phase III clinical trials in our COR program were designed to assess three doses of naltrexone ER (16mg, 32mg and 48mg) in combination with a 360mg dose of bupropion ER. All trials in the COR program were 56-week, randomized, double-blind, placebo-controlled trials.

The four Phase III clinical trials in the COR program are described as follows:

- COR-I: A trial designed to assess the safety, tolerability and efficacy of Contrave (32mg naltrexone ER plus 360mg bupropion ER) and NB16 (16mg naltrexone ER plus 360mg bupropion ER) versus placebo in 1,742 overweight/obese patients. This trial incorporated a typical diet and exercise regimen and was conducted across 34 U.S. centers.
- COR-II: A trial designed to assess the safety, tolerability and efficacy of Contrave versus placebo in 1,496 overweight/obese patients. This trial incorporated a typical diet and exercise regimen and was conducted across 36 U.S. centers. After week 28, patients not achieving at least 5% weight loss were re-randomized in a blinded fashion to assess whether increasing the dose to NB48 (48mg naltrexone ER plus 360mg bupropion ER) would result in additional weight loss.
- COR-Diabetes: A trial designed to assess the safety, tolerability and efficacy of Contrave versus placebo in 505 overweight/obese patients with Type 2 diabetes. This trial incorporated a typical diet and exercise regimen and was conducted across 53 U.S. centers.
- COR-BMOD: A trial designed to assess the safety, tolerability and efficacy of Contrave versus placebo in 793 overweight/obese patients in combination with an intensive behavior modification protocol, including dietary counseling, behavioral therapy and exercise. This trial was conducted across nine U.S. centers. This trial included the most intensive behavior modification regimen of the COR program, which resulted, as expected, in a high degree of weight loss among placebo patients.

The co-primary endpoints for all four Phase III clinical trials in the COR program were the proportion of patients achieving at least 5% weight loss and percent change in body weight compared to placebo. The co-primary endpoints for COR-I, COR-Diabetes and COR-BMOD were all measured at 56 weeks. The co-primary endpoints for COR-II were measured at 28 weeks. These endpoints were analyzed using a modified intent-to-treat, or ITT, last observation carried forward on treatment, or LOCF, of all randomized patients who had at least one post-baseline observation while on study drug. Contrave was administered twice a day with a three week escalation period in COR-I, COR-Diabetes and COR-BMOD. Contrave was administered twice a day with a four week escalation period in COR-II. All four Phase III clinical trials met their co-primary endpoints.

The 56-week results for all four clinical trials in the COR program are as follows:

	COR-I			
	ITT		Completers†	
	56 weeks		56 weeks	
	Contrave (n=471)	Placebo (n=511)	Contrave (n=296)	Placebo (n=290)
Mean Weight Loss (%)	6.1%*	1.3%	8.1%*	1.8%
Mean Weight Loss (lbs)	13.3*	3.0	17.5*	4.1
Greater than or equal to 5% weight loss (%)	48.0%*	16.4%	61.8%*	23.1%
Greater than or equal to 10% weight loss (%)	24.6%*	7.4%	34.5%*	10.7%

* Difference from placebo, $p<0.001$

† Those patients completing 56 weeks of treatment.

ITT, LOCF patients administered NB16 (n=471) experienced mean weight loss from baseline of 5.0% at 56 weeks; 39.5% of patients lost greater than or equal to 5% of their body weight at 56 weeks and 20.2% of patients lost greater than or equal to 10% of their body weight at 56 weeks.

	COR-II			
	ITT†		Completers**	
	56 weeks‡		56 weeks‡	
	Contrave (n=702)	Placebo (n=456)	Contrave (n=434)	Placebo (n=267)
Mean Weight Loss (%)	6.4%*	1.2%	8.2%*	1.4%
Mean Weight Loss (lbs)	13.8*	2.9	17.5*	3.4
Greater than or equal to 5% weight loss (%)	50.5%*	17.1%	64.9%*	21.7%
Greater than or equal to 10% weight loss (%)	28.3%*	5.7%	39.4%*	7.9%

† Co-primary endpoints for COR-II were the proportion of patients achieving at least 5% weight loss and percent change in body weight compared to placebo at 28 weeks. ITT patients (n=1,281) at 28 weeks experienced mean weight loss from baseline of 6.5% versus 1.9% for placebo; 55.6% of patients lost greater than or equal to 5% of their body weight at 28 weeks versus 17.5% for placebo and 27.3% of patients lost greater than or equal to 10% of their body weight at 28 weeks versus 7.0% for placebo.

** Those patients completing 56 weeks of treatment.

‡ Pre-specified exploratory analysis; Contrave patients not achieving 5% weight loss double weighted because NB48 patients were excluded from efficacy analysis. There was no statistical difference between patients re-randomized to Contrave or NB48.

* Difference from placebo, p<0.001

	COR-BMOD			
	ITT		Completers†	
	56 weeks		56 weeks	
	Contrave (n=482)	Placebo (n=193)	Contrave (n=301)	Placebo (n=106)
Mean Weight Loss (%)	9.3%*	5.1%	11.5%*	7.3%
Mean Weight Loss (lbs)	20.3*	11.0	25.0*	16.0
Greater than or equal to 5% weight loss (%)	66.4%*	42.5%	80.4%*	60.4%
Greater than or equal to 10% weight loss (%)	41.5%*	20.2%	55.2%*	30.2%

* Difference from placebo, p<0.001

† Those patients completing 56 weeks of treatment.

	COR-DIABETES			
	ITT		Completers†	
	56 weeks		56 weeks	
	Contrave (n=265)	Placebo (n=159)	Contrave (n=175)	Placebo (n=100)
Mean Weight Loss (%)	5.0%*	1.8%	5.9%*	2.2%
Mean Weight Loss (lbs)	11.6*	4.2	13.5*	5.1
Greater than or equal to 5% weight loss (%)	44.5%*	18.9%	53.1%*	24.0%
Greater than or equal to 10% weight loss (%)	18.5%*	5.7%	26.3%*	8.0%

* Difference from placebo, p<0.001

† Those patients completing 56 weeks of treatment.

Secondary endpoints included multiple measures of cardiometabolic risk, food cravings and eating control. Measures of hemoglobin A1c, or HbA1c, and other measures of glycemic control were also key secondary endpoints in the COR-Diabetes trial. Secondary endpoints that demonstrated clinically and statistically significant improvements over placebo across the entire COR program included cardiometabolic risk factors such as waist circumference, HDL cholesterol and triglycerides. Patients enrolled in the COR program also experienced reductions in the frequency and strength of food cravings and an increased ability to control their eating compared to placebo. In the COR-Diabetes trial, patients administered Contrave showed a reduction in HbA1c of 0.6% from baseline, compared to a 0.1% reduction in placebo.

The overall discontinuation rates across the COR program ranged from 42% to 51% for the Contrave treated groups compared to 41% to 50% for the placebo groups. The discontinuation rates due to adverse events across the COR program ranged from 19% to 29% for the Contrave treated groups compared to 10% to 15% for the placebo groups. The most frequent adverse events leading to discontinuation for patients taking Contrave were nausea, headache, vomiting and dizziness. Nausea was the leading adverse event resulting in discontinuation; however, for the majority of patients experiencing nausea, it was mild to moderate, transient and manageable. The most frequently observed treatment-emergent adverse events were nausea, constipation and headache. Across the entire COR program, seven serious adverse events were attributed by investigators as possibly related to Contrave treatment. These consisted of cholecystitis (gallbladder inflammation) (2), seizure (2), palpitations (1), paresthesia (1) and vertigo (1). In addition, there was one death of a patient on Contrave that was not attributed by investigators as related to Contrave treatment, but rather was attributed to a cardiovascular serious adverse event. At week 56, mean blood pressure was generally unchanged from baseline for Contrave patients, compared to placebo patients who tended to experience a slight decrease (approximately 2 mm Hg) from baseline. Contrave treatment did not appear to disrupt the normal circadian pattern of blood pressure. There was a slight increase in pulse (approximately 1 beat per minute) in Contrave patients, compared to placebo patients whose pulse was generally unchanged. There were no meaningful treatment effects on ECGs or laboratory measures including liver function tests. Treatment with Contrave was not associated with increases in symptoms of depression or suicidal ideation.

We believe that our clinical trial experience with Contrave has demonstrated and replicated the validity of our scientific hypothesis, specifically, that the administration of naltrexone with bupropion enables greater weight loss than bupropion alone and sustains weight loss beyond 24 weeks. 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.

The Light Study

Following the results of our COR program, we submitted a New Drug Application, or NDA, for Contrave to the FDA in March 2010. In January 2011, we received a complete response letter, or CRL, from the FDA regarding our NDA for Contrave. A CRL is issued by the FDA when the review of an NDA is completed and questions remain that preclude the approval of the NDA in its current form. The CRL for Contrave indicated that the FDA could not approve the NDA in its present form primarily due to concerns regarding the cardiovascular safety profile of Contrave when used long-term in a population of overweight and obese patients. The CRL stated that before our NDA could be approved, we must conduct a randomized, double-blind, placebo-controlled trial of sufficient size and duration to demonstrate that the risk of major adverse cardiac events, or MACE, in overweight and obese patients treated with Contrave does not adversely affect the drug's benefit-risk profile.

In September 2011, following a meeting with senior officials in the FDA's Office of New Drugs, or OND, we received written correspondence from the director of the OND detailing the OND's design requirements for a randomized, double- blind, placebo-controlled cardiovascular outcomes trial, or CVOT, for Contrave that would address the CRL. We initiated the CVOT, which we refer to as the Light Study, in June 2012 and completed screening in December 2012, which resulted in approximately 8,900 patients randomized to treatment. We enrolled a patient population that we predicted would have an annualized MACE rate between 1% and 2%. The FDA previously agreed that if the interim analysis of the Light Study meets the specified criteria to exclude cardiovascular risk, Contrave could be approved. The pre-specified criteria for the interim analysis is to exclude a hazard ratio of 2.0, using the upper bound of the 95% confidence interval, for excess risk MACE in patients receiving Contrave as compared to placebo. In November 2013, we announced successful results of the interim analysis of the Light Study. In addition to meeting the pre-specified criteria for excluding cardiovascular risk, no new safety signals were observed. Contrave was approved for commercial use by the FDA in September 2014.

The Light Study is a randomized, double-blind, placebo-controlled cardiovascular outcomes trial that is being conducted at approximately 265 sites in the United States. The primary objective of the Light Study is to

assess Contrave (32 mg naltrexone ER/360 mg bupropion ER) compared to placebo on the occurrence of MACE (cardiovascular death, nonfatal myocardial infarction or nonfatal stroke) in overweight and obese patients. Weight loss is not a primary or secondary objective of the Light Study as it is primarily a safety trial and the efficacy benchmark has already been established as acceptable from our Phase III COR program. After a double-blind lead-in period was conducted to exclude patients who exhibit characteristics predictive of lack of compliance or who do not tolerate treatment with Contrave well, approximately 8,900 eligible patients were randomized with either Contrave or placebo in a 1:1 ratio. The duration of the randomized treatment period (or patient follow-up period for those who discontinue study drug early) is estimated to be between 2-4 years for most patients. The estimated average duration of blinded study drug exposure is approximately 4-6 months at the time of the interim analysis depending on when the interim analysis occurs and 1.4 years at the time of the final analysis.

All patients, regardless of randomized treatment assignment, will participate in a weight management program tailored for the Light Study. We believe this is a significant value proposition to enhance retention in the Light Study. At week 16 there was an evaluation of weight loss relative to baseline observations. At that time, patients were discontinued from study drug if they had not lost at least 2% of their body weight or if they sustained (e.g., at 2 or more visits) increases in blood pressure (systolic or diastolic) of 10 mm Hg or greater, so only appropriate responders moved forward on the study drug after week 16. The Light Study is a large but streamlined trial without frequent site visits or intensive data collection, such as on-trial blood draws. Every two months between visits beyond week 26, patients will be asked to answer specific questions pertaining to compliance and hospitalizations (potential MACE or serious adverse events), using an internet- or telephone-based data collection system. Following FDA approval in September 2014, the responsibility for the continuation and completion of the Light Study trial was transferred to our partner, Takeda. The Light Study is currently expected to continue, blinded, until the trial is completed.

Post-Marketing Requirements. As part of the FDA approval of Contrave, we and Takeda agreed to several post-approval requirements, including studies to assess the safety and efficacy of Contrave for weight management in obese pediatric patients. There will also be a new randomized, double-blind, placebo-controlled study to evaluate the effects of long-term treatment with Contrave on the incidence of MACE in overweight and obese subjects with cardiovascular disease or multiple cardiovascular risk factors.

Open-Label Study for Smoking Cessation. We conducted an exploratory, open-label 24-week clinical trial of Contrave for smoking cessation in overweight or obese patients. This trial was conducted in 30 patients across three U.S. centers. The primary endpoint for this trial was the rate of smoking cessation as defined by patient-reported continuous abstinence during weeks 4-12. Secondary endpoints, which were measured at week 12 and 24, included: rate of smoking cessation as defined by patient-reported continuous abstinence during weeks 4-24; percent change from baseline in total body weight; and a number of other key measures. Additionally, measures of safety and tolerability were evaluated. The endpoints were analyzed using ITT, LOCF.

In this trial, Contrave significantly reduced cigarette use among obese patients trying to quit smoking and was not associated with clinically meaningful weight gain. The smoking cessation rates as measured by patient-reported continuous abstinence were 48.1% and 40.7% at week 12 and 24, respectively. Improvements were also seen in a number of key secondary endpoints. The most frequent adverse events were nausea, insomnia and constipation. These tended to be transient and mild or moderate in severity. No serious adverse events occurred. Five patients withdrew from this trial due to adverse events.

Open-Label Study for Obese Depressed Patients. We conducted an exploratory, open-label 24-week clinical trial assessing the safety and efficacy of Contrave in overweight or obese patients with major depression. This trial was a single-center trial conducted in 25 patients. The primary endpoint for this trial was the change from baseline in the Montgomery-Asberg Depression Rating Scale, or MADRS, total score at Week 12. Secondary endpoints included change from baseline in the MADRS total score at Week 24, as well a number of other key measures. Additionally, measures of safety and tolerability were evaluated. The endpoints were analyzed using ITT, LOCF.

In this trial, Contrave showed a clinically significant reduction in depressive symptoms in the study population, as evidenced by mean decreases from baseline in MADRS total scores of more than 50% at weeks 12 and 24. Improvements were also seen in a number of key secondary endpoints. The most frequent adverse events were nausea, constipation, headache and insomnia. These adverse events tended to be moderate in severity. No serious adverse events occurred during the trial that were attributed to treatment with Contrave. Ten patients withdrew from the trial due to adverse events.

The Ignite Study. In February 2013, we commenced a randomized, open-label clinical trial of 242 patients, which we refer to as the Ignite Study. The Ignite Study is designed to provide additional information regarding the real world weight loss potential of Contrave in combination with a commercially available comprehensive lifestyle intervention program, compared to patients who receive diet and exercise advice from the study site staff but who do not receive Contrave. Consistent with current labeling for recently approved anti-obesity medications, patients in the Ignite Study must achieve a certain amount of weight loss (at least 5% at week 16) and must not have a meaningful increase in blood pressure to remain on medication. The primary endpoint for this trial is change in body weight after 26 weeks. Secondary endpoints include the percentage of patients achieving at least 5% and 10% weight loss, waist circumference, lipids, and measures of glucose homeostasis, as well as a number of other key measures. The primary analysis population is the 26-week per-protocol population.

European Marketing Authorization Application. In October 2013, we submitted a centralized marketing authorization, or CMA, application for Contrave, under the name Mysimba, to the EMA. We utilized the EMA's centralized procedure, seeking approval of Mysimba in the European Economic Area, or EEA (which is comprised of the 28 Member States of the E.U., as well as Norway, Iceland and Liechtenstein), for the management of obesity, including weight loss and maintenance of weight loss, in conjunction with lifestyle modification. As part of this process, we have established the required pediatric investigation plan, or PIP, which has been agreed to by the EMA's Pediatric Committee. The centralized procedure, for which Mysimba is eligible, allows for the simultaneous market access of a product in all the Member States of the EEA. A CMA application is reviewed by the CHMP. After submission and validation of the CMA application, the CHMP generally has 210 days to complete its assessment and adopt an opinion on whether or not to recommend the granting of the CMA. The 210 day period does not include the anticipated "clock stops" at specified points in the procedure, typically at day 120 (Consolidated List of Questions) and at day 180 (List of Outstanding Issues). The clock stops allow time for us to address the outstanding questions or issues raised by the CHMP. At day 180, depending on the List of Outstanding Issues, an oral hearing with the CHMP may be required to address specific issues. Assuming a positive opinion from the CHMP, a final CMA is granted by the EC in the form of a binding decision on day 277 of the procedure counting form the date of start of centralized assessment procedure, not counting clock stops as noted above.

In December 2014, the CHMP adopted a positive opinion recommending the EC grant a CMA for Mysimba. The CHMP recently released minutes from their December meeting stating that the positive opinion for Mysimba was adopted by a majority vote with 31 members in favor and two opposed. Procedurally, a positive opinion and recommendation of the CHMP is then referred to the EC's Standing Committee, which is composed of representatives from each member state of the E.U. In a process that occurs either through a written procedure or in a meeting, the Standing Committee reviews the draft EC decision to grant marketing authorization. Draft decisions are adopted by majority vote. The EC recently informed us that at the request of one member state, the draft EC decision granting marketing authorization for Mysimba will be reviewed during a meeting of the Standing Committee to be held in March 2015. A positive decision by the Standing Committee would allow Mysimba to be placed on the market in all 28 E.U. member states, as well as Iceland, Liechtenstein and Norway.

Sales and Marketing

Contrave was developed to compete in historically large therapeutic markets traditionally served by primary care physicians. In order to effectively educate and promote Contrave to these physicians and maximize the value

of Contrave, in September 2010, we entered into a collaboration agreement with Takeda to develop and commercialize Contrave in the United States, Canada and Mexico. Subject to certain terms and conditions, the collaboration agreement allows us to co-promote Contrave in the United States. We currently retain marketing rights for Contrave outside the United States, Canada and Mexico. We may consider entering into additional collaborations with other pharmaceutical companies for territories outside the United States, Canada and Mexico with the sales force and marketing resources to adequately address the large primary care physician audience.

Contrave was recently launched commercially in the United States by our partner, Takeda, in October 2014. Takeda provides us with the sales, managed care, and marketing commercial expertise and capabilities to increase brand awareness and drive early trial, adoption, and long-term effective and safe usage of Contrave.

We are coordinating efforts with Takeda to ensure that we launch an integrated and innovative educational and promotional Contrave brand campaign to targeted health care providers that treat obesity as a chronic medical disease. By leveraging the knowledge-base and expertise of our experienced commercial team and the commercial team at Takeda, we believe we can continually improve our collective marketing strategies.

Maximizing the Value of Contrave in the U.S.

Our objective is to establish Contrave as the prescription product of choice for the treatment of obesity. Together with Takeda, we believe we are building awareness that obesity is a chronic disease and that modest weight loss is associated with reduced risk of cardio-metabolic diseases such as Type 2 diabetes and improved overall health.

Takeda has demonstrated the ability to successfully launch innovative products, penetrate primary care markets and drive the growth of multiple brands in highly competitive markets. Takeda brings large and experienced sales, national accounts, trade relations, operations and management teams providing ready access to primary care offices and key managed care accounts.

In order to continue to maximize the value, compete effectively, and successfully launch Contrave in this large emerging primary care obesity prescription weight loss market, we and Takeda are committed to providing our health care providers and their obese patients with access to a complete weight-management approach at an affordable value price focusing our commercialization efforts in the following areas:

- Physician education: Our physician education plan encompasses efforts to reach out with frequency to the highest prescribing primary care physicians and endocrinologists helping them identify appropriate and motivated patients, educating them on the clinical profile of Contrave, and enabling them to assess the clinical benefits of Contrave.
- Patient education: Our patient education plan encompasses efforts to reach out to appropriate and motivated patients that are obese or overweight with one or more cardio metabolic co morbidity through in office direct-to-patient education and direct-to-consumer education, including both traditional and digital channels, to educate them on the health benefits of modest weight loss, how to discuss their weight with their health care provider, how to safely and effectively take Contrave, and the weight management support program and tools available to them.
- Scale Down weight-management patient support program, or Scale Down: Scale Down is a clinically proven effective personalized weight-management program developed by Harvard-trained researchers that engages patients on their weight loss journey providing them with mobile weight-management support with a wireless scale that triggers daily personalized texts based on weigh-ins. This program helps patients keep track of their weight over time. Scale Down is available at no cost to all eligible patients taking Contrave.

- Contrave pharmacy savings card program: This program provides all eligible patients access to Contrave at their retail pharmacies at an affordable low cost. Patients prescribed Contrave with insurance coverage pay $55 for the first two months of therapy and then $45 per month thereafter. Patients without insurance coverage pay $70 per month for the first two months of therapy and then $60 per month thereafter.

Based on the existing burden of illness, the high and increasing health care cost associated with obesity and associated co-morbid diseases, the efficacy and safety profile of Contrave that was demonstrated through its clinical development program, and the health benefits associated with modest weight loss, we believe we are providing a strong value proposition to governmental authorities, private health insurers and other third-party payers. We understand that sufficient access and reasonable reimbursement are essential in order to optimize the commercial potential of Contrave.

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. We own or have exclusive rights to several patent application families currently pending in the United States with respect to various compositions, methods of use and formulations relating to Contrave. 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 by U.S. patent number 7,375,111, which we refer to as the Weber/Cowley composition patent, and U.S. patent number 7,462,626, which we refer to as the Weber/Cowley methods patent. Provided maintenance fees are paid, the Weber/Cowley composition patent is expected to expire in March 2025, and the Weber/Cowley methods patent is expected to expire in July 2024. Collectively, we refer to the Weber/Cowley composition patent and the Weber/Cowley methods patent as the Weber/Cowley patents. Each of these stems from a provisional patent application that we own but that is the subject of an agreement with the Oregon Heath & Science University, or OHSU, requiring us to pay them specified royalties on sales of products covered by the patent applications. This agreement is described in further detail below. The Weber/Cowley patents cover the current composition of Contrave and methods of administering it to treat obesity. We have also filed a number of international counterparts to these patent applications in foreign countries. The European Patent Office, or EPO, has granted the European version of the Weber/Cowley patent, which published as EP1617832 B1. This EP patent has issued in numerous countries throughout the European Union and provides coverage for Contrave until at least 2024. Use of our proprietary tri-layer Contrave tablet for weight loss is protected in the United States by U.S. patent numbers 8,088,786 and 8,318,788, which are expected to expire in February 2029 and November 2027, respectively. In addition, use of our proprietary sustained-release formulation of Contrave for weight loss is protected by U.S. patent number 8,916,195 which is expected to expire in February 2030. Additional patent applications related to Contrave remain pending in the U.S. and throughout the world.

We have also filed patent applications in the United States and certain foreign countries 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. Such steps have been taken in various foreign countries, including countries in Europe and Japan, with respect to our PCT filings directed to various treatment and formulation aspects of Contrave. Thus, we now have patent applications pending in those countries (along with our previous filings in the United States and certain non-PCT countries) that seek to provide further protection for Contrave. However, we cannot provide assurance that the claims in these patent applications will issue in their current form or at all.

We have received U.S. trademark registration number 3393576 for the mark CONTRAVE for use in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss. An

application for the CONTRAVE mark has been allowed in the United States in connection with certain printed materials and medical information services. We have also obtained foreign trademark registrations for the mark CONTRAVE in Canada, Europe and Japan. In addition, applications for a Contrave logo for use in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss, certain printed materials and medical information services has been filed in the U.S., and is pending in Canada. The Contrave logo is also registered in Europe and Japan.

We have received U.S. trademark registration number 3396021 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. We have obtained trademark registrations in Canada, Europe and Japan for the same mark. In addition, we have received U.S. trademark registration number 3396807 for our corporate name OREXIGEN for use in connection with pharmaceutical preparations for the treatment of disorders of the CNS, printed instructional, educational and teaching materials in the field of treatment and management of disorders of the CNS, and providing medical information in the field of disorders of the CNS. We have obtained trademark registrations in Canada, Europe and Japan for the same mark. We have obtained foreign trademark registrations for the corporate name Orexigen Therapeutics, Inc. in Europe and Japan.

Collaboration and Licensing Agreements

Collaboration Agreement with Takeda Pharmaceutical Company Limited

In September 2010, we entered into a collaboration agreement with Takeda to develop and commercialize Contrave in the United States, Canada and Mexico. Under the terms of the collaboration agreement, we received an upfront cash payment of $50 million from Takeda and payments totaling $100 million upon receipt of regulatory approval and the first commercial sale of Contrave in the United States. We are eligible to receive additional payments of over $900 million upon achieving certain anniversary, regulatory and sales-based milestones, including $45 million in anniversary milestones. We are also eligible to receive tiered royalty payments ranging from a minimum of 20% to a maximum of 35%, subject to customary reductions, on increasing levels of net sales in the United States, Canada and Mexico.

The collaboration agreement provides that Takeda will be responsible for commercialization costs and activities. Takeda has agreed to use commercially reasonable efforts in commercializing Contrave in the United States, Canada and Mexico in addition to specified commercial diligence commitments in the first three years in the United States after product launch, if at all. Subject to certain terms and conditions, the collaboration agreement also allows us to co-promote Contrave in the United States and, subject to certain limitations, Takeda shall be responsible for certain commercialization costs associated with our co-promote sales force.

We were responsible for all costs for development activities conducted prior to approval of the NDA for Contrave by the FDA in September 2014. Following the FDA approval, both parties conduct development activities; however, we have the right to perform a certain percentage of such activities. Once we have paid for $60 million of post-approval development activities, Takeda will generally be responsible for 75% of the post-approval development costs and we will be responsible for 25% of such costs, except for certain clinical safety trial costs for which we will be responsible for 50% of such costs.

As a part of the collaboration agreement, Takeda has committed to purchase its requirements of Contrave from us. Pursuant to an amendment to the collaboration agreement entered into in October 2013, Takeda assumed from us the responsibility to package Contrave for commercial sale. At any time during the term of the collaboration agreement, Takeda may elect, subject to certain terms and conditions, to transfer and assume the right and responsibility to manufacture Contrave in the United States, Canada and Mexico.

Both parties have agreed not to commercialize any other pharmaceutical product for the treatment of obesity or weight management through a specified date, other than Contrave and any product owned or controlled by either party as of the date of the collaboration agreement.

Unless earlier terminated, the term of the collaboration agreement shall expire on the first to occur of (1) on a country-by-country and product-by-product basis, upon the expiration of the specified royalty term in such country; or (2) in its entirety upon the expiration of the specified royalty term in all countries with respect to the last product covered under the agreement commercialized in such countries. Takeda has the right to terminate the agreement upon specified prior written notice. In addition, both parties have certain termination rights in the circumstance of unexpected product safety issues, and Takeda has certain termination rights in the circumstance of pre-specified post-approval regulatory requirements. Both parties may terminate the agreement immediately for insolvency of the other party, in the case of a patent challenge by the other party, and, upon certain specified notice, for uncured material breach of terms and conditions of the collaboration agreement.

In September 2014, we entered into a manufacturing services agreement with Takeda in accordance with the collaboration agreement. Pursuant to the manufacturing services agreement, among other things, we will supply to Takeda, and Takeda will, subject to certain exceptions as set forth in the collaboration and manufacturing services agreements, exclusively purchase from us, at our cost, all of Takeda's requirements of Contrave for commercialization in the United States, Canada and Mexico during the term of the collaboration agreement. The manufacturing services agreement will continue in full force and effect until the expiration or termination of the collaboration agreement. Notwithstanding the foregoing, the manufacturing services agreement will also terminate automatically (prior to the expiration or termination of the collaboration agreement) upon (1) the completion of the transfer of the right and responsibility to manufacture or have manufactured Contrave to Takeda pursuant to the collaboration agreement and (2) if elected by Takeda, the assignment to Takeda of all of the third party manufacturer agreements required for the manufacture of Contrave in the applicable territory.

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 the Weber/Cowley patents. These patents, as discussed above, cover the current composition of Contrave, including our ER 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 2025. We may unilaterally terminate the agreement 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 that stem from the assigned rights, and for any patents that have or may issue with respect thereto, including the Weber/Cowley 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, 2014, we have paid a total of approximately $118,000 in connection with the maintenance and prosecution of this patent. 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.

Duke University License Agreement

In February 2015, we terminated our license agreement with Duke University, or Duke. We do not expect to pay Duke any royalties on Contrave.

Manufacturing

To date, our products used in clinical trials have been produced by outside contractors under our supervision.

We use Patheon Pharmaceuticals and Patheon Inc., or collectively Patheon, to manufacture Contrave and placebo tablets for our clinical activities. Patheon currently provides our clinical quantities on a proposal-by-proposal basis under a master agreement for pharmaceutical development services that we originally entered into in February 2007, and amended and restated in March 2010. 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 a specified time period. In addition, we may terminate the agreement immediately for any business reason. To date, we have contracted for a sufficient amount of Contrave and placebo tablets to cover the supply needs for the Light Study.

In March 2010, we entered into a manufacturing services agreement with Patheon, pursuant to which Patheon agreed to manufacture commercial quantities of our Contrave tablet products. Under the terms of the manufacturing agreement, as amended by the parties in November 2013, we are required to purchase a certain percentage of our requirements for our Contrave tablet products intended for commercial sale, provided certain terms and conditions are met.

The initial term of the manufacturing agreement commenced on March 12, 2010 and continues in effect until December 31st of the year that is five years from the date Contrave first receives approval for marketing from the FDA or any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products. Upon expiration of the initial term, the agreement will be automatically renewed for additional two year terms. Patheon may terminate the manufacturing agreement at any time upon specified prior written notice to us. We may also terminate the agreement with specified prior written notice to Patheon, subject to our payment of certain termination amounts. Either party may terminate the agreement effective immediately upon written notice to the other in the event that (1) the other party dissolves, is declared insolvent or bankrupt by a court of competent jurisdiction, (2) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction, or (3) the agreement is assigned for the benefit of creditors. We may terminate the agreement upon specified prior written notice if any governmental or regulatory authority, including, but not limited to, the FDA, takes any action, or raises any objection, that prevents us from importing, exporting, purchasing, or selling our Contrave tablet products. We are also required to give specified advance notice if we intend to no longer order commercial supplies of our Contrave tablet products pursuant to the manufacturing agreement due to the product's discontinuation in the market. Patheon may terminate the agreement upon specified prior written notice

to us if we assign any of our rights under the agreement to an assignee that, in the opinion of Patheon acting reasonably, is (1) not a credit worthy substitute for us; or (2) a competitor of Patheon. Moreover, either party may terminate the agreement upon written notice to the other party where the other party has failed to remedy a material breach of any of its representations, warranties, or other obligations under the manufacturing agreement within a specified period of time following receipt of a written notice of the breach, subject to specified terms and conditions.

Patheon has produced and will produce our bulk Contrave tablet products using naltrexone and bupropion active pharmaceutical ingredient, or API, supplied from various sources, including but not limited to Cilag AG, and Mallinckrodt LLC.

In January 2009, we entered into a supply agreement with Cilag pursuant to which Cilag will manufacture commercial supplies of naltrexone for use in our drug products. Pursuant to the terms of the supply agreement, we shall pay certain specified prices for such supplies based on the volumes purchased, which prices may be adjusted, subject to specified limitations. In addition, from the period beginning on the first December 31st following marketing approval by the FDA for our drug product containing naltrexone and continuing through the term of the supply agreement, we are required to purchase from Cilag a specified percentage of our requirements for naltrexone intended for commercial sale in our drug products containing naltrexone, provided that certain terms and conditions are met.

The term of the supply agreement commenced in January 2009 and shall continue in effect until the date that is four years from the period beginning on the first December 31st following marketing approval by the FDA for our drug product containing naltrexone. Either party may terminate the agreement effective immediately upon written notice to the other in the event that (a) the other party dissolves, is declared insolvent or bankrupt by a court of competent jurisdiction, (b) a voluntary or involuntary petition of bankruptcy is filed in any court of competent jurisdiction, or (c) the agreement is assigned for the benefit of creditors. In addition, we may terminate the agreement effective immediately upon written notice in the event that (a) any regulatory agency takes any action, or raises any objection that prevents us from importing, exporting, purchasing or selling naltrexone, (b) our drug product containing naltrexone fails during clinical trials and we withdraw our NDA, (c) we determine, in our sole discretion, to no longer pursue the development and/or commercialization of a drug product containing naltrexone, or (d) a legal proceeding shall be instituted against Cilag, which is reasonably likely to materially adversely affect Cilag's ability to properly perform under the agreement or subject us to any material risk of liability or loss. Moreover, either party may terminate the agreement upon specified written notice to the other party of a failure by that party to perform or observe any material covenant, condition or agreement to be performed or observed by it under the supply agreement, unless such breach has been cured within the specified notice period.

During any period during the term of the supply agreement in which Cilag for any reason, including, without limitation, a force majeure, fails to deliver the requisite quantities of naltrexone included in any firm commitment purchase order placed by us, within a specified period after the date of delivery confirmed in writing by Cilag or if Cilag otherwise anticipates or notifies us that it will be unable to make delivery of all or a portion of the ordered naltrexone within a specified period after the confirmed date of delivery, then we may refuse such late shipment of naltrexone from Cilag and purchase such quantities under such firm commitment purchase order through a substitute third party supplier. In the event Cilag regains its ability to resume supplying under the supply agreement, our right to purchase naltrexone from the substitute supplier shall terminate.

We entered into a supply agreement with Mallinckrodt, effective January 2013, pursuant to which Mallinckrodt manufactured commercial supplies of naltrexone for use in Contrave. The initial term of this supply agreement terminated in December 2014. Until an additional agreement is executed by both parties, we plan to purchase our supplies of naltrexone from Mallinckrodt pursuant to purchase orders.

Other than our supply agreement with Cilag, we have no material, long-term commitments or supply agreements with any of our API suppliers. Although we may seek to establish additional 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 additional long-term agreements, including an additional agreement with Mallinckrodt, 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 alone tend to cause significant attrition over time, often resulting in regaining weight. When pharmaceutical therapies are recommended it is generally after behavioral modification alone has failed. In 2013, AACE published treatment guidelines for obese or overweight patients with type 2 diabetes or pre-diabetes that include anti-obesity pharmacotherapy in conjunction with lifestyle modification for certain patients. Consistent with proposed labeling and as demonstrated in our clinical studies, we believe behavioral modification in combination with Contrave is effective in achieving weight loss.

The pharmaceutical market for obesity reached approximately $218 million in 2014, up 68% from 2013. Total prescriptions for 2014 reached approximately 9.4 million prescriptions, up 10.4% from the previous year. Orlistat, phentermine/topiramate and lorcaserin are pharmaceutical products that have been approved for the treatment of obesity in the United States. 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 7.5 million prescriptions in the United States in 2014. Phentermine accounted for approximately $37 million in 2014 sales. Orlistat is marketed in the United States by Genentech under the brand name Xenical. Orlistat works by inhibiting lipase, an enzyme that aids in the absorption of fat in the gastrointestinal tract. In 2014, orlistat accounted for approximately 44,000 prescriptions in the United States, or approximately $17 million in sales. Orlistat was launched in 2007 over-the-counter in the United States at half the prescribed dose by GlaxoSmithKline under the brand name allí. According to GlaxoSmithKline, in 2008, allí accounted for approximately $105 million in sales. In June 2012, Arena obtained FDA approval for its product, lorcaserin, which was commercially launched in the United States under the name Belviq in June 2013. In July 2012, Vivus obtained FDA approval for its combination product, phentermine/topiramate. Vivus commercially launched its combination product in the United States under the name Qsymia in September 2012. In addition, in December, 2014, the FDA approved liraglutide injection for the treatment of obesity. In 2014, phentermine/topiramate accounted for approximately 548,000 prescriptions while lorcaserin accounted for approximately 479,000 prescriptions during the same period. Sales in 2014 for phentermine/topiramate and lorcaserin were approximately $79 million and $66 million, respectively.

Despite the large market opportunity for anti-obesity agents, there are relatively few competitive products in late stage clinical development. Companies pursuing pharmaceutical treatments for obesity include AstraZeneca, Athersys, Inc, Bristol-Myers Squibb, Johnson & Johnson, Norgine BV, and Zafgen, Inc.

There are also surgical approaches to treat severe obesity that are becoming increasingly accepted and could become competitors against our product candidates. Bariatric surgery, including gastric bypass and gastric banding procedures, is employed in more extreme cases, typically for patients with a BMI exceeding 40 or those with a BMI greater than 30 who are experiencing one or more obesity-related complications such as diabetes. Surgery is associated with significant side effects, potential complications and substantial costs and recovery time. Certain device implantations used as therapies, such as neuromodulation, are not yet approved by the FDA. In addition, other potential approaches which utilize various implantable devices or surgical tools are in development. Some of these approaches are in late stage development and may be approved for marketing. Companies such as Apollo Endosurgery, Boston Scientific, Covidien Ltd., EnteroMedics, Inc., GI Dynamics,

Inc., Johnson & Johnson, and Medtronic, Inc. are all active in the surgical and device space and may have substantially greater resources than we have.

In addition, we may face competition from generic products. Each of bupropion and naltrexone 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 that we believe may improve patient outcomes and provide further barriers to entry, including intellectual property protection, for potential competitors. We believe there cannot be an AB-equivalence designation for the generic versions of the constituents comprising Contrave because of differences in pharmacokinetics between the existing generically available formulations and doses and the formulations and doses we plan to use. For naltrexone, 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 issued, composition and methods-of-use 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 because the dosages, pharmacokinetic profile and titration regimens for Contrave 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 constituent of Contrave, naltrexone. 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 Contrave 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.

All states currently provide outpatient prescription drug coverage under their Medicaid programs. States that elect to offer outpatient prescription drug coverage must provide coverage for all FDA-approved drugs of every manufacturer that has entered into a rebate agreement with HHS under the Medicaid Rebate Program, with certain exceptions. For example, state Medicaid programs, administered by individual states for qualifying low-income individuals, are permitted to exclude coverage for weight loss drugs.

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. In the fourth quarter of 2011, the Centers for Medicare & Medicaid Services announced that the Medicare program was adding new benefit coverage for prevention with the objective of treating obesity. The new benefit provides for screening for obesity and counseling for eligible beneficiaries by primary care providers in physician's offices. The benefit includes face to face counseling for up to 12 total months. 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

In general, private commercial plans offer coverage for oral weight loss products only if the benefit is selected by employers. Many plans require prior authorization. Thus, our product may not achieve broad coverage. Moreover, the amount of any coverage provided under the various plans may be minimal. Government policy is a key player in setting trends for coverage of obesity treatments. Private payers may be more likely to add coverage of weight loss products if Medicare provides coverage. We do not expect the success of our obesity product to be entirely contingent on third-party payer coverage and reimbursement, but rather, on acceptance by physicians and people who want to lose weight and are willing to pay for the drugs out of pocket.

Government Regulation

In the United States, 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 drug, including a new dosage form or use of a previously approved drug, can be marketed in the United States.

New Drug Application (NDA)

An approved NDA 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.

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

Preclinical tests include laboratory evaluation, as well as animal studies to evaluate pharmacology and toxicity. 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, issues a clinical hold raising 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 a clinical trial can begin. 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, protocol and informed consent forms for any clinical trial and the IRB must monitor the trial 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 Good Clinical Practice, or GCP, as set forth in the FDA guidance, and related regulations, including regulations for informed consent.

For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following three or four 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 when the drug is too toxic to be ethically given to healthy individuals.
- *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. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the drug. Such post approval trials are typically referred to as Phase IV studies.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The cost of preparing and submitting an NDA is substantial. The Prescription Drug User Fee Act, which has been reauthorized four times by Congress, requires the payment of user fees with the submission of NDAs, including 505(b)(2) NDAs. These application fees are substantial ($2,335,200 in the FDA's Fiscal Year 2015) and will likely increase in future years. The FFDCA provides for waiver of the application fee for the first NDA for a small business under certain circumstances. In February 2010, we were granted a waiver of this application fee for our Contrave NDA. This one time waiver will not be available to us upon submission of NDAs, if any, for our other product candidates in the future. Manufacturers and sponsors of approved drugs are subject to annual product and establishment fees of $569,200 per manufacturing establishment and $110,370 per product. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for non-priority drug products have been reviewed within ten to twelve months while most applications for priority review drugs, that is, drugs that the FDA determines represent a significant improvement over existing therapy, are reviewed in six to eight months. The review process is often extended by the submission of additional information or

clarification during the review. 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.

Before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with cGMP and GCP is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied. The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied, or it may require additional data including additional pivotal Phase III clinical trials. 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 we do.

Upon completion of its review of the NDA, FDA issues an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA's goal is to review such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions which can materially affect the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Special Protocol Assessment

An SPA is a written agreement with the FDA on the details of the design and planned analysis for a clinical trial. It is intended to form the basis for an NDA and may only be changed through a written agreement between the sponsor and the FDA. An SPA is generally binding upon the FDA unless the FDA determines that there are public health concerns unrecognized at the time the SPA agreement was entered into, other new scientific concerns regarding product safety or efficacy arise, or if the sponsor fails to comply with the agreed upon trial protocols.

The Hatch-Waxman Act

In 1984, Congress enacted the Hatch-Waxman Act. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. ANDA applicants are not required to conduct or submit results of pre-clinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

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

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

The ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which the FDA cannot grant effective approval of an ANDA based on that listed drug.

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 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 for previously approved products. 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 for which the Section 505(b)(2) applicant has submitted its own data. The FDA requires companies to perform additional studies or measurements to support the change from the approved product. We submitted our initial NDA for Contrave 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. As with ANDAs, described above, 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 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. When we submitted our NDA for Contrave, we made

paragraph IV certifications that Contrave does not infringe the bupropion patents listed in the Orange Book and sent the appropriate notice to the patent holder and NDA holder once we received confirmation from the FDA that our NDA was sufficiently complete to permit a substantive review. 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 notification, 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.

Upon FDA approval of Contrave, we received three years of Hatch-Waxman marketing exclusivity for such product. Under this form of exclusivity, the FDA would be precluded from approving a generic drug application or, in some cases, another 505(b)(2) application for a drug product for the protected conditions of approval (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.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. The Best Pharmaceuticals For Children Act, or BPCA, provides sponsors with an additional 6-month period of market exclusivity on all forms of the drug containing the active moiety, if the sponsor submits results of pediatric studies specifically requested by FDA under BPCA. In order to receive the BPCA exclusivity, the drug must have other existing patent or exclusivity protection in effect.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. We and our contract manufacturers are required to comply with applicable FDA manufacturing requirements contained in the FDA's 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 for commercial distribution. 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. In addition, prescription drug manufacturers in the United States must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities, and have procedures in place to identify and properly handle suspect and illegitimate products.

Adverse experiences associated with the use of the drug must be reported to the FDA and could result in the imposition of market restrictions 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.

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.

The FDA can require post-approval studies and clinical trials if the FDA finds, after approving the drug, that scientific data, including information regarding related drugs, render 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 prohibits, restricts or otherwise imposes regulatory requirements on certain activities, including 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 federal civil and criminal investigations and prosecutions. State enforcement actions relating to promotional violations are also becoming more common.

As part of the FDA approval of Contrave, we and Takeda agreed to several post-approval requirements, including studies to assess the safety and efficacy of Contrave for weight management in obese pediatric patients. There will also be a new randomized double-blind, placebo-controlled study to evaluate the effects of long-term treatment with Contrave on the incidence of MACE in overweight and obese subjects with cardiovascular disease or multiple cardiovascular risk factors.

Other Regulatory Requirements

The FDA can require a drug-specific Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the drug outweighs the risks. 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, a sponsor must submit a proposed REMS as part of its application, or if the request is made post-approval, not later than 120 days after the FDA notifies the drug sponsor. 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 how a drug may be prescribed or dispensed or other measures that the FDA deems necessary to assure the safe use of the drug. REMS programs must be evaluated on an ongoing basis and the FDA may require changes needed to address ongoing safety issues or corrective actions to address any noncompliance.

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 federal government 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.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The PPACA amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, PPACA amended the federal false claims law such that a violation of the federal healthcare program anti-kickback statute can serve as a basis for liability under the federal false claims law. The majority of states also have statutes or regulations similar to the federal anti-kickback statute and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Furthermore, pursuant to PPACA, the Centers for Medicare & Medicaid Services, or CMS, has issued a final rule that requires manufacturers of prescription drugs to collect and report information on payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians and their immediate family members. Manufacturers were required to begin collecting information on August 1, 2013, with the first reports due in 2014. The reported data was posted in searchable form on a public website beginning September 30, 2014. Failure to submit required information may result in civil monetary penalties. Furthermore, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual physicians in these states. Other states prohibit various other marketing-related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Massachusetts and Nevada require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties. Companies must also be registered or licensed by the federal and state governments prior to manufacturing or distributing prescription drug products.

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.

European Union Drug Review and Approval

In the EEA (which is comprised of the 28 Member States of the European Union, as well as, through the Treaty of the European Economic Area, Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of MA:

The CMA, which is issued by the European Commission in the form of a binding decision through the Centralized Procedure, based on the opinion of the CHMP of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. A medicinal product can be progressively authorized in two or more EEA Member States. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Contrave is eligible for the Centralized Procedure. In October 2013, we submitted a CMA supporting potential approval of Contrave, under the name Mysimba, under the centralized procedure. After submission and validation of a CMA, the EMA's CHMP generally has 210 days to complete its assessment and adopt an opinion on whether or not to recommend the granting of the CMA. The 210 day period does not include the anticipated "clock stops" at specified points in the procedure, typically at day 120 (Consolidated List of Questions) and at day 180 (List of Outstanding Issues). The clock stops allow time for us to address the outstanding questions or issues raised by the CHMP. At day 180, depending on the List of Outstanding Issues, an oral hearing with the CHMP may be required to address specific issues. Assuming a positive opinion from the CHMP, final marketing authorization is generally granted by the European Commission on day 277 of the procedure, counting from the start date of the centralized assessment procedure, not counting clock stops as noted above.

In December 2014, the CHMP adopted a positive opinion recommending the EC grant a CMA for Mysimba. The CHMP recently released minutes from their December meeting stating that the positive opinion for Mysimba was adopted by a majority vote with 31 members in favor and two opposed. Procedurally, a positive opinion and recommendation of the CHMP is then referred to the Standing Committee, which is composed of representatives from each member state of the E.U. In a process that occurs either through a written procedure or in a meeting, the Standing Committee reviews the draft EC decision to grant marketing authorization. The EC recently informed us that at the request of one member state, the draft EC decision granting marketing authorization for Mysimba will be reviewed during a meeting of the Standing Committee being held in March 2015. A positive decision issued by the EC will allow Mysimba to be placed on the market in all 28 E.U. member states, as well as Iceland, Liechtenstein and Norway.

Prior to submission of the CMA for Mysimba, we also established an agreed-to pediatric investigation plan with the EMA's Pediatric Committee. The EMA's Pediatric Committee also agreed to grant a waiver from the obligation to carry out pediatric clinical trials in certain subsets of the pediatric population. The EMA's Pediatric Committee's opinion was validated by an EMA decision adopted in August 2013.

DEA Regulation

Naltrexone, one of the components of Contrave, is manufactured from semi-synthetic opiates. Although naltrexone is not a narcotic or a controlled substance, manufacturing of naltrexone 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. Even though neither Contrave nor naltrexone is a controlled substance, 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.

Government Programs for Marketed Drugs

Medicaid, the 340B Drug Pricing Program, and Medicare

Federal law requires that a pharmaceutical manufacturer, as a condition of having its products receive federal reimbursement under Medicaid and Medicare Part B, must pay rebates to state Medicaid programs for all units of its covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program under either a fee-for-service arrangement or through a managed care organization. This federal requirement is effectuated through a Medicaid drug rebate agreement between the manufacturer and the Secretary of Health and Human Services. CMS administers the Medicaid drug rebate agreements, which provide, among other things, that the drug manufacturer will pay rebates to each state Medicaid agency on a quarterly basis and report certain price information on a monthly and quarterly basis. The rebates are based on prices reported to CMS by manufacturers for their covered outpatient drugs. For non-innovator products, generally generic drugs marketed under ANDAs, the rebate amount is 13% of the average manufacturer price, or AMP, for the quarter. The AMP is the weighted average of prices paid to the manufacturer (1) directly by retail community pharmacies and (2) by wholesalers for drugs distributed to retail community pharmacies. For innovator products, drugs that are marketed under NDAs or BLAs, the rebate amount is the greater of 23.1% of the AMP for the quarter or the difference between such AMP and the best price for that same quarter. The best price is essentially the lowest price available to non-governmental entities. Innovator products may also be subject to an additional rebate that is based on the amount, if any, by which the product's AMP has increased since launch.

The statutory definition of AMP was recently amended, and there are many ambiguities in the revised provision. In February 2012, CMS published a proposed rule further defining AMP and providing clarification on other parts of the rebate program. Until the rule is finalized, manufacturers are required to make reasonable assumptions when interpreting the statute and calculating AMP.

The terms of participation in the Medicaid drug rebate program impose an obligation to correct the prices reported in previous quarters, as may be necessary. Any such corrections could result in additional or lesser rebate liability, depending on the direction of the correction. In addition to retroactive rebates, if a manufacturer were found to have knowingly submitted false information to the government, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

A manufacturer must also participate in a federal program known as the 340B drug pricing program in order for federal funds to be available to pay for the manufacturer's drugs under Medicaid and Medicare Part B. Under this program, the participating manufacturer agrees to charge certain safety net healthcare providers no more than an established discounted price for its covered outpatient drugs. The formula for determining the discounted price is defined by statute and is based on the AMP and the unit rebate amount as calculated under the Medicaid drug rebate program, discussed above.

Federal law also requires that manufacturers report data on a quarterly basis to CMS regarding the pricing of drugs that are separately reimbursable under Medicare Part B. These are generally drugs, such as injectable products, that are administered "incident to" a physician service and are not generally self-administered. The pricing information submitted by manufacturers is the basis for reimbursement to physicians and suppliers for drugs covered under Medicare Part B. As with the Medicaid drug rebate program, federal law provides for civil monetary penalties for failing to provide required information, late submission of required information, and false information.

Medicare Part D provides prescription drug benefits for seniors and people with disabilities. Medicare Part D beneficiaries have a gap in their coverage (between the initial coverage limit and the point at which catastrophic coverage begins) where Medicare does not cover their prescription drug costs, known as the coverage gap. However, by 2020, Medicare Part D beneficiaries will pay 25% of drug costs after they reach the initial coverage limit—the same percentage they were responsible for before they reached that limit—thereby closing the coverage gap. The cost of closing the coverage gap is being borne by innovator companies and the government through subsidies. Beginning in 2011, each manufacturer of drugs approved under NDAs or BLAs was required to enter into a Medicare Part D coverage gap discount agreement and provide a 50% discount on those drugs dispensed to Medicare beneficiaries in the coverage gap, in order for its drugs to be reimbursed by Medicare Part D.

Federal Contracting/Pricing Requirements

Manufacturers are also required to make their covered drugs, which are generally drugs approved under NDAs or BLAs, available to authorized users of the Federal Supply Schedule, or FSS, of the General Services Administration. The law also requires manufacturers to offer deeply discounted FSS contract pricing for purchases of their covered drugs by the Department of Veterans Affairs, the Department of Defense, or DoD, the Coast Guard, and the Public Health Service (including the Indian Health Service) in order for federal funding to be available for reimbursement or purchase of the manufacturer's drugs under certain federal programs. FSS pricing to those four federal agencies for covered drugs must be no more than the Federal Ceiling Price, or FCP, which is at least 24% below the Non-Federal Average Manufacturer Price, or Non-FAMP, for the prior year. The Non-FAMP is the average price for covered drugs sold to wholesalers or other middlemen, net of any price reductions.

The accuracy of a manufacturer's reported Non-FAMPs, FCPs, or FSS contract prices may be audited by the government. Among the remedies available to the government for inaccuracies is recoupment of any overcharges to the four specified federal agencies based on those inaccuracies. If a manufacturer were found to have knowingly reported false prices, in addition to other penalties available to the government, the law provides for civil monetary penalties of $100,000 per incorrect item. Finally, manufacturers are required to disclose in FSS contract proposals all commercial pricing that is equal to or less than the proposed FSS pricing, and subsequent to award of an FSS contract, manufacturers are required to monitor certain commercial price reductions and extend commensurate price reductions to the government, under the terms of the FSS contract Price Reductions Clause. Among the remedies available to the government for any failure to properly disclose commercial pricing and/or to extend FSS contract price reductions is recoupment of any FSS overcharges that may result from such omissions.

Tricare Retail Pharmacy Network Program

The DoD provides pharmacy benefits to current and retired military service members and their families through the Tricare healthcare program. When a Tricare beneficiary obtains a prescription drug through a retail pharmacy, the DoD reimburses the pharmacy at the retail price for the drug rather than procuring it from the

manufacturer at the discounted FCP discussed above. In order for the DoD to realize discounted prices for covered drugs (generally drugs approved under NDAs or BLAs), federal law requires manufacturers to pay refunds on utilization of their covered drugs sold to Tricare beneficiaries through retail pharmacies in DoD's Tricare network. These refunds are generally the difference between the Non-FAMP and the FCP and are due on a quarterly basis. Absent an agreement from the manufacturer to provide such refunds, DoD will designate the manufacturer's products as Tier 3 (non-formulary) and require that beneficiaries obtain prior authorization in order for the products to be dispensed at a Tricare retail network pharmacy. However, refunds are due whether or not the manufacturer has entered into such an agreement.

Branded Pharmaceutical Fee

A branded pharmaceutical fee is imposed on manufacturers and importers of "branded prescription drugs," generally drugs approved under NDAs or BLAs. Beginning in 2011, an aggregate annual fee to be paid by these manufacturers is set at $28 billion over 10 years, of which $2.5 billion was payable in 2011, $2.8 billion in 2012, $2.8 billion in 2013, and $3.0 billion in 2014. This annual fee is apportioned among the participating companies based on each company's sales of qualifying products to or utilization by certain U.S. government programs during the preceding calendar year. The fee became effective January 1, 2011, and is not deductible for U.S. federal income tax purposes. Utilization of generic drugs, generally drugs approved under ANDAs, is not included in a manufacturer's sales used to calculate its portion of the fee.

Outside the United States

Within the European Union, approved products are paid for by a variety of payors, with governments being the primary source of payment. Governments may determine or influence reimbursement of products. Governments may also set prices or otherwise regulate pricing. Negotiating prices with governmental authorities can delay commercialization of our products, if approved. Governments may use a variety of cost-containment measures to control the cost of products, including price cuts, mandatory rebates, value-based pricing, and reference pricing (i.e., referencing prices in other countries and using those reference prices to set a price). Budgetary pressures in many European Union countries are continuing to cause governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates, and expanded generic substitution and patient cost-sharing. If budget pressures continue, governments may implement additional cost-containment measures.

Employees

As of February 23, 2015, we had 47 full-time employees and three part-time employees, consisting of clinical development, clinical science, regulatory affairs, marketing, medical affairs, technical operations, legal, finance and administration. We consider our relations with our employees to be good.

As our business continues to grow, and we transition from primarily a drug development company to a commercial product organization, we expect to experience changes in our executive team, including potential departures and the addition of new executives with other areas of expertise that will add value to our business.

Research and Development

Our research and development expenses totaled $57.4 million, $56.7 million and $73.7 million in the years ended December 31, 2014, 2013 and 2012, respectively.

About Orexigen

We were incorporated in Delaware in September 2002. Our principal offices are located at 3344 N. Torrey Pines Court, Suite 200, La Jolla, California 92037, and our telephone number is (858) 875-8600. 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 contained in this report and our other periodic reports and other filings we make from time to time with the SEC, 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 our other filings with the SEC 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

Our success for the foreseeable future is dependent solely on the success of our recently approved product, Contrave® (naltrexone HCI and bupropion HCI) extended release, or ER, tablets.

To date the majority of our resources have been focused on the research and development of Contrave. On September 10, 2014, the U.S. Food and Drug Administration, or the FDA, notified us that it had approved our New Drug Application, or NDA, for Contrave extended-release tablets as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index, or BMI, of 30 kg/m2 or greater (obese), or 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition. We and our collaboration partner, Takeda Pharmaceutical Company Limited, or Takeda, are now focused on the commercialization of Contrave. Takeda commercially launched Contrave in October 2014. Our ability to generate revenue for the foreseeable future will depend solely on the commercial success of Contrave. Accordingly, any failure or significant delay in the successful commercialization of Contrave will have a material and adverse impact on our business.

We are dependent on our collaboration with Takeda to further develop and commercialize Contrave in the United States, Canada and Mexico. This collaboration places a large part of the commercialization and the development outside our control, and poor performance under or failure to maintain the collaboration agreement between us and Takeda could have an adverse impact on our business.

In September 2010, we entered into a collaboration agreement with Takeda for the development and commercialization of Contrave in the United States, Canada and Mexico. Under the collaboration agreement, as amended, Takeda is also responsible for the packaging of Contrave for commercial sale. We cannot be certain that our collaboration with Takeda will continue. Both we and Takeda have the right to terminate the collaboration agreement, in certain circumstances, prior to its expiration, including a right by Takeda to terminate the agreement upon specified prior written notice. If the agreement is terminated prior to its expiration, we may not be able to find another collaborator for the commercialization and further development of Contrave, and even if we elected to pursue commercialization and further development of Contrave on our own, we might not be able to do so successfully and would experience substantially increased capital requirements that we might not be able to fund.

Our dependence on Takeda and the collaboration agreement subjects us to a number of risks, including:

- Takeda may not perform as expected and we may not be able to control the amount and timing of resources that Takeda may devote to commercialization, commercial packaging, development of Contrave in Mexico or Canada, or the post-approval development of Contrave in the United States;
- we and Takeda could disagree as to our ongoing or future post-approval development plans, including lifecycle plans for Contrave, which may result in Takeda not funding such activity; and Takeda may delay clinical trials or stop a clinical trial;
- there may be disputes between us and Takeda, including disagreements regarding the collaboration agreement and decisions related to development plans, regulatory actions or intellectual property, that

may result in (a) the delay of (or prevent entirely) the achievement of regulatory and commercial objectives that would result in milestone payments, (b) the delay or termination of the commercialization, commercial packaging or development of Contrave, and/or (c) costly litigation or arbitration that diverts our management's attention and resources;

- the ongoing discussions between us and Takeda may not result in an executed amended and restated collaboration agreement with Takeda and if an amended and restated agreement is executed, that agreement may not reflect the non-binding term sheet, in whole or in part, that the parties entered into in September 2014;
- Takeda may not comply with applicable regulatory guidelines (including the post-marketing requirements and the cardiovascular outcomes trial, or CVOT) with respect to the commercialization, commercial packaging or development of Contrave, which could adversely impact the sales of Contrave and could result in administrative or judicially imposed sanctions, including warning letters, civil and criminal penalties, injunctions, product seizures or detention, product recalls, total or partial suspension of production and refusal to approve any new drug applications;
- Takeda may not provide us with timely and accurate information regarding sales activities and supply forecasts, which could adversely impact our ability to comply with our manufacturing and supply obligations under the collaboration agreement and our and Takeda's ability to commercialize Contrave;
- Takeda may experience financial difficulties;
- business combinations or significant changes in Takeda's business strategy may also adversely affect Takeda's ability to perform its obligations under our collaboration agreement;
- Takeda may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation; and
- notwithstanding the non-competition requirements in the collaboration agreement, Takeda could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors.

Any failure of Takeda to adequately perform its obligations under our collaboration agreement or the termination of such agreement, or an amendment of the terms of such agreement on terms that are not favorable to us, could have a material and adverse impact on our ability to successfully commercialize Contrave, and our business.

If Contrave does not achieve broad market acceptance, the revenues, including any milestone or royalty payments we may be eligible to receive under our collaboration agreement with Takeda, that we generate from its sales will be limited.

The commercial success of our recently launched product, Contrave, or any other 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 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 timing of market introduction of our products as well as competitive products;
- 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, the "black box" warning(s) and pregnancy precautions associated with the active pharmaceutical ingredients, or APIs, in Contrave and included in Contrave's product label;
- availability of alternative treatments and the potential or perceived advantages or disadvantages of such treatments, including, in the case of Contrave, a number of competitive products approved for the treatment of weight loss or expected to be commercially launched in the near future;
- pricing and cost effectiveness;
- our Risk Evaluation and Mitigation Strategy, or REMS, if any are imposed;
- the effectiveness of our, or our current or any future collaborators' sales and marketing strategies;
- our and our collaborative partner's 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 Contrave does not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not generate sufficient revenue from our product, and we may not become or remain profitable. In addition, our and our collaborative partner's efforts to educate the medical community and third-party payors on the benefits of our product may require significant resources and may never be successful.

Even though Contrave received regulatory approval from the FDA, it will still be subject to ongoing and continued regulatory review and post-marketing requirements, which may result in significant expense and limit our ability to commercialize this product.

Even though U.S. regulatory approval has been obtained for Contrave, the FDA has imposed restrictions on its indicated uses and marketing and imposed ongoing requirements for post-marketing studies and other activities. For example, the approved use of Contrave is limited as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial BMI of 30 kg/m2 or greater (obese), or 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition. The label also contains a "boxed" warning regarding the potential for suicidal thoughts and behaviors and neuropsychiatric reactions as a side effect of the drug. We are also required to conduct a number of post-marketing studies. We are required to conduct a series of studies in obese pediatric patients to evaluate the safety and efficacy of Contrave for weight management in pediatric populations. We are also required to perform a group of short-term trials, including a thorough QT study, single-dose pharmacokinetic studies in renal and hepatic impairment, and a drug-drug interaction study. Finally, we will need to conduct a new placebo-controlled cardiovascular outcomes trial, or CVOT, with a pre-specified goal to exclude a hazard ratio of 1.4, with the upper bound of the 95% confidence interval. A new trial design for the CVOT needs to be worked out among us, Takeda and the FDA, and we have committed to have a final protocol complete by April 2015 and final study results by January 2022. We expect to pay a substantial portion of the CVOT. Any issues relating to these restrictions or post-marketing requirements (including a delay in conducting the post-marketing required studies) could have an adverse impact on our ability to achieve market acceptance of or continue marketing Contrave in the United States and for us to generate revenue from its sale in the United States. To the extent that Contrave is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

Contrave will also be subject to ongoing FDA requirements governing the manufacturing, labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market information. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice, or cGMP, regulations and good clinical practice, or GCP, requirements for any clinical trials that we conduct post-approval.

Approved products, manufacturers and manufacturers' facilities are subject to continual review and periodic inspections. Later discovery of previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, problems with the facility where the product is manufactured, or failure to comply with regulatory requirements, may result in, among other things, restrictions on that product or on us or a collaborative partner, including:

- withdrawal of the product from the market or voluntary or mandatory product recalls
- warning letters or untitled letters;
- civil or criminal penalties, including fines;
- withdrawal of regulatory approval;
- suspension of any ongoing clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- restrictions on operations, including restrictions on the marketing or manufacturing of the product or the imposition of costly new manufacturing requirements; or
- seizure or detention, or refusal to permit the import or export of products.

In addition, the FDA's policies may change and additional government regulations may be enacted that could impact the marketing of Contrave. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Our clinical trials, including the CVOT and other post-marketing required studies, may fail to demonstrate acceptable levels of safety or efficacy of Contrave, which could prevent or significantly delay Contrave's regulatory approval in countries outside the United States and may adversely impact our ability to maintain regulatory approval in the United States.

Contrave is prone to the risks of failure inherent in drug development, even following approval from the FDA. Even though U.S. regulatory approval has been obtained for Contrave, the FDA has imposed ongoing requirements for post-marketing studies. We are required to conduct a number of post-marketing studies, including a series of studies in obese pediatric patients to evaluate the safety and efficacy of Contrave for weight management in pediatric populations, a group of short-term trials, including a thorough QT study, single-dose pharmacokinetic studies in renal and hepatic impairment, and a drug-drug interaction study. Finally, we will need to conduct a new CVOT with a pre-specified goal to exclude a hazard ratio of 1.4, with the upper bound of the 95% confidence interval. A new trial design for the CVOT needs to be worked out among us, Takeda and the FDA, and we have committed to have a final protocol complete by April 2015 and final study results by January 2022. Any issues relating to these post-marketing requirements (including a delay in conducting the post-marketing required studies and issues relating to the safety or efficacy of Contrave) could have an adverse impact on our ability to receive regulatory approval outside the United States, achieve market acceptance of or continue marketing Contrave in the United States and for us to generate revenue from its sale in the United States. To the extent that Contrave is approved for sale in other countries, we may be subject to similar restrictions and requirements imposed by laws and government regulators in those countries.

Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well-controlled clinical trials, 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.

In addition, we may need to complete additional preclinical testing of any product candidate to evaluate safety and toxicity and the FDA may require us to conduct additional clinical trials. The results from the preclinical and clinical trials that we have completed for Contrave 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 Contrave (outside the United States) and maintain approval for Contrave in the United States. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, including post-marketing clinical trials, even after promising results in earlier trials. If Contrave is not shown to be safe and effective in clinical trials, our clinical development program 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 any other product candidates that we may develop, in-license or acquire would prevent receipt or maintenance of regulatory approval and, ultimately, the commercialization of that product candidate.

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

Contrave competes with well-established prescription drugs for the treatment of obesity, including Xenical® (orlistat), marketed by Genentech, Inc. Orlistat has also been launched by GlaxoSmithKline in over-the-counter form under the brand name allí®, which represents additional competition and potential negative pricing pressure. Orlistat is marketed by a pharmaceutical company 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 Contrave. The availability of a large number of branded prescription products, including drugs that are prescribed off-label, generic products and over-the-counter products could limit the demand for, and the price we or our collaborative partner are able to charge for Contrave and any future products. Vivus, Inc. commercially launched its combination product, phentermine/topiramate, in the United States under the name Qsymia in September 2012. Eisai Inc., the collaboration partner of Arena Pharmaceuticals, Inc., or Arena, commercially launched lorcaserin in the United States under the name Belviq in June 2013. Vivus, Arena and Eisai may already have built a significant competitive advantage as we and our collaborative partner begin to market Contrave. Moreover, Novo Nordisk's product, Saxenda, recently received FDA approval and is expected to commercially launch in the first half of 2015. These products represent additional competition and potential negative pricing pressure with respect to Contrave. Further, if safety concerns about these products' use arise after their launch, such concerns may materially and adversely affect the commercialization of Contrave.

Currently, there are a number of drug products in development for obesity which could become competitors against our product. These include products being developed by AstraZeneca, Athersys, Inc., Johnson & Johnson, Norgine BV, A/S, Novo Nordisk, and Zafgen, Inc.

There are also surgical approaches to treat severe obesity that are becoming increasingly accepted and could become competitors against our product. Two of the most well established surgical procedures are gastric bypass surgery and adjustable gastric banding. In addition, other potential approaches which utilize various implantable devices or surgical tools are in development, including an endoscopic approach for treating obesity. Some of these approaches are in late stage development and may be approved for marketing. Companies such as Allergan, Inc., Boston Scientific, Covidien Ltd., EnteroMedics, Inc., GI Dynamics, Inc., Johnson & Johnson and Medtronic, Inc. are all active in this space and may have substantially greater resources than we have.

New developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the nutritional, pharmaceutical and medical technology industries at a rapid pace. These developments may render our product 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 more rapidly develop products than we did or may do in the future or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product. Our competitors may also develop drugs or surgical approaches that are more effective, more useful and less costly than ours and may also be more successful in manufacturing and marketing their products. In addition, our competitors may be more effective in commercializing 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.

We and our collaborative partner are subject to uncertainty relating to reimbursement policies which, if not favorable to Contrave, could hinder or prevent Contrave's commercial success.

Our ability and our collaborative partner's ability to commercialize our approved product 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 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 or our collaborative partner will be able to obtain third-party coverage or reimbursement for our product in whole or in part.

The obesity therapy 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 Part D prescription drug program for eligible seniors and disabled individuals. Medicare is a federal governmental third-party payor whose policies often are emulated or adopted by other payors. Although the Centers for Medicare & Medicaid Services, or CMS, which administers the Medicare program, has removed longstanding policy language that obesity itself cannot be considered an illness, the agency interprets the Part D exclusion of weight loss drugs as applying to novel obesity therapies. However, CMS has since issued a national policy covering bariatric surgery for co-morbid conditions associated with obesity, and extended coverage under the Medicare program for intensive behavioral therapy for beneficiaries with obesity. The benefit provides for screening for obesity and counseling for eligible beneficiaries by primary care providers in physician's offices. Although third-party payors' willingness to cover and reimburse 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.

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 does not receive adequate coverage or reimbursement, the market acceptance and commercial success of our product may be limited.

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

As part of our corporate strategy, we may 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.

Disclosure of interim results of ongoing clinical trials or delays in the commencement, the transfer and delivery of clinical trial information or completion of clinical trials or the requirement to conduct additional clinical trials could result in increased costs to us and delay or limit our ability to continue development programs, maintain or receive additional regulatory approvals and/or generate revenues.

Disclosure of interim results of ongoing clinical trials, including disclosure of interim results related to the protection of intellectual property, or delays in the commencement, the transfer and delivery of clinical trial information or completion of clinical trials could significantly affect our product development costs or adversely impact our ability to maintain or receive additional regulatory approvals. We do not know whether clinical trials will begin on time or whether clinical trials will be completed on schedule, if at all. The commencement, transfer and delivery of clinical trial information 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, including regulatory approval of the design of 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 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 the restrictions imposed by the design and length of a clinical trial;
- retaining patients who have initiated a clinical trial, including the Light Study, 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;
- the status of our collaborative relationship with Takeda with respect to the post-marketing requirements for Contrave and any additional clinical trials required for Contrave; and
- timely collection, review and analysis of our clinical trial data.

Clinical trials may also be delayed or terminated as a result of disclosure of interim results, including ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, a collaborative partner, 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;
- lack of adequate funding or other resources to continue the clinical trial;
- 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
- logistical and operational challenges inherent in complex clinical trials.

Additionally, changes in regulatory requirements and guidance for developing products for weight management may occur and we may need to initiate new clinical trials or change protocols of existing clinical trials to account for these changes. For instance, based on the FDA's interpretation of the input received from the March 2012 EMDAC meeting, the FDA may issue final guidance on developing products for weight management. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion or termination of clinical trials, may also ultimately lead to the termination of a development program and/or the denial of regulatory approval of a product candidate, including the denial of an NDA or regulatory approval outside the United States.

Contrave may cause undesirable side effects that could delay or prevent commercialization, limit the commercial profile of an approved label, result in significant negative consequences following marketing approval or delay or prevent regulatory approval.

Undesirable side effects caused by our product could cause regulatory authorities to withdraw or limit their approval of the product or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. Contrave has been evaluated in four completed Phase III clinical trials, which we refer to collectively as the Contrave Obesity Research, or COR, program. Across the entire COR program, seven patients experienced serious adverse events that were attributed by investigators as possibly related or related to Contrave treatment. These consisted of cholecystitis (gallbladder inflammation) (2), seizure (2), palpitations (1), paresthesia (1) and vertigo (1). The most frequently observed treatment-emergent adverse events were nausea,

constipation, headache, vomiting, dizziness, insomnia, dry mouth and diarrhea. Nausea was the leading adverse event resulting in discontinuation; however, for the majority of patients experiencing nausea, it was mild to moderate, transient and manageable. In the Light Study interim analysis, there were no unexpected new safety signals observed. Serious adverse events and adverse events leading to discontinuation were generally consistent with the overall safety profile established in the COR program. These safety conclusions may change in connection with the ongoing conduct of the Light Study or the required post-marketing CVOT.

The safety data we have disclosed to date represents our interpretation of the data at the time of disclosure and it is subject to our further review and analysis. Serious adverse events have been reported to the FDA and study investigators as required in accordance with current guidelines and standards. Serious adverse events that are not characterized by clinical investigators as possibly related to our study drug or adverse events that occur in small numbers may not be disclosed to the public until such time the various documents submitted to the FDA as part of the approval process are made public. We are unable to determine if the subsequent disclosure of adverse events will have an adverse effect on our stock price. In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA. The FDA may not agree with our methods of analysis or our interpretation of the results.

In addition, the constituent drugs of our product each has its own side effect profile that is included in the respective current product label. Contrave's label includes the side effect profiles of each of its constituent drugs, including a "boxed" warning regarding the potential for suicidal thoughts and behaviors and neuropsychiatric reactions as a side effect of the drug. Moreover, patients in our clinical trials may experience side effects that are indicated in the constituent drugs' labels, as was the case with the side effects experienced by patients in our clinical trials of Contrave. In addition, while the constituent drugs that make up Contrave have post-marketing safety records and while we have tested these constituent drugs in combination in our clinical trials of Contrave to date, the safety of the combined use of the constituents of Contrave is not yet fully known, and any future trials may produce side effects not observed to date. Any of the side effects of Contrave, or its individual constituent drugs, could limit the commercial profile of the approved label.

Further, if we or others, including our collaborative partner, identify undesirable side effects caused by the recently launched Contrave, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as an additional "boxed" warning with Contrave or an additional contraindication;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we or our collaborative partner may decide to remove the products from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product; and
- our reputation may suffer.

Any of these events could prevent us and our collaborative partner from achieving or maintaining market acceptance of Contrave or any other affected product candidate and could substantially increase the costs of commercializing Contrave and significantly impact our ability and our collaborative partner's ability to successfully commercialize Contrave and generate revenues.

We rely primarily on third parties to assist us in the conduct of 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 commercialize our product within our expected timeframes or at all.

We are currently working with a number of CROs for monitoring, oversight and statistical support for the Light Study. In addition, we expect to use a CRO to assist us with the additional post-marketing requirements for

Contrave, including the post-marketing CVOT. The third parties with whom we contract for execution of our clinical trials play a significant role in the conduct of our clinical trials and the subsequent collection, review and analysis of data. These third parties, including 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. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and that our regulatory filings are consistent with regulatory requirements. Our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs that assist us with our clinical studies are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and regulatory authorities may not accept the clinical data in support of our marketing applications or in connection with our post-marketing commitments. We cannot assure you that upon inspection by a given regulatory authority, such authority will determine that any clinical trial complied with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP regulations. If our CROs, consultants or independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard or fails to comply with regulatory requirements, it may adversely impact the commercialization of our product. In addition, the execution of clinical trials, the subsequent compilation, review and analysis of the data produced and the preparation of regulatory applications requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties provide the necessary resources and communicate and coordinate with one another. If these third parties are unable to provide the necessary resources or coordinate and communicate with one another, our clinical trials may be delayed or the completion and analysis of the data and the related regulatory applications may be delayed or compromised. Moreover, these third parties may also have relationships with other commercial entities, some of which may compete with us. If these third parties also contract to provide services for our competitors, it could adversely affect our business.

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

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 and commercial supplies. These supplies include the formulations of our product's APIs from our API suppliers, the tablets combining those components and the bottles used to package these tablets for commercial use and use in clinical trials. If the contract manufacturers upon whom we rely fail to produce our product in the volumes required on a timely basis, we may face delays in the continued development and commercialization of Contrave. In addition, pursuant to an amendment to our collaboration agreement with Takeda, effective in September 2013, Takeda assumed from us the responsibility to package Contrave for commercial sale in the United States, Canada and Mexico, and in September 2014, we entered into a manufacturing services agreement with Takeda to supply to Takeda all of Takeda's requirements of Contrave for commercialization in the United States.

In March 2010, we entered into a long-term manufacturing services agreement, or manufacturing agreement, with Patheon Pharmaceuticals and Patheon Inc., which we collectively refer to as Patheon, pursuant to which Patheon has agreed to manufacture commercial quantities of our Contrave tablet products. Under the terms of the manufacturing agreement, as amended by the parties in November 2013, we are required to purchase from Patheon a certain percentage of our requirements for Contrave tablet products intended for commercial sale, provided certain terms and conditions are met. The initial term of the manufacturing agreement commenced in March 2010 and shall continue in effect until December 31, 2019. Upon expiration of the initial term, the agreement will be automatically renewed for additional two year terms. Patheon may terminate the manufacturing agreement at any time upon specified prior written notice to us. We may also terminate the manufacturing agreement with specified prior written notice to Patheon, subject to our payment of certain

termination amounts. Either party may terminate the manufacturing agreement effective immediately upon written notice to the other in the event that (a) the other party dissolves, is declared insolvent or bankrupt by a court of competent jurisdiction, (b) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction, or (c) the manufacturing agreement is assigned for the benefit of creditors. We may terminate the manufacturing agreement upon specified prior written notice if any governmental or regulatory authority, including, but not limited to, the FDA, takes any action, or raises any objection, that prevents us from importing, exporting, purchasing or selling Contrave tablet products. We are also required to give specified advance notice if we intend to no longer order commercial supplies of Contrave tablet products pursuant to the manufacturing agreement due to the product's discontinuance in the market. Patheon may terminate the manufacturing agreement upon specified prior written notice to us if we assign any of our rights under the manufacturing agreement to an assignee that, in the opinion of Patheon acting reasonably, is (a) not a credit worthy substitute for us, or (b) a competitor of Patheon. Moreover, either party may terminate the manufacturing agreement upon written notice to the other party where the other party has failed to remedy a material breach of any of its representations, warranties, or other obligations under the manufacturing agreement within a specified period of time following receipt of a written notice of the breach, subject to specified terms and conditions.

If we change to other manufacturers in the future, 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 demonstrate successful technology transfer of the processes necessary for the production of our product.

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 for commercial production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, shortages of qualified personnel and production capacity, equipment failures as well as compliance with strictly enforced federal, state and foreign regulations, which include product requirements established by the FDA or other regulatory agencies and stability requirements in other foreign countries that our current product candidate formulations may not be able to meet. If our manufacturers were to encounter any of these difficulties in the United States or in other foreign countries or otherwise fail to comply with their obligations to us, or if we or our collaborative partner do not accurately forecast our demand, our ability or our collaborative partner's ability to support the commercial sale of Contrave or to provide product to patients in our and our collaborative partner's clinical trials would be jeopardized. Any delay or interruption in our ability to meet commercial demand for Contrave will result in the loss of potential revenues. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining a clinical trial program and, depending upon the period of delay, require us or such collaborative partner 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. While we are ultimately responsible for ensuring that our contract manufacturers operate in accordance with cGMP requirements and have implemented a quality oversight program, 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 successfully commercialize Contrave or obtain regulatory approval for or successfully complete any required clinical trials, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay in the sale of Contrave or any of its clinical trials, entail higher costs or result in our or Takeda being unable to effectively commercialize Contrave. 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 and Takeda may be unable to meet demand for Contrave and would lose potential revenues.

There are labeled adverse side effects to the individual use of bupropion and naltrexone.

A key constituent of Contrave 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 "boxed" 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 "boxed" warning statement. 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 "boxed" warning be extended to cover adults up to their mid-20's. The package insert for Contrave includes a "boxed" warning regarding the potential for suicidal thoughts and behaviors and neuropsychiatric reactions as a side effect of the drug. To the extent that any additional warnings or labeling changes related to suicidal thinking and behavior in adults are required, we expect that any such additional warnings or other labeling changes will also be required on labeling for Contrave. In July 2009, the FDA issued a news release announcing that it was requiring manufacturers to put a "boxed" warning on the prescribing information for smoking cessation drugs including Zyban®, which is a branded form of bupropion. The warning highlights the risk of serious mental health events including changes in behavior, depressed mood, hostility, and suicidal thoughts. Although Contrave is not intended to be promoted for or used in the treatment of major depression or smoking cessation, a similar warning is included in the labeling for Contrave, particularly because it is likely that there will be obese patients who smoke or depressed obese patients who will use Contrave.

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 included children or adolescents in the Contrave clinical trials, the FDA required us to create a Medication Guide for Contrave. These warnings and other requirements may have the effect of limiting the market acceptance by our collaborative partner's targeted physicians and patients of Contrave.

The other constituent of Contrave, naltrexone, has been approved by the FDA for the treatment of alcohol and opioid dependence. The FDA has directed the manufacturers of naltrexone for these indications to include in their product labels a "boxed" warning and expanded warnings statements regarding hepatotoxicity, or liver toxicity. A similar warning statement is included in the labeling for Contrave.

Each of the constituent drugs included in the Contrave combination 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. In addition, although Contrave is not known to be teratogenic, it appears from a recent FDA action, in which the FDA stated that weight loss offers no potential benefit to a pregnant woman and may result in fetal harm, that the FDA is likely to classify all weight loss pharmaceutical products as Category X. Contrave, the obesity therapeutics approved by the FDA in 2012 and orlistat all have Category X pregnancy precautions.

Any of these known side effects and any associated warning statements or classification or categorization of risk may limit the commercial profile of the approved label for Contrave and prevent us or Takeda from achieving or maintaining market acceptance of Contrave.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and we may be subject to fines, penalties or injunctions if we are determined to be promoting the use of our products for unapproved or "off-label" uses, resulting in damage to our reputation and business.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about approved drugs, such as Contrave. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling, also known as "off-label" promotion. Physicians may nevertheless use our product for their patients in a manner that is inconsistent with the approved label, as the FDA does not restrict or regulate a physician's choice of treatment within the practice of medicine. If the FDA determines that our promotional materials or training or the statements made by our sales representatives constitute promotion of an off-label use, it could request that we modify our training or promotional materials or subject us to regulatory or enforcement actions, which could have an adverse impact on our reputation and financial results.

If the suppliers upon whom we rely for API fail to produce such ingredients in the volumes that we or Takeda require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we or Takeda may face delays in the further development or commercialization of Contrave.

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. The failure or inability of our API suppliers to satisfy our API requirements on a timely basis could delay the commercialization of Contrave.

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 Substances Act or applicable foreign equivalents. As such, manufacturers of naltrexone API must be registered with the Drug Enforcement Administration, or DEA, or applicable foreign equivalents. 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 currently exist a limited number of manufacturers of this API. Therefore, API costs for naltrexone are greater than for the other constituents of our product. Demand for Contrave may require amounts of naltrexone greater than the currently available worldwide supply or our or our collaborative partner's current forecasts for the supply to us of Contrave or its components. Any lack of sufficient quantities of naltrexone would limit our or Takeda's ability to continue to commercialize Contrave and complete any additional required clinical trials. 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 at the appropriate quantities, quality or price.

In January 2009, we entered into a long-term supply agreement with Cilag AG, pursuant to which Cilag will manufacture commercial supplies of naltrexone for use in our drug products. The supply agreement shall continue in effect until December 31, 2018. Either party may terminate the supply agreement effective immediately upon written notice to the other in the event that (a) the other party dissolves, is declared insolvent or bankrupt by a court of competent jurisdiction, (b) a voluntary or involuntary petition of bankruptcy is filed in any court of competent jurisdiction, or (c) the supply agreement is assigned for the benefit of creditors. In addition, we may terminate the supply agreement effective immediately upon written notice in the event that (a) any regulatory agency takes any action, or raises any objection that prevents us from importing, exporting, purchasing or selling a finished product containing naltrexone, (b) the product containing naltrexone fails during clinical trials and we withdraw our NDA, (c) we determine, in our sole discretion, to no longer pursue the development and/or commercialization of a product containing naltrexone, or (d) a legal proceeding shall be instituted against Cilag, which is reasonably likely to materially adversely affect Cilag's ability to properly perform under the supply agreement or subject us to any material risk of liability or loss. Moreover, either party

may terminate the agreement upon specified written notice of a failure by the other party to perform or observe any material covenant, condition or agreement to be performed or observed by it under the supply agreement, unless such breach has been cured within the specified notice period.

We entered into a supply agreement with Mallinckrodt, effective January 2013, pursuant to which Mallinckrodt manufactured commercial supplies of naltrexone for use in Contrave. The initial term of this supply agreement terminated in December 2014. Until an additional agreement is executed by both parties, we plan to purchase our supplies of naltrexone from Mallinckrodt pursuant to purchase orders.

Other than our agreement with Cilag, we have no other material, long-term commitments or supply agreements with any of our other API suppliers. Although we may seek to establish additional 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 additional long-term agreements, including an additional agreement with Mallinckrodt, on commercially reasonable terms, or at all. Consequently, we and our collaborative partner may not be able to successfully commercialize Contrave if we are unable to secure long-term supply commitments for its API components.

In addition, our API suppliers must comply with cGMP requirements enforced by the FDA through its facilities inspection program and must maintain and comply with their respective DMFs on file with the FDA. These requirements include, among other things, quality control, quality assurance and the generation and maintenance of records and documentation. Suppliers of our API may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. While we are ultimately responsible for ensuring that our contract manufacturers operate in accordance with cGMP requirements and have implemented a quality oversight program, 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 suppliers' failure to adhere to applicable laws or for other reasons, we may not be able to successfully commercialize Contrave, and we may be held liable for an injuries sustained as a result. Any of these factors could cause a delay of clinical trials or commercialization of Contrave, entail higher costs or result in our and Takeda being unable to effectively commercialize our product. Furthermore, if our suppliers fail to deliver the required commercial quantities of API on a timely basis, pursuant to the required specifications set forth in their respective DMF and at commercially reasonable prices, and we are unable to timely secure and qualify additional suppliers with applicable regulatory authorities, we and Takeda may not be able to successfully commercialize Contrave and/or we and Takeda partner may be unable to meet demand for our product and would lose potential revenues.

Contrave is a combination of generically-available pharmaceutical products, and our success is dependent on our ability and Takeda's ability to compete against off-label generic substitutes and demonstrate the advantages of our proprietary combination products.

Off-label use occurs when physicians prescribe a drug that is approved by the FDA for one indication for a different, unapproved indication. We believe that a practitioner seeking safe and effective therapy is not likely to prescribe such off-label generics in place of Contrave because the dosage strengths, pharmacokinetic profiles and titration regimens recommended for Contrave are not available using existing generic preparations of immediate release, or IR, naltrexone and bupropion ER, and there are no oral generic ER formulations of naltrexone. However, a physician could seek to prescribe off-label generics in place of Contrave. Such off-label prescriptions could significantly diminish the market potential of our product and significantly impact our ability and Takeda's ability to generate revenues.

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, as well as the differences in its 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 should limit 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, which could significantly diminish their market potential and significantly impact our ability and our collaborative partner's ability to successfully commercialize our product and generate revenues.

In addition, although we believe the current market prices for the generic forms of naltrexone 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 have limited sales and marketing experience and resources, and if we do not enter into additional collaboration or co-promotion arrangements, we may not be able to effectively market and sell Contrave outside the United States, Canada or Mexico, and our ability to generate revenues may be delayed or limited.

We are developing Contrave 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 effectively promote to these physician groups, we entered into a collaboration agreement with Takeda in September 2010 to further develop and commercialize Contrave in the United States, Canada and Mexico. In order to expand the market opportunity outside of these countries for Contrave we must either establish additional 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 developing our own sales and marketing presence. We may not be able to enter into additional collaboration or co-promotion arrangements on acceptable terms, if at all. If we are unable to enter into additional collaboration or co-promotion arrangements for Contrave outside the United States, Canada and Mexico and we must develop our own sales and marketing presence to address the large market of general and family practitioners and internists in these areas, we will require additional capital and our ability to market and sell our product and generate revenues from our product may be delayed or limited. We also face competition in our search for collaborators, co-promoters and sales force personnel. If our competitors are able to establish collaboration or co-promotion arrangements with pharmaceutical companies who have substantially greater resources than we have, our ability to successfully commercialize Contrave outside the United States, Canada and Mexico will be limited and as a result our competitors may be more successful in marketing and selling their products in these areas. Even if we do enter into additional collaboration or co-promotion arrangements with third parties, we will be reliant on such third parties to successfully develop and/or commercialize our product in these areas. These third parties may fail to develop or effectively commercialize our product because they cannot obtain the necessary regulatory approvals, decide to pursue a competitive potential product that may be developed outside of the collaboration or fail to devote the resources necessary to realize the full commercial potential of our product, especially in light of the resources being devoted by our competitors' collaboration and co-promotion partners. Any such failures would negatively affect our ability to generate revenues from sales of Contrave outside the United States, Canada and Mexico.

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 Contrave, because our NDA for Contrave relied, in part, upon the FDA's findings of safety and effectiveness for the previously-approved products that are incorporated into Contrave. Similar legislation for active substances with well-established medicinal use exists in the European Union under article 10a of European Directive 2001/83/EC, which allows for reference to scientific literature if active substances have been approved for at least ten years with recognized efficacy and an acceptable level of safety. There also are alleviations under article 10b of European Directive 2001/83/EC of the obligation to provide scientific references relating to individual active substances in combination products if such individual active substances have been previously authorized in the European Union, although not the obligation to provide results of new pre-clinical tests or new clinical trials relating to such combination products, which could provide an alternative pathway in Europe. 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 have taken advantage of Section 505(b)(2) for approval of Contrave, the FDA may also require us to perform additional studies or measurements to support changes from the previously-approved products incorporated into our product.

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 make certifications to the FDA with respect to 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 relevant 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 505(b)(2) 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. We have made paragraph IV certifications that Contrave does not infringe the bupropion ER formulation patents listed in the Orange Book, and have sent the appropriate notice to the patent holder and NDA holder. We have obtained three years of Hatch-Waxman marketing exclusivity for Contrave from the date of approval by the FDA on September 10, 2014. Under this form of exclusivity, the FDA is precluded from approving a 505(b)(2) NDA or ANDA for the same 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 might not prevent the FDA from approving a 505(b)(1) NDA that relies on its own clinical data. Further, if another company obtains approval for an identical 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, unless we conduct additional studies in support of a 505(b)(1) NDA.

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, efficacy and manufacturing. 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. For example, although Vivus obtained FDA approval for its combination product, phentermine/topiramate, in October 2012, the CHMP adopted an opinion recommending against the approval of the marketing authorization application for such product due to concerns about its long-

term effects on the heart and blood vessels, particularly due to the effects of the phentermine component, its long-term psychiatric effects (depression and anxiety were reported in the studies) and cognitive effects (such as problems with memory and attention) related to the topiramate component, as well as known risks with topiramate being potentially harmful to the unborn baby if taken by pregnant women. The CHMP also noted that there was a high probability that, if approved, Vivus' product would not be used strictly for the intended patients. Vivus requested a re-examination of the CHMP's opinion. After considering the grounds for this request, the CHMP re-examined the initial opinion, and confirmed the refusal of the marketing authorization in February 2013. Further, according to Vivus, the CHMP indicated that a pre-approval CVOT would be necessary to establish the long-term safety of its product. Additionally, although Arena obtained FDA approval for its product, lorcaserin, in May 2013, Arena announced that it has notified the EMA that it is withdrawing its marketing authorization application for lorcaserin in the European Union due to the CHMP's view that certain major objections remain outstanding that preclude a recommendation for approval of such marketing authorization application and Arena's belief that it cannot resolve the major objections related to the results of non-clinical studies prior to the time the CHMP would issue its final opinion. We may face similar negative recommendations with respect to any regulatory filings we submit for Contrave in the European Union and other geographies.

In October 2013, we submitted a CMA application for Contrave, under the name Mysimba, to the EMA, utilizing the EMA's centralized procedure, seeking approval of Contrave in the European Economic Area, or EEA, (which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein) for the management of obesity, including weight loss. As part of this process, we have established the required pediatric investigation plan, or PIP, which has been agreed to by the EMA's Pediatric Committee. The centralized procedure allows for the simultaneous market access of a product in all the Member States of the EEA. A CMA application is reviewed by the CHMP. After submission and validation of the CMA application, the CHMP generally has 210 days to complete its assessment and adopt an opinion on whether or not to recommend the granting of the Community MA. The 210 days period does not include the anticipated "clock stops" at specified points in the procedure, typically at day 120 (Consolidated List of Questions) and at day 180 (List of Outstanding Issues). The clock stops allow time for us to address the outstanding questions or issues raised by the CHMP. After day 180, depending on the List of Outstanding Issues, an oral hearing with the CHMP may be required to address specific issues. Assuming a positive opinion from the CHMP, the European Commission has to adopt a decision granting the CMA, based on the CHMP opinion. The European Commission usually adopts this decision within 67 days after receipt of the CHMP opinion, not counting clock stops as noted above.

In February 2014, we received from the CHMP the Day 120 Consolidated List of Questions regarding our Contrave CMA. The CHMP's key questions were consistent with the issues raised by the FDA during the course of Contrave development and the initial review of the NDA, such as manufacturing and quality, non-clinical studies, dosing regimen, and, most significantly, cardiovascular safety. We believe the questions were adequately addressed in our response based in part on the interim analysis of the Light Study.

In July 2014, we received the day 180 List of Outstanding Issues, or the Day 180 LOI, from the CHMP for our Mysimba CMA. The Day 180 LOI raised new issues. Specifically, the CHMP requested further justification of the balance of benefits and risks of Contrave treatment as well as additional information regarding post-approval risk minimization measures and pharmacovigilance activities. Details were also requested of our third-party suppliers of bupropion related to the starting materials. We submitted our response to the Day 180 LOI in September 2014. In October 2014, we received a second Day 180 LOI from CHMP. In December 2014, the CHMP adopted a positive opinion recommending the EC grant a CMA for Mysimba. The CHMP recently released minutes from their December meeting stating that the positive opinion for Mysimba was adopted by a majority vote with 31 members in favor and two opposed. Procedurally, a positive opinion and recommendation of the CHMP is then referred to the EC's Standing Committee, which is composed of representatives from each member state of the E.U. In a process that occurs either through a written procedure or in a meeting, the Standing Committee reviews the draft EC decision to grant marketing authorization. Draft decisions are adopted by majority vote. The EC recently informed us that, at the request of one member state, the draft EC decision

granting marketing authorization for Mysimba will be reviewed during a meeting of the Standing Committee to be held in March 2015. A positive decision issued by the EC would allow Mysimba to be placed on the market in all 28 E.U. member states, as well as Iceland, Liechtenstein and Norway. While we believe we adequately addressed the CHMP's requests, the EMA may ask for additional or different data in connection with its review of the CMA which could result in additional delays in its potential approval. We can provide no assurance that the CMA will be approved on this timeframe, or at all. As described above, such effects include the risks that Contrave may not be approved for all indications requested, which could limit the uses of our product and have an adverse effect on its commercial potential or require costly, post-marketing follow-up studies.

We can provide no assurance that the CMA will be approved on this timeframe, or at all. Failure to obtain regulatory approval for Contrave 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 Contrave may not be approved for all indications requested, which could limit the uses of Contrave and have an adverse effect on their commercial potential or require costly, post-marketing follow-up studies.

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

The use of our product in clinical trials and the sale of our product 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;
- 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.

Although we have commercial product liability insurance, which includes coverage for our ongoing and future clinical trials we perform, 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. 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.

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

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems to contain healthcare costs and improve quality. While reform proposals often involve expanding coverage to more individuals, healthcare 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.

In March 2010, the President signed into law one of the most significant health reform measures in decades. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the PPACA, substantially changes the way healthcare is financed by both governmental and private insurers, including several payment reforms that establish payments to hospitals and physicians based in part on quality measures, subjects biologic products to potential competition by lower-cost "biosimilars," and significantly impacts the pharmaceutical and medical device industries. The PPACA includes, among other things, the following measures:

- annual, non-deductible fees on any entity that manufactures or imports certain prescription branded drugs and biologics;
- increased Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program for both branded and generic drugs and expanded rebates owed by manufacturers to include rebates on Medicaid managed care utilization;
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical research;
- requirements for manufacturers to discount drug prices to eligible patients in the coverage gap by 50% at the pharmacy level and for mail order services in order for their outpatient drugs to be covered under Medicare Part D;
- an increase in the number of entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a licensure framework for follow-on biologic products.

The PPACA provisions on comparative clinical effectiveness research extend the initiatives of the American Recovery and Reinvestment Act of 2009, also known as the stimulus package, which included $1.1 billion in funding to study the comparative effectiveness of healthcare treatments and strategies. This stimulus funding was designated for, among other things, conducting, supporting or synthesizing research that compares and evaluates the risks and benefits, clinical outcomes, effectiveness and appropriateness of products. The PPACA also appropriates additional funding to comparative clinical effectiveness research. Although Congress has indicated that this funding is intended to improve the quality of healthcare, it remains unclear how the research will impact current Medicare coverage and reimbursement or how new information will influence other third-party payor policies.

In addition, the PPACA provides for a prevention and health promotion outreach and education campaign to raise public awareness of health improvement, including obesity reduction and obesity-related services that are available to Medicaid enrollees. The PPACA also provides funding for projects designed to reduce childhood obesity.

Other legislative changes have also been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and will stay in effect through 2024, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals.

In the European Union and some other international markets, the government provides health care at low cost to consumers and regulates pharmaceutical prices, patient eligibility or reimbursement levels to control costs for the government-sponsored health care system. Many countries have announced or implemented measures to reduce health care costs to constrain their overall level of government expenditures. These measures vary by

country and may include, among other things, patient access restrictions, suspensions on price increases, prospective and possibly retroactive price reductions and other recoupments and increased mandatory discounts or rebates, recoveries of past price increases, and greater importation of drugs from lower-cost countries to higher-cost countries. If our product is approved in these markets, these measures may negatively impact our revenues. In addition, certain countries set prices by reference to the prices in other countries where approved products are marketed. Thus, our inability to secure adequate prices for our products, if approved, in a particular country may not only limit the marketing of these products within that country, but may also adversely affect our ability to obtain acceptable prices in other markets. This may create the opportunity for third party cross border trade or influence our decision to sell or not to sell a product, if approved, thus adversely affecting our revenues.

We cannot predict what effect the PPACA or other healthcare reform or cost control initiatives that may be adopted in the future will have on our business. 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 and our collaborative partner's ability to set a price we believe is fair for our approved product;
- our or our collaborative partner's ability to generate revenues and achieve or maintain profitability; and
- the availability of capital.

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 retention efforts may be particularly challenging in light of our historical regulatory interactions with our Contrave NDA and our workforce reductions completed in February and June 2011. Our industry has experienced a high rate of turnover of management personnel in recent years. As our business continues to grow, and we transition from primarily a drug development company to a commercial product organization, we expect to experience changes in our executive team, including potential departures and the addition of new executives with other areas of expertise that will add value to our business. We may also experience some departures from our current executive team as individuals transition to new experiences and/or retirement. 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 successful development and commercialization of our product, our ability to raise additional capital and our ability to implement our overall business strategy.

We are highly dependent on the development, regulatory, commercial and financial expertise of our senior management, particularly Michael A. Narachi, our President and Chief Executive Officer. 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. If we lose any members of our senior management team, including Mr. Narachi, we may not be able to find suitable replacements, and our business may be harmed as a result. We are not aware of any key personnel who has plans to retire or leave our company in the immediate 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.

In addition, we have scientific and clinical advisors who assist us in formulating our product development and clinical and regulatory 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.

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 laws that may affect our ability to operate include:

- the federal healthcare program Anti-Kickback Statute (as amended by the PPACA, which modified the intent requirement of the Anti-Kickback Statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation), 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 promote pharmaceutical products and provide coding and billing advice to customers, and under the PPACA, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal false claims laws;
- 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.

Additionally, the compliance environment is changing, with more states mandating implementation of compliance programs, compliance with industry ethics codes, and spending limits, and other states requiring reporting to state governments of gifts, compensation, and other remuneration to physicians. The PPACA also imposes new reporting and disclosure requirements on device and drug manufacturers for any "transfer of value" made or distributed to prescribers and other healthcare providers. Such information is now publicly available in a searchable format. In addition, device and drug manufacturers are also required to report and disclose any investment interests held by physicians and their immediate family members during the preceding calendar year. Manufacturers were required to begin collecting requisite information on August 1, 2013, with the first reports due in 2014. Failure to submit requisite information may result in civil monetary penalties of up to an aggregate of $150,000 per year (and up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests not reported in an annual submission. Finally, under the PPACA, effective April 1, 2012, pharmaceutical manufacturers and distributors must provide the U.S. Department of Health and Human Services with an annual report on the drug samples they provide to physicians. The shifting regulatory environment, along with the requirement to comply with multiple jurisdictions with different compliance and/or reporting requirements, increases the possibility that a pharmaceutical company may run afoul of one or more laws.

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, exclusion from governmental health care programs, 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 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.

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, could result in delays in our regulatory 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 could be delayed.

Risks Related to Intellectual Property

Our market opportunity for Contrave may be limited by the relatively small number of issued U.S. patents and foreign patents that we own or in-license. In addition, although we have additional U.S. and international patent applications pending which seek further protection of our product, these applications may not issue on a timely basis or at all.

Contrave is currently protected by U.S. patent number 7,375,111, which we refer to as the Weber/Cowley composition patent, and U.S. patent number 7,462,626, which we refer to as the Weber/Cowley methods patent. Provided maintenance fees are paid, the Weber/Cowley composition patent is expected to expire in March 2025, and the Weber/Cowley methods patent is expected to expire in July 2024. Collectively, we refer to the Weber/Cowley composition patent and the Weber/Cowley methods patent as the Weber/Cowley patents. We own the Weber/Cowley patents, but they are subject to our license agreement with Oregon Health & Science University, or OHSU. The Weber/Cowley patents cover the current composition of Contrave and methods of administering it to treat obesity. We and/or our licensors have filed a number of international counterparts to the Weber/Cowley patents in foreign countries. A European counterpart application to the Weber/Cowley patent has issued in the European Patent Office, or EPO, and provides protection for Contrave in the various EPO countries in which the

patent has been registered. Several international counterparts to the Weber/Cowley patents have also issued in other foreign jurisdictions. However, we cannot provide assurance that other pending international counterparts will issue on a timely basis or at all. There is also no assurance that the currently pending claims in those foreign countries will not be rejected, that any such rejections and any future rejections will ultimately be overcome, nor that any claims that may issue will be sufficiently broad to protect Contrave in those foreign countries. Furthermore, we cannot be certain that the scope of any issued 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. If a competitor is willing to challenge the scope or validity of the Weber/Cowley patents, the competitor could file an NDA seeking approval for three years after the date we obtained approval from the FDA of the NDA for Contrave.

We have also filed patent applications, directed to various treatment and formulation aspects of Contrave, in the United States and certain foreign countries under the Patent Cooperation Treaty, or PCT. Use of our proprietary tri-layer Contrave tablet for weight loss is protected in the United States by U.S. patent numbers 8,088,786 and 8,318,788, which are expected to expire in February 2029 and November 2027, respectively. Corresponding patents have issued in several foreign countries. In addition, the dose escalation schedule of Contrave is protected by U.S. patent 8,722,085, which is expected to expire in November 2027. U.S. patent number 8,815,889, directed to methods of treating insulin resistance using Contrave, including in obese patients, issued in August 2014, and is expected to expire in July 2024. The PCT 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. Such steps have been taken in various foreign countries, including Europe and Japan, with respect to a number of our PCT filings. Thus, we now have patent applications pending in those foreign countries, along with our previous filings in the United States and certain non-PCT countries. These filings seek to provide further protection for Contrave in the United States and overseas; however, we cannot provide assurance that the claims in the other patent applications will issue in their current form or at all.

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.

While we have filed patent applications in many countries outside the United States, and have obtained some patent coverage for Contrave in certain foreign countries, we do not currently have widespread patent protection for Contrave outside the United States and have no protection in many foreign jurisdictions. Even if international patent applications 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 and/or compulsory licensing 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 and our collaborative partner may face competition from the off-label use of other dosage forms of the generic components in our product. In addition, others may attempt to commercialize our product combination in the countries of the European Union, Canada, Mexico, Japan or other markets, in some of which, we do not have patent protection for our product. Due to the lack of patent protection for these combinations in some 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 component of our product (naltrexone IR) in those other territories. The off-label use of the generic IR component in the United States or the importation of the generic IR component from foreign markets could adversely affect the commercial potential for our product and adversely affect our overall business and financial results.

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

We have in-licensed and otherwise contracted for rights to our product, and we may enter into similar licenses in the future to supplement our product pipeline. Under the relevant agreements, we are subject to

commercialization, development, sublicensing, royalty, insurance and other obligations. If we or our collaborative partner 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.

Restrictions on our patent rights relating to Contrave may limit our and Takeda's ability to prevent third parties from competing against us.

Our success will depend on our and Takeda's ability to obtain and maintain patent protection for Contrave, 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 will be considered novel and unobvious by the PTO and courts.

In addition to composition of matter patents and patent applications, we also have issued and filed method of use patents and patent applications. This type of patent protects the use of Contrave 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 key 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 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 and Takeda 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 and Takeda 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 or Takeda 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 and our collaborative partner's ability to develop, manufacture, market and sell our product 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 collaborative partner are developing products. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product 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 or proprietary technologies. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us or Takeda, which may later result in issued patents that Contrave 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 and/or proprietary technologies infringe their intellectual property rights. If one of these patents is found to cover Contrave, proprietary technologies or their uses, we or Takeda could be enjoined by a court and required to pay damages and could be unable to commercialize our product or use our proprietary technologies unless we or they obtained a license to the patent. A license may not be available to us or Takeda 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 or our collaborative partner 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 Takeda 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 product 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 ER, naltrexone ER, our finished Contrave tablets combining these components, and the packaging for these tablets from third-party manufacturers. Each aspect of product design, formulation, manufacturing, packaging, and use has the potential to implicate third-party patent rights. We have taken various measures to reduce the potential for infringement. However, we could be exposed to potential patent infringement liability from other third parties who hold patents on various formulations of bupropion and naltrexone.

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 or Takeda from adopting or marketing a particular formulation or product, or could expose us to patent infringement liability.

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 Weber/Cowley patents covering Contrave, as well as our other issued patents, are due to be paid to the PTO in several stages over the lifetimes of the 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 issued and 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.

We have received U.S. trademark registration number 3396021 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. We have obtained trademark registrations in Canada, the European Union, and Japan for the same mark. In addition, we have received U.S. trademark registration number 3396807 for our corporate name OREXIGEN for use in connection with pharmaceutical preparations for the treatment of disorders of the central nervous system, or CNS, printed instructional, educational and teaching materials in the field of treatment and management of disorders of the CNS, and providing medical information in the field of disorders of the CNS. We have obtained trademark registrations in Canada, the European Union, and Japan for the same mark and have pending applications in Brazil and Russia. We have obtained foreign trademark registrations for the corporate name Orexigen Therapeutics, Inc. in the European Union and Japan. We have received U.S. trademark registration number 3393576 for the mark CONTRAVE for use in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss. An intent-to-use application for the CONTRAVE mark has been filed in the United States in connection with certain printed materials and medical information services. We have also obtained foreign trademark registrations for the mark CONTRAVE in Canada, Europe and Japan and have pending applications in Brazil, Canada, and Russia. In addition, applications for a Contrave logo for use in connection with pharmaceutical preparations for use in the treatment of obesity and inducing weight loss, certain printed materials and medical information services are pending in the U.S. and Canada. The Contrave logo is registered in Europe and 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. 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 have focused primarily on developing our first approved product, Contrave. 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. As of December 31, 2014, we had an accumulated deficit of approximately $552.0 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 to continue to incur significant and increasing operating losses for the foreseeable future and such losses have had, and will continue to have, an adverse effect on our stockholders' equity. Because of the numerous risks and uncertainties associated with developing and commercializing 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 significant revenue from our product and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. With the exception of the amortization of the upfront payment of $50.0 million from Takeda upon execution of the collaboration agreement and regulatory and development milestones totaling $100.0 million from Takeda, we have not generated any significant revenue, and we do not know when, or if, we will generate any significant revenue. Takeda commercially launched Contrave in October 2014. Our ability to generate revenue depends on a number of factors, including, but not limited to, Takeda's ability to effectively commercialize Contrave and our ability to:

- successfully manage our collaborative relationship with Takeda to effectively launch, market and sell Contrave in the United States, Canada and Mexico;
- successfully complete future trials for Contrave, including the required post-marketing studies;
- maintain regulatory approval of Contrave;
- manufacture commercial quantities of Contrave at acceptable cost levels; and
- identify and enter into one or more additional strategic collaborations to effectively market and sell Contrave outside the United States, Canada and Mexico, if approved.

We anticipate incurring significant costs associated with the continued development and commercialization of our approved product, Contrave. We will not achieve profitability until well after the commercial launch of Contrave, if ever. If we or Takeda are unable to generate product revenues, we will not become sustainably profitable and may be unable to continue operations without continued funding.

We may need additional funds and/or need to enter into additional collaborative or other agreements in order to fund post-marketing studies for Contrave or clinical trials outside the United States for Contrave, and commercialize Contrave outside the United States, Canada and Mexico, and we may be unable to raise capital when needed or enter into such an agreement, which would force us to delay, reduce or eliminate development and commercialization activities required for Contrave, and our commercialization efforts for Contrave outside such countries.

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, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least the next 12 months. 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 additional capital to:

- fund our operations and to conduct post-marketing requirements for Contrave;
- commercialize Contrave outside the United States, Canada and Mexico;
- co-promote Contrave in the United States; and
- qualify and outsource the commercial-scale of our products under cGMP.

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

- the successful commercialization of Contrave.
- the rate of progress and cost of clinical activity, including the new CVOT for Contrave, and the scope and cost of the additional post-marketing requirements for Contrave, including expenses to support the trials and milestone payments that may become payable;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish with respect to Contrave;
- the costs of establishing sales, marketing and distribution capabilities in order to commercialize Contrave should we elect to do so;
- the costs involved in enforcing or defending patent claims or other intellectual property rights;
- the costs and timing of additional regulatory approvals for Contrave; and
- the extent to which we in-license, acquire or invest in other indications, products, technologies and businesses.

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, milestone payments, debt, receivables or royalty 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 may be affected by numerous factors, including:

- the level of underlying demand for Contrave, wholesalers' buying patterns with respect to Contrave and Takeda's ability to successfully market Contrave under our collaboration agreement;
- variations in the level of expenses related to our product or future development programs;
- regulatory developments affecting our product or those of our competitors;
- the timing of future payments, if any, we may receive under our collaboration agreement with Takeda;
- our execution of any additional collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;

- addition or termination of clinical trials or funding support; and
- any intellectual property infringement lawsuit in which we may become involved.

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, receivables and royalty financings typically contain covenants that restrict operating activities and may impair our ability to in-license potential products or product candidates. Debt, receivables and royalty financings may also be coupled with an equity component, such as warrants to purchase stock, which could also result in dilution of our existing stockholders' ownership.

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 our product.

We sold $115 million aggregate principal amount of 2.75% Convertible Senior Notes in December 2013, which may impact our financial results, result in the dilution of existing stockholders, and restrict our ability to take advantage of future opportunities.

In December of 2013, we sold $115 million aggregate principal amount of 2.75% Convertible Senior Notes due 2020, or the 2020 Notes. We will be required to pay interest on the 2020 Notes until they come due, are called by us, or are converted, and the payment of that interest will reduce our net income. The sale of the 2020 Notes may also affect our earnings per share figures, as accounting requirements require that we include in our calculation of earnings per share the number of shares of our common stock into which the 2020 Notes are convertible. On June 27, 2014, our stockholders approved a flexible conversion option that allows us to pay the conversion right on these 2020 Notes in cash and/or shares. The flexible conversion right may allow us to exclude from the earnings per share calculation the shares of our common stock into which the 2020 Notes are convertible. However, we cannot guarantee that the flexible conversion option would result in the accounting treatment described above. The 2020 Notes may be converted, under the conditions and at the premium specified in those 2020 Notes, into shares of our common stock and/or into the cash equivalent of shares of our common stock. If converted into shares, the 2020 Notes will result in the dilution of our shareholders. If converted into cash, the 2020 Notes may require the payment of significant additional amounts above the initial principal. The payment of the interest payments, the repayment of the principal, and the potential payment of the conversion premium will require the use of a substantial amount of our cash, and if such cash is not available, we may be required to sell other assets or enter into alternate financing arrangements at terms that may or may not be desirable. The existence of the 2020 Notes and the obligations we incurred by issuing them may restrict our ability to take advantage of certain future opportunities, such as engaging in future debt or equity financing activities, which may reduce or impair our ability to acquire new businesses or invest in our existing businesses.

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. 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., or Nasdaq, have imposed various 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 devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations result in increased legal and financial compliance costs and will make some activities more time-consuming and costly.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure. In particular, we are required to 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 have incurred and continue to 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 may need to hire additional accounting and financial staff with appropriate experience and technical accounting knowledge. Moreover, if we do not comply with the requirements of Section 404, 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.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations could be materially negatively affected by economic conditions generally, both in the U.S. and elsewhere around the world. Domestic and international equity markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue and the markets continue to remain volatile, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may further decline. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

We may lose the ability to use our net operating loss carryforwards, which could prevent or delay us from offsetting future taxable income.

We have incurred substantial losses during our history and do not expect to become profitable in 2015 and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Our federal and state net operating loss carryforwards begin to expire in 2024 and 2015, respectively. Additionally, the future utilization of our net operating loss carryforwards and credits to offset future taxable income is subject to annual limitations, pursuant to Sections 382 and 383 of the Internal Revenue Code, as a result of ownership changes that have occurred in prior years or may occur in the future, which could defer our ability to utilize or prevent us from fully utilizing our net operating loss carryforwards, or NOLs, and credits, which could have an adverse effect on our results of operations. We completed an ownership change analysis in accordance with Section 382 from inception through December 31, 2014. As a result of the study, it was determined that we experienced several ownership changes during this period with the last one occurring in December 2014. The analysis to determine the limitation of NOLs and federal credits as a result of the ownership changes has not been finalized. When this analysis is finalized, we will reassess the amount of net operating losses and federal credits subject to limitation under Section 382.

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. Over the last several years, the overall capital markets have been highly volatile. Since the commencement of trading in connection with our initial public offering, or IPO, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During the quarter ended December 31, 2014, the price per share for our common stock on the Nasdaq Global Market has ranged from a low sale price of $3.11 to a high sale price of $6.94. 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:

- announcements regarding the commercial sales for Contrave;
- FDA or international regulatory actions, including failure to receive regulatory approval outside the United States for Contrave;
- announcements regarding our clinical trials, including the Light Study, the Ignite Study and the post-marketing required clinical trials, including the CVOT, for Contrave;
- announcements regarding Vivus', Arena's and Eisai's approved obesity products, including sales, safety and efficacy results, and their respective regulatory submissions and/or the results of their respective clinical trials;
- announcements regarding our other competitors' regulatory submissions and/or the results of their clinical trials;
- announcements regarding our collaborative relationship with Takeda;
- announcements regarding bupropion or naltrexone;
- announcements regarding manufacturing or supply developments for Contrave;
- failure of any of our product to achieve commercial success;
- developments concerning current or future strategic collaborations;
- 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 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;
- healthcare reform measures and other third-party coverage and reimbursement policies; 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.

Any future sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could adversely affect the price of our common stock. We cannot predict

the effect, if any, that market sales of any such shares of common stock or the availability of any such shares of common stock for sale would have on the market price of our common stock.

In addition, 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 may be able to sell in the public market, subject to the limitations of Rule 144 of the Securities Act of 1933, as amended. 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, directors, principal stockholders and their respective 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 February 18, 2015, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates together controlled approximately 29% of our outstanding common stock, assuming no exercise of outstanding options or warrants. 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 66 $^{2}/_{3}$% 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. 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 and could subject us to significant liabilities.

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 and other types of shareholder litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

In May 2013, we received a shareholder demand alleging that certain option grants to our President and Chief Executive Officer, Michael A. Narachi, our Chief Business Officer and acting-Chief Financial Officer, Joseph P. Hagan, and our Senior Vice President, General Counsel and Secretary, Heather D. Turner, in 2011 were granted in excess of the 1,500,000 share limit set forth in Section 3.3 of the Orexigen Therapeutics, Inc. 2007 Equity Incentive Award Plan, or Plan, as to the number of shares of our common stock with respect to which one or more stock awards may be granted to any one eligible participant during any of our fiscal years. We refer to this limit as the 162(m) Award Limit. Our board of directors established a demand review committee composed of independent directors to conduct an investigation with respect to the shareholder demand and to make recommendations to our board of directors. The demand review committee engaged independent counsel as part of its investigation and evaluated (1) the terms of the Plan, (2) the initial issuance procedures for the option grants to Mr. Narachi, Mr. Hagan and Ms. Turner during 2011, (3) the authority available to the compensation committee of our board of directors under its charter and the Plan, (4) the expectations of the award recipients and (5) the intent of our board of directors and the compensation committee regarding the availability of an exemption from the deductibility limitations of Section 162(m) of the Internal Revenue Code for such option grants. Following its investigation, the demand review committee determined that the 162(m) Award Limit first became effective as of June 2, 2011, and that, therefore, awards granted under the Plan prior to June 2, 2011, did not count toward the 162(m) Award Limit. The demand review committee determined that the awards granted to Mr. Hagan between June 2, 2011 and December 31, 2011 did not exceed the 162(m) Award Limit. The demand review committee further determined that the options granted to Mr. Narachi and Ms. Turner, including the portion of such awards in excess of the 162(m) Award Limit, were validly approved under the Plan, although the

portion of those awards in excess of the 162(m) Award Limit does not qualify as performance-based compensation under Section 162(m). In September 2013, the compensation committee amended the Plan, with the approval of our board of directors, to take the following actions: (1) to clarify that the 162(m) Award Limit only applies to awards or the portion thereof intended to qualify as performance-based compensation under Section 162(m); and (2) to confirm that the compensation committee has the authority to make awards in excess of the 162(m) Award Limit, which board action we refer to as the Plan Amendment. The Plan Amendment is deemed effective as of June 10, 2011, consistent with the authority of the compensation committee as administrator of the Plan as of that date. Any grants under the Plan in excess of the 162(m) Award Limit are not intended to qualify as performance-based compensation under Section 162(m).

On December 6, 2013, a plaintiff claiming to be a shareholder of ours filed a derivative lawsuit purportedly on behalf of us against certain of our officers and the members of our board of directors, in the Superior Court for the State of California, County of San Diego, captioned *Wilkin v. Narachi, et al*. On December 9, 2013, the same shareholder who made a demand on the board in May 2013 filed a derivative lawsuit purportedly on behalf of us against certain of our officers and current and former members of our board of directors in the United States District Court, for the Southern District of California, captioned *Turgeman v. Narachi, et al*. Both of the lawsuits assert claims for breach of fiduciary duty, waste and unjust enrichment based on, among other things, the alleged grant of stock options to certain officers in excess of the 162(m) Award Limit, repricing stock options allegedly in violation of our equity incentive plan, the board of directors' conduct in responding to the May 2013 shareholder demand, and making allegedly false and misleading statements. Both of the lawsuits seek, among other things, declaratory relief, corporate governance reforms, rescission of certain stock option awards, rescission of the Plan Amendment, injunctive relief, damages, restitution, disgorgement and attorney's fees. On July 23, 2014, we and the individual defendants filed a motion to dismiss the *Turgeman* complaint. The judge has not yet ruled on the motion. We and the individual defendants filed a motion to dismiss the *Wilkin* complaint on August 13, 2014. On October 24, 2014, the judge granted the motion to dismiss with leave to amend the complaint. The plaintiff did not file an amended complaint within the court-ordered deadline but filed a motion to stay the action. On January 29, 2015, the judge denied the motion to stay and dismissed the lawsuit with prejudice. On February 6, 2015, the parties filed a stipulation with the court in which plaintiff waived his right to appeal and the parties agreed to a judgment dismissing the lawsuit. We are awaiting the judge's signature on the final judgment. Although management believes that the claims lack merit and intends to defend against them vigorously, there are uncertainties inherent in any litigation and we cannot predict the outcome.

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 use as our corporate headquarters in La Jolla, California. In September 2008, we entered into an amendment to lease an additional 9,312 square feet bringing the total leased space to 31,541 square feet. In February 2012, we entered into a partial lease termination agreement to reduce the amount of leased office space at our corporate headquarters to a total of 22,229 square feet of leased space. In February 2013, we entered into an amendment to extend our lease to September 2017. 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 May 2013, we received a shareholder demand alleging that certain option grants to our President and Chief Executive Officer, Michael A. Narachi, our Chief Business Officer and acting-Chief Financial Officer, Joseph P.

Hagan, and our Senior Vice President, General Counsel and Secretary, Heather D. Turner, in 2011 were granted in excess of the 1,500,000 share limit set forth in Section 3.3 of the Orexigen Therapeutics, Inc. 2007 Equity Incentive Award Plan, or Plan, as to the number of shares of our common stock with respect to which one or more stock awards may be granted to any one eligible participant during any of our fiscal years. We refer to this limit as the 162(m) Award Limit. Our board of directors established a demand review committee composed of independent directors to conduct an investigation with respect to the shareholder demand and to make recommendations to our board of directors. The demand review committee engaged independent counsel as part of its investigation and evaluated (1) the terms of the Plan, (2) the initial issuance procedures for the option grants to Mr. Narachi, Mr. Hagan and Ms. Turner during 2011, (3) the authority available to the compensation committee of our board of directors under its charter and the Plan, (4) the expectations of the award recipients and (5) the intent of our board of directors and the compensation committee regarding the availability of an exemption from the deductibility limitations of Section 162(m) of the Internal Revenue Code for such option grants. Following its investigation, the demand review committee determined that the 162(m) Award Limit first became effective as of June 2, 2011, and that, therefore, awards granted under the Plan prior to June 2, 2011, did not count toward the 162(m) Award Limit. The demand review committee determined that the awards granted to Mr. Hagan between June 2, 2011 and December 31, 2011 did not exceed the 162(m) Award Limit. The demand review committee further determined that the options granted to Mr. Narachi and Ms. Turner, including the portion of such awards in excess of the 162(m) Award Limit, were validly approved under the Plan, although the portion of those awards in excess of the 162(m) Award Limit does not qualify as performance-based compensation under Section 162(m). In September 2013, the compensation committee amended the Plan, with the approval of our board of directors, to take the following actions: (1) to clarify that the 162(m) Award Limit only applies to awards or the portion thereof intended to qualify as performance-based compensation under Section 162(m); and (2) to confirm that the compensation committee has the authority to make awards in excess of the 162(m) Award Limit, which board action we refer to as the Plan Amendment. The Plan Amendment is deemed effective as of June 10, 2011, consistent with the authority of the compensation committee as administrator of the Plan as of that date. Any grants under the Plan in excess of the 162(m) Award Limit are not intended to qualify as performance-based compensation under Section 162(m).

On December 6, 2013, a plaintiff claiming to be a shareholder of ours filed a derivative lawsuit purportedly on behalf of us against certain of our officers and the members of our board of directors, in the Superior Court for the State of California, County of San Diego, captioned *Wilkin v. Narachi, et al* . On December 9, 2013, the same shareholder who made a demand on the board in May 2013 filed a derivative lawsuit purportedly on behalf of us against certain of our officers and current and former members of our board of directors in the United States District Court, for the Southern District of California, captioned *Turgeman v. Narachi, et al* . Both of the lawsuits assert claims for breach of fiduciary duty, waste and unjust enrichment based on, among other things, the alleged grant of stock options to certain officers in excess of the 162(m) Award Limit, repricing stock options allegedly in violation of our equity incentive plan, the board of directors' conduct in responding to the May 2013 shareholder demand, and making allegedly false and misleading statements. Both of the lawsuits seek, among other things, declaratory relief, corporate governance reforms, rescission of certain stock option awards, rescission of the Plan Amendment, injunctive relief, damages, restitution, disgorgement and attorney's fees. On July 23, 2014, we and the individual defendants filed a motion to dismiss the *Turgeman* complaint. The judge has not yet ruled on the motion. We and the individual defendants filed a motion to dismiss the *Wilkin* complaint on August 13, 2014. On October 24, 2014, the judge granted the motion to dismiss with leave to amend the complaint. The plaintiff did not file an amended complaint within the court-ordered deadline but filed a motion to stay the action. On January 29, 2015, the judge denied the motion to stay and dismissed the lawsuit with prejudice. On February 6, 2015, the parties filed a stipulation with the court in which plaintiff waived his right to appeal and the parties agreed to a judgment dismissing the lawsuit. We are awaiting the judge's signature on the final judgment. Although management believes that the claims lack merit and intends to defend against them vigorously, there are uncertainties inherent in any litigation and we cannot predict the outcome.

Item 4. Mine Safety Disclosure.

Not applicable.

PART II

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

Market Information

Our common stock is traded on the Nasdaq Global Market under the symbol "OREX."

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, 2014:		
Fourth Quarter	$6.94	$3.11
Third Quarter	6.53	4.23
Second Quarter	7.02	4.76
First Quarter	7.82	5.48
Year Ended December 31, 2013:		
Fourth Quarter	$7.05	$4.60
Third Quarter	7.84	5.60
Second Quarter	7.34	5.55
First Quarter	6.68	4.98

On February 23, 2015, the last reported sale price of our common stock on the Nasdaq Global Market was $6.04. As of February 23, 2015, there were 31 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. 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.

Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2014.

Plan Category	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:	17,958,969	$ 3.59	5,269,668(1)
Equity compensation plans not approved by security holders:	—	N/A	2,500,000(2)
Total	17,958,969	$ 3.59	7,769,668

(1) Represents shares reserved for issuance under the 2004 Stock Plan, the 2007 Equity Incentive Award Plan, as amended, or the 2007 Plan or the 2013 Employee Stock Purchase Plan. The 2007 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 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 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

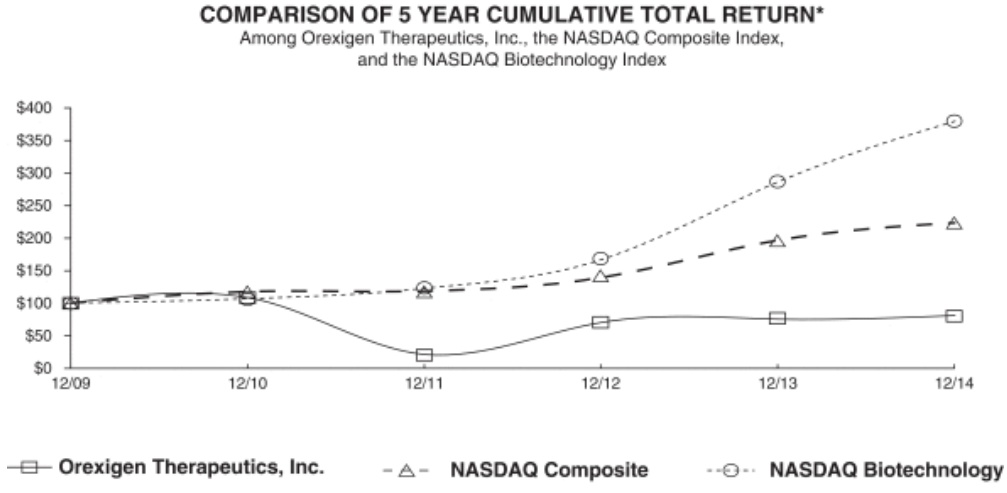
January 1, 2008. The annual increase in the number of shares shall be equal to the lesser of (i) 15% of our outstanding common stock on the applicable January 1, (ii) 6,000,000 shares of common stock, or (iii) a lesser amount determined by our board of directors. The 2007 Plan provides that the maximum number of shares that may be granted pursuant to the exercise of incentive stock options granted under the plan is 40,000,000 shares. The 2013 Employee Stock Purchase Plan was approved in June 2013.

(2) Represents shares reserved for issuance under the 2007 Plan to individuals not previously an employee or non-employee director of ours (or following a bona fide period of non-employment with us), as an inducement material to each individual's entering into employment with us, or the Inducement Reserve, within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules, or Rule 5635(c)(4). The 2007 Plan was amended in October 2009 to provide for the reservation of 500,000 shares of our common stock to be issued pursuant to the Inducement Reserve without stockholder approval, as permitted under Rule 5635(c)(4). The 2007 Plan was further amended without stockholder approval in February 2010 to reserve an additional 2,000,000 shares of our common stock to be issued pursuant to the Inducement Reserve.

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.



*$100 invested on 12/31/09 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

	December 31, 2009	December 31, 2014
Orexigen Therapeutics, Inc.	$ 100	$ 81
Nasdaq Composite Index	$ 100	$ 224
Nasdaq Biotechnology Index	$ 100	$ 380

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 on Form 10-K.

	Years Ended December 31,				
	2014	2013	2012	2011	2010
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Revenues:					
Collaborative agreement	$ 54,229	$ 3,428	$ 3,428	$ 3,428	$ 1,143
Royalties	1,292	—	—	971	88
Total revenues	55,521	3,428	3,428	4,399	1,231
Operating expenses:					
Research and development	57,412	56,748	73,680	12,780	28,131
General and administrative	28,639	23,878	19,987	19,502	24,495
Total operating expenses	86,051	80,626	93,667	32,282	52,626
Loss from operations	(30,530)	(77,198)	(90,239)	(27,883)	(51,395)
Other income (expense):					
Interest income	88	65	147	46	124
Interest expense	(7,083)	(538)	(2)	(221)	(644)
Total other income (expense)	(6,995)	(473)	145	(175)	(520)
Net loss	$ (37,525)	$(77,671)	$(90,094)	$(28,058)	$(51,915)
Basic and diluted net loss per share[1]	$ (0.32)	$ (0.80)	$ (1.27)	$ (0.58)	$ (1.10)
Shares used to calculate net loss per share[1]	118,240	96,491	70,739	48,273	47,377

(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,				
	2014	2013	2012	2011	2010
	(In thousands)				
Balance Sheet Data:					
Cash and cash equivalents and investment securities, available-for-sale	$ 205,537	$ 176,996	$ 137,403	$ 147,593	$ 92,366
Working capital	181,612	155,429	113,780	141,013	78,580
Total assets	212,981	180,121	139,154	149,700	96,846
Long-term convertible debt	83,908	80,031	—	—	—
Accumulated deficit	(552,000)	(514,475)	(436,804)	(346,710)	(318,652)
Total stockholders' equity	22,344	41,862	75,469	99,706	33,788

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 on Form 10-K. 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 on Form 10-K.

Overview

Background

We are a biopharmaceutical company focused on the treatment of obesity. Our sole product, Contrave, is approved in the United States by the U.S. Food and Drug Administration, or FDA, as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index, or BMI, of 30 kg/m^2 or greater (obese), or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition. Contrave is a combination of generic drug components, each of which has already received regulatory approval for other indications and been commercialized in the United States and in a majority of the member countries of the European Union.

On September 10, 2014, the FDA notified us that it had approved our NDA for Contrave extended-release. We and our collaboration partner, Takeda Pharmaceutical Company Limited, or Takeda, are now focused on the commercialization of Contrave. Takeda commercially launched Contrave in October 2014. As part of the approval of Contrave by the FDA, we and Takeda agreed to several post-marketing requirements, including studies to assess the safety and efficacy of Contrave for weight management in obese pediatric patients. We are also required to conduct a new randomized double-blind, placebo-controlled study to evaluate the effects of long-term treatment with Contrave on the incidence of major adverse cardiovascular, or CV, events in overweight and obese subjects with CV disease or multiple CV risk factors, as well as a group of short-term trials including a thorough QT study, single-dose pharmacokinetic studies in renal and hepatic impairment, and a drug-drug interaction study.

In October 2013, we submitted a marketing authorization application for Contrave, under the name Mysimba, to the European Medicines Agency, or EMA. This submission is being reviewed by the EMA's Committee for Medicinal Products for Human Use, or CHMP, for the first time. In December 2014, the CHMP adopted a positive opinion recommending the European Commission, or EC, grant a centralized marketing authorization, or CMA, for Mysimba. The CHMP recently released minutes from their December meeting stating that the positive opinion for Mysimba was adopted by a majority vote with 31 members in favor and two opposed. Procedurally, a positive opinion and recommendation of the CHMP is then referred to the EC's Standing Committee for Medicinal Products, or Standing Committee, which is composed of representatives from each member state of the E.U. In a process that occurs either through a written procedure or in a meeting, the Standing Committee reviews the draft EC decision to grant marketing authorization. Draft decisions are adopted by majority vote. The EC recently informed us that at the request of one member state, the draft EC decision granting marketing authorization for Mysimba will be reviewed during a meeting of the Standing Committee being held in March 2015. A positive decision by the Standing Committee would allow Mysimba to be placed on the market in all 28 E.U. member states, as well as Iceland, Liechtenstein and Norway.

In December 2013, we issued $115.0 million in aggregate principal amount of 2.75% Convertible Senior Notes due 2020, or the 2020 Notes, in an offering to qualified institutional buyers conducted in accordance with Rule 144A under the Securities Act of 1933, as amended. Net cash proceeds from the issuance of the 2020 Notes were approximately $110.5 million, after deducting initial purchasers' discounts and commissions and estimated offering expenses payable by us.

Our primary activities since incorporation have been organizational activities, including recruiting personnel, conducting research and development, including clinical trials, and raising capital. We have incurred significant net losses since our inception. As of December 31, 2014, we had an accumulated deficit of $552.0 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, performing manufacturing-related activities, and general and administrative expenses. We expect to continue to incur losses for the next several years. Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support our cost structure, and until that time, we may need to continue to raise additional equity or debt financing.

Revenues

We generated approximately $55.5 million in revenue in 2014, resulting from the sublicensing of technology and amounts earned under our collaboration agreement with Takeda. In September 2010, we entered into a collaboration agreement with Takeda to develop and commercialize Contrave in the United States, Canada and Mexico. Under the collaboration agreement, we received an upfront, nonrefundable cash payment of $50.0 million from Takeda and this amount is being recognized ratably over the estimated life of the agreement. In September 2014, we also recognized two regulatory/development milestones, consisting of $20.0 million due to us upon regulatory approval in the United States and $10.0 million due to us upon the delivery of launch supplies to Takeda. In October 2014, we earned and were paid a $70.0 million milestone from Takeda for the shipment of Contrave to pharmacy wholesalers in preparation for the commercial launch. This milestone payment was determined to not meet the definition of a substantive milestone. As a result, we recognized $20.8 million in 2014 with $49.2 million deferred which will be recognized over the remaining estimated life of the agreement. Additionally, we recognized $1.3 million in royalties earned for the sale of Contrave by Takeda in 2014.

Other than the amortization of the upfront payment of $50.0 million and regulatory/development milestones totaling $100.0 million from Takeda, our ability to generate revenue in the near term will depend solely on the success of Takeda sales of Contrave in the U.S. Takeda commercially launched Contrave in October 2014. We are eligible to receive tiered royalty payments ranging from a minimum of 20% to a maximum of 35%, subject to customary reductions, on increasing levels of net sales of Contrave in the United States, Canada and Mexico. Given the early stage of commercialization, it is difficult to predict the amount of future sales of Contrave or the related revenues we will generate. Future sales of Contrave will depend on, among other factors, the availability and use of Contrave, Takeda's ability to effectively launch, market and sell Contrave and coverage and reimbursement by third-party payors.

Takeda accounted for 100% of revenue for each of the years ended December 31, 2014, 2013 and 2012.

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 consisted primarily of costs associated with clinical trials managed by our contract research organizations, or CROs, product development efforts, raw materials, inventory, and manufacturing-related expenses. 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. The clinical trial expenses included 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.

Our internal research and development resources are not directly tied to any individual research project and are primarily deployed across our Contrave and other programs. We have developed Contrave in parallel with other projects 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.

The following table summarizes our research and development expenses for the year ended December 31, 2014. Costs that are not attributable to a specific research program are included in the "Other" category (in thousands):

Costs of external service providers:	
Obesity	$42,163
Other	356
Subtotal	42,519
Internal costs	10,439
Stock-based compensation	4,454
Total research and development costs	$57,412

At this time, due to the risks inherent in the drug development process, we are unable to estimate with any certainty the costs we will incur for the post-marketing requirements of Contrave and any additional clinical trials required for potential approval of Contrave, under the name Mysimba, by the EMA. Specifically, we cannot quantify the development expenses associated with completion of the Light Study for Contrave. Prior to its commencement, we anticipated that the costs to conduct the Light Study to the interim analysis would be approximately $100.0 million. We believe the costs we have incurred to date and expect to incur in the future in connection with the conduct of the Light Study are consistent with our original projection. Until we are able to finalize the protocol, we are unable to predict the cost of the new CV outcomes trial that we and Takeda are responsible for conducting. Future development expenses will depend on the timing of the Light Study, the new CV outcomes trial and any other additional clinical trials for Contrave, if any, our financial resources and ongoing assessments as to Contrave's commercial potential. Clinical development timelines, the probability of success and development costs can differ materially from expectations. The lengthy process of completing our clinical trials, including the Light Study, 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, including the Light Study, 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. Contrave became commercially available in the U.S. in October 2014.

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 general and administrative expenses to remain generally unchanged.

Interest and Other (Expense), Income net

Interest and Other (Expense), Income net, consists principally of interest expense incurred on the 2020 Notes, offset by income earned on marketable securities.

Income Taxes

At December 31, 2014, we have federal and state net operating loss carryforwards of approximately $398.1 million and $392.4 million, respectively, not considering the IRC Section 382 annual limitation discussed below. The federal and state net operating loss carryforwards begin to expire in 2024 and 2015, respectively, unless previously utilized. At December 31, 2014, we have federal and state research and development tax credit

carryforwards of $18.5 million and $5.5 million, respectively. The federal research and development tax credit carryforwards begin to expire in 2024 unless previously utilized and the state tax credits carry forward indefinitely. Under Sections 382 and 383 of Internal Revenue Code, substantial changes in our ownership may limit the amount of net operating loss carryforwards and federal tax credit carry forwards that could be utilized annually in the future to offset taxable income, and tax, respectively. The Company has completed an ownership change analysis in accordance with Section 382 from inception through December 31, 2014. As a result of the analysis, it was determined that the Company experienced several ownership changes during this period with the last one occurring in December 2014. The analysis to determine the limitation of NOLs and federal credits as a result of the ownership changes has not been finalized. Based on our preliminary analysis of the limitation of our net operating losses and federal credits, we have removed deferred tax assets for net operating losses of $254.1 million and $231.1 million for federal and state, respectively, and federal research and development credits of $9.6 million from our deferred tax asset schedule and have recorded a corresponding decrease to our valuation allowance. When this analysis is finalized, we will reassess the amount of net operating losses and federal credits subject to limitation under Section 382. Due to the existence of the valuation allowance, future changes in the deferred tax assets related to these tax attributes will not impact our effective tax rate.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations are based upon our financial statements, which are prepared in accordance with accounting principles that are generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, related disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. We continually evaluate our estimates and judgments, the most critical of which are those related to accounting for research and development expenses and stock-based compensation costs. We base our estimates and judgments on historical experience and other factors that we believe to be reasonable under the circumstances. Materially different results can occur as circumstances change and additional information becomes known.

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 or are expected to be 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, patient visits to clinical sites for routine testing associated with the clinical trials, and progress of clinical 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. In October 2014, the Company transferred the responsibility for conducting the Light Study to Takeda pursuant to the terms of the collaboration agreement, as amended.

Revenue Recognition

We have a collaboration agreement with Takeda Pharmaceutical Company Limited ("Takeda") which contains multiple elements, including nonrefundable upfront fees, payments associated with achieving specific development milestones and royalties based on specified percentages of net product sales, if any.

Prior to the revised multiple element and milestone method of revenue recognition guidance adopted by us on January 1, 2011, nonrefundable, up-front license fees and milestone payments with standalone value that are not dependent on any future performance by us under the agreements were recognized as revenue upon the

earlier of when payments were received or collection was assured, but were deferred if we had continuing performance obligations. If we had continuing involvement through contractual obligations under such agreements, such up-front fees were deferred and recognized over the period for which we continued to have a performance obligation. The collaboration agreement with Takeda has continuing obligations, and as a result the up-front fees were deferred upon receipt.

Effective January 1, 2011, for multiple element agreements entered into or materially modified after December 31, 2010, we follow the provisions of ASU No. 2009-13. In order to account for the multiple-element arrangements, we identify the deliverables included within the agreement and evaluate which deliverables represent separate units of accounting. Analyzing the arrangement to identify deliverables requires the use of judgment, and each deliverable may be an obligation to deliver services, a right or license to use an asset, or another performance obligation. A delivered item is considered a separate unit of accounting when the delivered item has value to the partner on a standalone basis based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research capabilities of the partner and the availability of research expertise in this field in the general marketplace. Arrangement consideration is allocated at the inception of the agreement to all identified units of accounting based on their relative selling price. The relative selling price for each deliverable is determined using vendor-specific objective evidence, or VSOE, of selling price or third-party evidence of selling price if VSOE does not exist. If neither VSOE nor third-party evidence of selling price exists, we use our best estimate of the selling price for the deliverable. The amount of allocable arrangement consideration is limited to amounts that are fixed or determinable. The consideration received is allocated among the separate units of accounting, and the applicable revenue recognition criteria are applied to each of the separate units. Changes in the allocation of the sales price between delivered and undelivered elements can impact revenue recognition but do not change the total revenue recognized under any agreement. Upfront license fee payments are recognized upon delivery of the license if facts and circumstances dictate that the license has standalone value from the undelivered items, which generally include research and development services and the manufacture of drug products, the relative selling price allocation of the license is equal to or exceeds the upfront license fee, persuasive evidence of an arrangement exists, our price to the partner is fixed or determinable, and collectability is reasonably assured. The adoption of this new accounting standard did not have a material impact on our results of operations or financial position.

Upfront license fee payments are deferred if facts and circumstances dictate that the license does not have standalone value. The determination of the length of the period over which to defer revenue is subject to judgment and estimation and can have a material impact on the amount of revenue recognized in a given period.

The terms of our collaboration agreements provide for milestone payments upon achievement of certain regulatory/development and sales-based events. Effective January 1, 2011, we adopted on a prospective basis the guidance under ASU No. 2010-17, "*Revenue Recognition-Milestone Method*". Under the Milestone Method of accounting, we recognize consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is substantive in its entirety. A milestone is considered substantive when it meets all of the following three criteria: 1) The consideration is commensurate with either the entity's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, 2) The consideration relates solely to past performance, and 3) The consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. A milestone is defined as an event (i) that can only be achieved based in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting from the entity's performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (iii) that would result in additional payments being due us. Any milestone payments received prior to satisfying these revenue recognition criteria were recorded as deferred revenue in the accompanying consolidated financial statements.

Royalties to be received based on sales of our licensed products by partners will be recognized as earned.

Convertible Senior Notes

In December 2013, we issued the 2020 Notes. The 2020 Notes are accounted for in accordance with Financial Accounting Standards Board, or FASB, ASC 470, formerly FSP APB 14-1, *Accounting for Convertible Debt Instruments That May be Settled in Cash upon Conversion (Including Partial Cash Settlement)*. ASC Subtopic 470-20 requires the issuer of convertible debt that may be settled in shares or cash upon conversion at their option, such as the 2020 Notes, to account for the liability (debt) and equity (conversion option) components separately. The guidance requires the carrying amount of the liability component to be estimated by measuring the fair value of a similar liability that does not have an associated conversion feature. To measure the fair value of the liability component, we used an income approach, discounting the future contractual cash flows due under the 2020 Notes by a market interest rate. The market interest rate was determined to be 8.69%. Assumptions used in the estimate represent what market participants would use in pricing the liability component, including market interest rates, credit standing, and yield curves, all of which are defined as Level 2 observable inputs. The estimated implied interest rate was applied to the 2020 Notes, which resulted in a fair value of the liability component of $79.7 million upon issuance, calculated as the present value of implied future payments based on the $115.0 million aggregate principal amount. The $31.3 million difference between the cash proceeds of $111.0 million and the estimated fair value of the liability component was recorded in additional paid-in capital as the 2020 Notes. The liability component will be accreted to redemption value over the term of the 2020 Notes.

Stock-Based Compensation

We account for stock-based compensation to employees in accordance with the fair value method of accounting for stock-based compensation arrangements which requires us to expense the estimated fair value of non-cash, stock-based payments to employees. Share-based payment transactions with employees are recognized in the financial statements based on their fair value and recognized as compensation expense over the vesting period.

We grant options to purchase our common stock to our employees, directors and non-employees under our 2007 equity incentive award plan. Stock-based compensation expense for the years ended December 31, 2014, 2013 and 2012 was $15.3 million, $11.6 million and $7.6 million, respectively. At December 31, 2014, total unrecognized estimated stock-based compensation expense related to non-vested stock options granted prior to that date was $26.7 million, which is expected to be recognized over a weighted-average period of 1.8 years.

We calculate the fair value of stock option grants using the Black-Scholes option-pricing model. The determination of the fair value of stock-based payment awards on the date of grant using an option-pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables. These variables include, but are not limited to, our expected stock price volatility over the term of the awards, risk-free interest rate and the expected term of the awards.

The weighted average expected life of an award is based on historical forfeiture experience, exercise activity, and on the terms and conditions of the stock awards. For options granted during the year ended December 31, 2014, we have calculated a weighted average expected term of 5.6 years. The expected volatility is based on the historical volatility of our common stock over the most recent period commensurate with the estimated expected term of the stock awards. For purposes of estimating the fair value of stock options granted during 2014 using the Black-Scholes model, we used an estimated weighted average stock price volatility of 107.3%.

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 (weighted-average risk-free interest rate of 1.8% for the year ended December 31, 2014). The assumed dividend yield was based on our expectation of not paying dividends in the foreseeable future.

For 2014, 2013 and 2012, we have reduced stock-based compensation expense recognized in the Statement of Operations to reflect estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if

necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures were estimated to be approximately 10.0% for all years ended December 31, 2014, 2013 and 2012 based on historical experience.

Equity instruments issued to non-employees are recorded at their fair value and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

Income Taxes

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. We provide 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.

We follow the provisions of the Income Taxes Topic of the FASB Accounting Standards Codification, that defines a recognition threshold and measurement attributes for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The topic also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. Under the topic, 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.

Results of Operations

Comparison of year ended December 31, 2014 to year ended December 31, 2013

Revenues. Revenues increased to $55.5 million for the year ended December 31, 2014 from $3.4 million in 2013, and represent revenue recognized under our collaboration agreement with Takeda. The increase of approximately $52.1 million in 2014 was due primarily to recognition of two regulatory/development milestones, consisting of $20.0 million payable upon regulatory approval of Contrave in the United States and $10.0 million payable upon the delivery of Contrave launch supplies to Takeda. In the fourth quarter of 2014, we also recognized $20.8 million of a $70.0 million milestone we received from Takeda for the shipment of Contrave to pharmacy wholesalers in preparation for the commercial launch. Additionally, we recognized $1.3 million of royalty revenue for the sales of Contrave by Takeda in 2014.

Research and Development Expenses. Research and development expenses increased to $57.4 million for the year ended December 31, 2014 from $56.7 million in 2013. This increase of approximately $700,000 was due primarily to an increase in pre-launch expenses for Contrave including raw materials, inventory and manufacturing-related expenses of $10.1 million, an increase in salaries and personnel related costs of $1.1 million and an increase in stock-based compensation expense of $1.0 million. These increases were partially offset by an $11.3 million decrease in expenses in connection with our Contrave CVOT, related proprietary product formulation work and consulting activities.

General and Administrative Expenses. General and administrative expenses increased to $28.6 million for the year ended December 31, 2014 from $23.9 million in 2013. This increase of approximately $4.7 million was due primarily to increases in stock-based compensation expense of approximately $2.7 million, salaries and personnel related costs of approximately $900,000 and an increase in professional fees of approximately $898,000.

Interest Income. Interest income increased to $88,000 for the year ended December 31, 2014 from $65,000 in 2013. This decrease of approximately $23,000 was primarily due to an increase in average investment balances and higher interest rates as compared to 2013.

Interest Expense. Interest expense increased to $7.1 million for the year ended December 31, 2014 from $538,000 in 2013. This increase of approximately $7.0 million was primarily due to an increase of $2.9 million in interest expense for the 2020 Notes and increase of $3.6 million in the amortization of the discount of the liability component of the 2020 Notes.

Comparison of year ended December 31, 2013 to year ended December 31, 2012

Revenues. Revenues for each of the years ended December 31, 2013 and 2012 were $3.4 million and represent revenue recognized under our collaboration agreement with Takeda in each year.

Research and Development Expenses. Research and development expenses decreased to $56.7 million for the year ended December 31, 2013 from $73.7 million in 2012. This decrease of approximately $16.9 million was due primarily to a decrease in expenses in connection with the Light Study, related proprietary product formulation work and consulting activities of $23.2 million. The decrease was partially offset by increases in salaries and personnel related costs of $3.0 million, stock-based compensation expense of $1.6 million and expenses related to regulatory filings of $1.3 million.

General and Administrative Expenses. General and administrative expenses increased to $23.9 million for the year ended December 31, 2013 from $20.0 million in 2012. This increase of approximately $3.9 million was due primarily to increases in stock-based compensation expense of approximately $2.4 million, professional fees of $1.0 million and salaries and personnel related costs of approximately $837,000.

Interest Income. Interest income decreased to $65,000 for the year ended December 31, 2013 from $147,000 in 2012. This decrease of approximately $82,000 was primarily due to a decrease in average investment balances and lower interest rates as compared to 2012.

Interest Expense. Interest expense increased to $538,000 for the year ended December 31, 2013 from $2,000 in 2012. This increase of approximately $536,000 was primarily due to $220,000 in interest accrued for the 2020 Notes and $315,000 in amortization of the discount of the liability component of the 2020 Notes.

Liquidity and Capital Resources

Since inception, our operations have been financed primarily through the issuance of equity and debt securities. Through December 31, 2014, we received net proceeds of approximately $574.2 million from the issuance of equity and debt securities 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;
- 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;
- in January and February 2008, we issued and sold a total of 7,326,435 shares of common stock for aggregate net proceeds of $74.9 million;

- in July 2009, we issued and sold a total of 11,500,000 shares of common stock for aggregate net proceeds of $81.6 million;
- in December 2011, we issued and sold a total of 5,646,173 shares of common stock and common stock warrants to purchase up to 56,461,730 shares for aggregate net proceeds of $86.9 million;
- in October 2012, we issued and sold a total of 11,000,000 shares of common stock for aggregate net proceeds of $56.5 million; and
- in December 2013, we issued the 2020 Notes for aggregate net proceeds of $110.5 million.

As of December 31, 2014, we had $104.2 million in cash and cash equivalents and an additional $101.3 million in investment securities, available-for-sale. As of December 31, 2014, our holdings primarily consisted of treasury-backed money market funds, treasuries and other instruments that are insured, guaranteed or supported by the U.S. federal government, and corporate debt obligations. We maintain established guidelines relating to diversification and maturities of our investments to preserve principal and maintain liquidity.

Net cash provided by operating activities was $26.9 million in 2014 and net cash used in operating activities was $70.8 million for 2013. 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 and manufacturer expenses and professional fees. In 2014, we received a milestone payment from Takeda for $70.0 million, of which a portion has been deferred and will be amortized over the remaining estimated life of the collaboration agreement.

Net cash used in investing activities was $23.6 million and $21.3 million for 2014 and 2013, respectively. These amounts are primarily the result of the net purchases and maturities of investment securities.

Net cash provided by financing activities was $2.7 million and $111.9 million for 2014 and 2013, respectively. The net cash provided by financing activities in 2014 was a result of proceeds from the issuance of common stock due to exercises of stock options and purchases under the employee stock purchase plan. The net cash provided by financing activities for 2013 was primarily as a result of the issuance of the 2020 Notes for aggregate net proceeds of $110.5 million.

We cannot be certain if, when or to what extent we will receive cash inflows from the commercialization of our product candidates beyond the milestones related to Contrave. We will incur substantial additional development expenses to conduct the Light Study and the new CV outcomes trial for Contrave. We initiated the Light Study in June 2012. Prior to its commencement, we anticipated that the costs to conduct the Light Study to the interim analysis would be approximately $100.0 million. We believe the costs we have incurred to date and expect to incur in the future in connection with the conduct of the Light Study are consistent with our original projection. Until we are able to finalize the protocol, we are unable to predict the cost of the new CV outcomes trial that we and Takeda are responsible for conducting.

We have entered into a license agreement to acquire the rights to develop and commercialize Contrave. Pursuant to this agreement, we obtained exclusive and non-exclusive licenses to the patent rights and know-how for selected indications and territories. Pursuant to our 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. We are also obligated to pay royalties on any net sales of the applicable licensed product(s), including Contrave. Our royalty payable to OHSU at December 31, 2014 for Contrave sales was approximately $65,000.

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

- the successful commercialization of Contrave;
- the success and costs of approval of our CMA for Mysimba in the E.U;

- the rate of progress and cost of the Light Study, the new CVOT for Contrave and the scope and cost of the additional post-marketing requirements for Contrave;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish with respect to Contrave;
- the costs of establishing sales, marketing and distribution capabilities in order to commercialize Contrave should we elect to do so;
- the costs involved in enforcing or defending patent claims or other intellectual property rights;
- the costs and timing of regulatory approvals for Contrave, if at all; and
- the extent to which we in-license, acquire or invest in other indications, products, technologies and businesses.

Although it is difficult to predict future liquidity requirements, we believe that our existing cash and cash equivalents and investment securities, available-for-sale, and anticipated product revenue 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, debt, potential milestone payments under our existing collaboration agreement, receivables or royalty financings and potential future corporate collaborations and licensing arrangements. However, we cannot be sure that our existing cash and investment resources and future product revenue 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 and/or our pre-commercialization and commercialization activities, 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. Debt, receivables and royalty financings may be coupled with an equity component, such as warrants to purchase stock, which could also result in dilution of our existing stockholders' ownership. If we raise additional funds through debt, receivables or royalty financings, the terms of such financings may involve significant cash payment obligations as well as covenants and specific financial requirements that may restrict our ability to operate our business.

Any turbulence in the U.S. and international markets and economies may adversely affect our ability to access the capital markets and obtain additional financing on terms acceptable to us, or at all.

Contractual Obligations and Commitments

The following table describes our long-term contractual obligations and commitments as of December 31, 2014 (in thousands):

	Payments Due by Periods				
	Total	Less Than 1 Year	1-3 Years	4-5 Years	After
Debt obligations	$115,000	$ —	$ —	$ —	$115,000
Interest on debt obligations[1]	18,712	3,163	6,325	6,325	2,899
Purchase obligations	2,623	2,623	—	—	—
Operating lease obligations	2,880	1,053	1,827	—	—
Total	$139,215	$ 6,839	$ 8,152	$ 6,325	$117,899

(1) Interest on the 2020 Notes calculated at 2.75%

We have not included certain license obligations which may require additional payments due upon the occurrence of certain milestones related to regulatory or commercial events. We may also be required to pay royalties on any net sales of the licensed products. License payments may increase 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.

Recently Issued Accounting Standards

In May 2014, the FASB issued new accounting guidance related to revenue recognition. This new standard will replace all current generally accepted accounting principles guidance on this topic and eliminate all industry-specific guidance. The new revenue recognition standard provides a unified model to determine when and how revenue is recognized. The core principle is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration for which the entity expects to be entitled in exchange for those goods or services. This guidance will be effective for fiscal years beginning after December 16, 2016, including interim periods within that reporting period, and can be applied either retrospectively to each period presented or as a cumulative-effect adjustment as of the date of adoption. Early adoption is prohibited. We are evaluating the impact of adopting this new accounting standard on our financial statements and related disclosures.

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 and investment securities, available-for-sale, as of December 31, 2014 consisted primarily of money market funds, U.S. government agency securities 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.

Our cash is invested in accordance with an investment policy approved by our board of directors which specifies the categories, allocations, and ratings of securities we may consider for investment. We do not believe our cash, cash equivalents and investment securities have significant risk of default or illiquidity. We made this determination based on discussions with our investment advisors and a review of our holdings. While we believe our cash, cash equivalents and investment securities are well diversified and do not contain excessive risk, we cannot provide assurance that in the future our investments will not be subject to adverse changes in market value.

In addition, domestic and international equity markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue and the markets continue to remain volatile, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary and our stock price may further decline. In addition, we maintain significant amounts of cash and cash equivalents that are not federally insured. If economic instability continues, we cannot provide assurance that we will not experience losses on these investments.

Item 8. Financial Statements and Supplementary Data

Index to Financial Statements

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. as of December 31, 2014 and 2013, and the related statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Orexigen Therapeutics, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Orexigen Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated February 27, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California
February 27, 2015

OREXIGEN THERAPEUTICS, INC.

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

	December 31, 2014	December 31, 2013
ASSETS		
Current assets:		
Cash and cash equivalents	$ 104,243	$ 98,121
Accounts receivable	2,571	77
Investment securities, available-for-sale	101,294	78,875
Inventory	1,198	—
Deferred tax asset	547	—
Prepaid expenses and other current assets	1,473	1,209
Total current assets	211,326	178,282
Property and equipment, net	857	630
Other long-term assets	621	1,032
Restricted cash	177	177
Total assets	$ 212,981	$ 180,121
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,243	$ 4,787
Accrued clinical trial expenses	10,690	7,886
Accrued expenses	6,552	6,751
Deferred revenue, current portion	8,229	3,429
Total current liabilities	29,714	22,853
Long-term convertible debt	83,908	80,031
Deferred revenue, less current portion	76,114	35,143
Deferred tax liabilities	547	—
Other long-term liabilities	354	232
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2014 and 2013, no shares issued and outstanding at December 31, 2014 and 2013	—	—
Common stock, $0.001 par value, 300,000,000 shares authorized at December 31, 2014 and 2013; 123,460,598 and 104,970,200 shares issued and outstanding at December 31, 2014 and 2013, respectively	123	105
Additional paid-in capital	574,247	556,235
Accumulated other comprehensive loss	(26)	(3)
Accumulated deficit	(552,000)	(514,475)
Total stockholders' equity	22,344	41,862
Total liabilities and stockholders' equity	$ 212,981	$ 180,121

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.

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

	Years Ended December 31,		
	2014	2013	2012
Revenues:			
Collaborative agreement	$ 54,229	$ 3,428	$ 3,428
Royalties	1,292	—	—
Total revenues	55,521	3,428	3,428
Operating expenses:			
Research and development	57,412	56,748	73,680
General and administrative	28,639	23,878	19,987
Total operating expenses	86,051	80,626	93,667
Loss from operations	(30,530)	(77,198)	(90,239)
Other income (expense):			
Interest income	88	65	147
Interest expense	(7,083)	(538)	(2)
Total other income (expense)	(6,995)	(473)	145
Net loss	$ (37,525)	$(77,671)	$(90,094)
Net loss per share—basic and diluted	$ (0.32)	$ (0.80)	$ (1.27)
Shares used to compute basic and diluted net loss per share	118,240	96,491	70,739

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.

STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Years Ended December 31,		
	2014	2013	2012
Net loss	$(37,525)	$(77,671)	$(90,094)
Other comprehensive income (loss)			
Unrealized gains (losses) on investment securities	(23)	(18)	17
Other comprehensive income (loss)	(23)	(18)	17
Comprehensive loss	$(37,548)	$(77,689)	$(90,077)

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2011	61,285	$ 61	$446,357	$ (2)	$(346,710)	$ 99,706
Issuance of common stock and warrants, net of issuance costs	11,000	11	56,520	—	—	56,531
Net exercise of warrants	11,131	11	—	—	—	11
Stock-based compensation expense	—	—	7,570	—	—	7,570
Exercise of common stock options	998	1	1,727	—	—	1,728
Unrealized gain on securities, available-for-sale	—	—	—	17	—	17
Net loss					(90,094)	(90,094)
Balance at December 31, 2012	84,414	84	512,174	15	(436,804)	75,469
Net exercise of warrants	19,895	20	—	—	—	20
Exercise of common stock options	616	1	1,074	—	—	1,075
Issuance of common stock for Employee Stock Purchase Plan	45	—	242	—	—	242
Issuance of convertible senior notes, equity portion, net of issuance costs	—	—	31,178	—	—	31,178
Stock-based compensation expense	—	—	11,567	—	—	11,567
Unrealized gain on securities, available-for-sale	—	—	—	(18)	—	(18)
Net loss					(77,671)	(77,671)
Balance at December 31, 2013	104,970	105	556,235	(3)	(514,475)	41,862
Net exercise of warrants	17,295	17	—	—	—	17
Exercise of common stock options	1,112	1	2,285	—	—	2,286
Issuance of common stock for Employee Stock Purchase Plan	84	—	431	—	—	431
Stock-based compensation expense	—	—	15,296	—	—	15,296
Unrealized gain on securities, available-for-sale	—	—	—	(23)	—	(23)
Net loss					(37,525)	(37,525)
Balance at December 31, 2014	123,461	$ 123	$574,247	$ (26)	$(552,000)	$ 22,344

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
(In thousands)

	Years Ended December 31,		
	2014	2013	2012
Operating activities			
Net loss	$ (37,525)	$ (77,671)	$ (90,094)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Amortization of premium on investment securities, available-for-sale	751	815	500
Accretion of debt discount	3,877	313	—
Amortization of debt issuance costs	43	3	—
Depreciation	139	94	313
Loss on disposal of equipment	—	—	42
Stock-based compensation	15,296	11,567	7,570
Changes in operating assets and liabilities:			
Accounts receivable	(2,494)	—	—
Inventory	(1,198)	—	—
Prepaid expenses and other current assets	(175)	205	(365)
Accounts payable and accrued expenses	2,107	(2,291)	17,306
Other assets	112	(686)	—
Deferred rent and lease incentives	124	262	(186)
Deferred revenue	45,771	(3,428)	(3,428)
Net cash provided by (used) in operating activities	26,828	(70,817)	(68,342)
Investing activities			
Purchases of investment securities, available-for-sale	(130,390)	(85,647)	(78,921)
Maturities and sales of investment securities, available-for-sale	107,196	65,011	65,211
Purchases of property and equipment	(246)	(640)	—
Restricted cash	—	—	365
Net cash used in investing activities	(23,440)	(21,276)	(13,345)
Financing activities			
Proceeds from issuance of convertible notes, net	—	110,545	—
Proceeds from issuance of common stock and warrants	2,734	1,337	58,270
Net cash provided by financing activities	2,734	111,882	58,270
Increase (decrease) in cash and cash equivalents	6,122	19,789	(23,417)
Cash and cash equivalents at beginning of period	98,121	78,332	101,749
Cash and cash equivalents at end of period	$ 104,243	$ 98,121	$ 78,332
Supplemental Disclosure of Cash flow Information:			
Interest paid	$ 3,119	$ —	$ —
Unrealized gain (loss) on investment securities, available-for-sale	$ (23)	$ (18)	$ 17
Supplemental Disclosure of Non-Cash Investing Information:			
Purchases of equipment included in accounts payable	$ 120	$ —	$ —

See accompanying notes.

OREXIGEN THERAPEUTICS, INC.

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 of pharmaceutical product candidates for the treatment of 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, raising capital, and preparing for the marketing and commercialization of its sole product, Contrave, in the United States. Contrave was launched commercially in the United States by the Company's partner, Takeda Pharmaceutical Company Limited ("Takeda"), in October 2014. The Company has experienced losses since its inception, and as of December 31, 2014, had an accumulated deficit of $552.0 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 may need to continue to raise additional equity or debt financing.

2. Summary of Significant Accounting Policies

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

As of December 31, 2014, restricted cash represents a certificate of deposit pledged as collateral for a letter of credit issued by the Company in connection with the execution of an operating lease.

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 and Accounts Receivable

Takeda accounted for 100% of revenue for each of the years ended December 31, 2014, 2013 and 2012. Takeda also accounted for 100% of our accounts receivable as of December 31, 2014 and 2013.

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

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. The Company has not recognized any impairment losses as of December 31, 2014.

Research and Development Costs

All research and development costs are charged to expense as incurred and consist principally of costs related to clinical trials, 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 require estimates of total costs incurred based on patients enrolled, progress of clinical 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.

Inventory

Inventories are stated at the lower of cost (using a first-in, first-out basis) or market. Inventory costs including raw materials and finished goods that may be associated with its products prior to regulatory approval are charged to research and development expense prior to such approval on a country-specific basis.

Income Taxes

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.

The Company follows the provisions of the Income Taxes Topic of the Financial Accounting Standards Board ("FASB") Accounting Standards Codification that defines a recognition threshold and measurement attributes for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. Under the Income Taxes Topic, 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.

Revenue Recognition

The Company has entered into agreements with Takeda which contain multiple elements, including nonrefundable upfront fees, payments associated with achieving specific development milestones and royalties based on specified percentages of net product sales, if any.

Prior to the revised multiple element and milestone method of revenue recognition guidance adopted by the Company on January 1, 2011, nonrefundable, up-front license fees and milestone payments with standalone value that are not dependent on any future performance by the Company under the agreements were recognized as revenue upon the earlier of when payments were received or collection was assured, but were deferred if the Company had continuing performance obligations. If the Company had continuing involvement through contractual obligations under such agreements, such up-front fees were deferred and recognized over the period for which the Company continued to have a performance obligation. The collaboration agreement with Takeda has continuing obligations, and as a result the up-front fees were deferred upon receipt.

Effective January 1, 2011, for multiple element agreements entered into or materially modified after December 31, 2010, the Company follows the provisions of Accounting Standards Update ("ASU") No. 2009-13. In order to account for the multiple-element arrangements, the Company identifies the deliverables included within the agreement and evaluates which deliverables represent separate units of accounting. Analyzing the arrangement to identify deliverables requires the use of judgment, and each deliverable may be an obligation to deliver services, a right or license to use an asset, or another performance obligation. A delivered item is considered a separate unit of accounting when the delivered item has value to the partner on a standalone basis based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research capabilities of the partner and the availability of research expertise in this field in the general marketplace. Arrangement consideration is allocated at the inception of the agreement to all identified units of accounting based on their relative selling price. The relative selling price for each deliverable is determined using vendor-specific objective evidence ("VSOE") of selling price or third-party evidence of selling price if VSOE does not exist. If neither VSOE nor third-party evidence of selling price exists, we use our best estimate of the selling price for the deliverable. The amount of allocable arrangement consideration is limited to amounts that are fixed or determinable. The consideration received is allocated among the separate units of accounting, and the applicable revenue recognition criteria are applied to each of the separate units. Changes in the allocation of the sales price between delivered and undelivered elements can impact revenue recognition but do not change the total revenue recognized under any agreement. Upfront license fee payments are recognized upon delivery of the license if facts and circumstances dictate that the license has standalone value from the undelivered items, which generally include research and development services and the manufacture of drug products, the relative selling price allocation of the license is equal to or exceeds the upfront license fee, persuasive evidence of an arrangement exists, the Company's price to the partner is fixed or determinable, and collectability is reasonably assured.

Upfront license fee payments are deferred if facts and circumstances dictate that the license does not have standalone value. The determination of the length of the period over which to defer revenue is subject to judgment and estimation and can have a material impact on the amount of revenue recognized in a given period.

The terms of the Company's partnership agreements provide for milestone payments upon achievement of certain regulatory/development and sales-based events. Effective January 1, 2011, the Company adopted on a

prospective basis the guidance under ASU No. 2010-17, "*Revenue Recognition-Milestone Method*". Under the Milestone Method of accounting, the Company recognizes consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is substantive in its entirety. A milestone is considered substantive when it meets all of the following three criteria: 1) The consideration is commensurate with either the entity's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, 2) The consideration relates solely to past performance, and 3) The consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. A milestone is defined as an event (i) that can only be achieved based in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting from the entity's performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (iii) that would result in additional payments being due to the Company. Any milestone payments received prior to satisfying these revenue recognition criteria were recorded as deferred revenue in the accompanying consolidated financial statements.

Royalties to be received based on sales of the Company's licensed products by partners will be recognized as earned.

Convertible Senior Notes

In December 2013, the Company issued $115.0 million in aggregate principal amount of 2.75% convertible senior notes due 2020 (the "2020 Notes"). The 2020 Notes are accounted for in accordance with FASB ASC 470, formerly FSP APB 14-1, *Accounting for Convertible Debt Instruments That May be Settled in Cash upon Conversion (Including Partial Cash Settlement).* ASC Subtopic 470-20 requires the issuer of convertible debt that may be settled in shares or cash upon conversion at their option, such as the 2020 Notes, to account for the liability (debt) and equity (conversion option) components separately. The guidance requires the carrying amount of the liability component to be estimated by measuring the fair value of a similar liability that does not have an associated conversion feature. To measure the fair value of the liability component, the Company used an income approach, discounting the future contractual cash flows due under the 2020 Notes by a market interest rate. The market interest rate was determined to be 8.69%. Assumptions used in the estimate represent what market participants would use in pricing the liability component, including market interest rates, credit standing, and yield curves, all of which are defined as Level 2 observable inputs. The estimated implied interest rate was applied to the 2020 Notes, which resulted in a fair value of the liability component of $79.7 million upon issuance, calculated as the present value of implied future payments based on the $115.0 million aggregate principal amount. The $31.3 million difference between the cash proceeds of $111.0 million and the estimated fair value of the liability component was recorded in additional paid-in capital as the 2020 Notes. The liability component will be accreted to redemption value over the term of the 2020 Notes.

Stock-Based Compensation

The Company measures and recognizes compensation expense for all stock-based payment awards made to employees, non-employee directors and consultants, including stock options and employee stock purchases related to the Company's 2013 Employee Stock Purchase Plan, based on estimated fair values. Compensation costs related to all equity instruments granted are recognized at the grant-date fair value of the awards. Additionally, the Company includes 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.

The fair value of each option award was 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,		
	2014	2013	2012
Expected life (in years)	5.6	6.0	6.0
Expected volatility	107.3%	92.7%	87.5%
Risk-free interest rate	1.8%	1.2%	1.1%
Expected dividend yield	0.0%	0.0%	0.0%
Per share grant-date fair value	$ 5.01	$4.35	$2.26

The weighted average expected life of an award is based on historical forfeiture experience, exercise activity, and on the terms and conditions of the stock awards. The expected volatility is based on the historical volatility of the Company's common stock over the most recent period commensurate with the estimated expected term of the stock awards. 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.

Total stock-based compensation expense recognized during the years ended December 31, 2014, 2013 and 2012 was comprised of the following (in thousands):

	Years Ended December 31,		
	2014	2013	2012
General and administrative	$10,842	$ 8,162	$5,755
Research and development	4,454	3,405	1,815
	$15,296	$11,567	$7,570

At December 31, 2014, total unrecognized estimated share-based compensation expense related to non-vested stock options granted prior to that date was $26.7 million, which is expected to be recognized over a weighted-average period of 1.8 years.

Comprehensive Loss

The Company records all components of comprehensive income, including net income, in the financial statements in the period in which they are recognized. Comprehensive loss consists of net loss and certain changes in stockholders' equity that are excluded from net loss. Comprehensive loss for each of the years ended December 31, 2014, 2013 and 2012 has been reflected in the Statements of Comprehensive Loss. Accumulated other comprehensive income (loss), which is included in stockholders' equity, represents unrealized gains and losses on investment securities, available-for-sale.

Comprehensive loss includes net loss and unrealized gains and losses on investments. The Company discloses the accumulated balance of other comprehensive loss as a separate component of stockholder's equity.

Net Loss Per Share

The Company computes basic loss per share by dividing the net loss available to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss assumes the conversion, exercise or issuance of all potential common stock equivalents, unless the effect of inclusion would be anti-dilutive. For purposes of this calculation, common stock

equivalents include the Company's stock options and Employee Stock Purchase Plan (ESPP), warrants and the shares to be issued upon the conversion of the convertible senior notes. No shares related to the assumed conversion of the convertible senior notes were included in the diluted net loss calculation for the years ended December 31, 2014, 2013 and 2012 because the inclusion of such shares would have had an anti-dilutive effect. The shares to be issued upon exercise of certain outstanding stock options and common stock warrants were excluded from the diluted net loss calculation for all periods presented because such shares are anti-dilutive.

(In thousands, except per share amounts)	Years Ended December 31,		
	2014	2013	2012
Historical			
Numerator:			
Net loss	$ (37,525)	$(77,671)	$(90,094)
Denominator:			
Weighted average common shares outstanding	118,240	96,491	70,739
Denominator for basic and diluted net loss per share	118,240	96,491	70,739
Net loss per share—basic and diluted	$ (0.32)	$ (0.80)	$ (1.27)

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

	As of December 31,		
	2014	2013	2012
Shares underlying convertible senior notes	14,042	14,042	—
Common stock warrants outstanding	572	17,870	37,768
Common stock options outstanding	17,959	16,902	13,839
	32,573	48,814	51,607

Recently Issued Accounting Standards

In May 2014, the FASB issued new accounting guidance related to revenue recognition. This new standard will replace all current generally accepted accounting principles guidance on this topic and eliminate all industry-specific guidance. The new revenue recognition standard provides a unified model to determine when and how revenue is recognized. The core principle is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration for which the entity expects to be entitled in exchange for those goods or services. This guidance will be effective for fiscal years beginning after December 16, 2016, including interim periods within that reporting period, and can be applied either retrospectively to each period presented or as a cumulative-effect adjustment as of the date of adoption. Early adoption is prohibited. The Company is evaluating the impact of adopting this new accounting standard on its financial statements and related disclosures.

3. Investment Securities, Available-for-Sale

The Company invests its excess cash in investment securities, principally debt instruments of financial institutions, corporations with investment grade credit ratings and government agencies. Regardless of maturity date, the Company intends to use all available-for-sale securities in current operations; therefore, these assets have been classified as short-term. A summary of the estimated fair value of investment securities, available-for-sale, is as follows at December 31, 2014 and December 31, 2013 (in thousands):

December 31, 2014	Maturity in Years	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. government agency securities	Less than 1	$ 87,895	$ 4	$ (27)	$ 87,872
Corporate debt securities	Less than 1	5,074	—	(1)	5,073
U.S. government agency securities	More than 1	8,351	—	(2)	8,349
Total investment securities		$101,320	$ 4	$ (30)	$101,294

December 31, 2013	Maturity in Years	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. government agency securities	Less than 1	$77,877	$ 4	$ (7)	$77,874
U.S. Treasury securities	Less than 1	1,001	—	—	1,001
Total investment securities		$78,878	$ 4	$ (7)	$78,875

Gross realized gains and losses on available-for-sale securities were immaterial during the years ended December 31, 2014, 2013 and 2012.

4. Fair Value Measurements

The following table presents information about the Company's financial assets measured at fair value on a recurring basis as of December 31, 2014, and indicates the fair value hierarchy of the valuation techniques utilized by the Company to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access. The Company classifies money market funds as Level 1 assets. Fair values determined by Level 2 inputs utilize inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets and liabilities in active markets, and inputs other than quoted prices that are observable for the asset or liability, such as interest rates and yield curves that are observable at commonly quoted intervals. The Company classifies commercial paper holdings, U.S. Treasury securities, U.S. government agency securities and asset-backed security holdings as Level 2 assets. Level 3 inputs are unobservable inputs for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. The Company does not hold any Level 3 assets. In certain cases, the inputs used to measure fair value may fall into different levels of the fair value hierarchy. In such cases, the level in the fair value hierarchy within which the fair value measurement in its entirety falls has been determined based on the lowest level input that is significant to the fair value measurement in its entirety. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires judgment, and considers factors specific to the asset or liability.

Assets that have recurring measurements are shown below (in thousands):

Description	Balance as of December 31, 2014	Fair Value Measurement at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial instruments owned:				
Money market funds	$ 97,966	$ 97,966	$ —	$ —
U.S. government agency securities	100,720	—	100,720	—
Corporate debt securities	5,073	—	5,073	—
Total financial instruments owned	$ 203,759	$ 97,966	$ 105,793	$ —

Description	Balance as of December 31, 2013	Fair Value Measurement at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial instruments owned:				
Money market funds	$ 96,910	$ 96,910	$ —	$ —
U.S. Treasury securities	1,001	—	1,001	—
U.S. government agency securities	77,874	—	77,874	—
Total financial instruments owned	$ 175,785	$ 96,910	$ 78,875	$ —

5. Inventory

Upon receiving U.S. Food and Drug Administration ("FDA") approval of Contrave in September 2014, the Company began to capitalize certain inventory costs for Contrave, which were recorded as research and development expenses prior to such approval.

Inventory consists of the following (in thousands):

	December 31, 2014	December 31, 2013
Raw materials	$ 755	$ —
Work in process	58	—
Finished goods	385	—
	$1,198	$ —

6. Property and Equipment

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

	Useful Life in Years	December 31, 2014	December 31, 2013
Furniture and fixtures	5	$ 1,079	$ 1,079
Computer equipment and software	3 to 5	521	422
Leasehold improvements	5	557	557
Manufacturing equipment	5	640	—
Asset under construction		120	518
		2,917	2,576
Accumulated depreciation		(2,060)	(1,946)
Property and equipment, net		$ 857	$ 630

Depreciation expense was $139,000, $94,000 and $313,000 for each of the years ended December 31, 2014, 2013 and 2012, respectively.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2014	2013
Accrued compensation related expenses	$4,666	$4,774
Accrued research and development expenses	1,187	1,273
Accrued interest on convertible notes	264	220
Accrued legal and professional expenses	156	355
Other accrued expenses	279	129
	$6,552	$6,751

8. Commitments and Contingencies

2.75% Convertible Senior Notes due 2020

In December 2013, the Company issued $115.0 million in aggregate principal amount of 2.75% convertible senior notes due 2020 ("2020 Notes") in an offering to qualified institutional buyers conducted in accordance with Rule 144A under the Securities Act of 1933, as amended. Debt issuance costs of approximately $488,000 were primarily comprised of legal, accounting and other professional fees, the majority of which were recorded in other noncurrent assets and are being amortized to interest expense over the seven-year term of the 2020 Notes.

Upon conversion, the 2020 Notes will be settled in shares of the Company's common stock (together with cash in lieu of any fractional shares). However, if the Company receives stockholder approval in accordance with the Nasdaq Listing Standards, the Company will settle conversions of the 2020 Notes through payment or delivery, as the case may be, of cash, shares of the Company's common stock or a combination thereof, at the Company's election. The conversion rate for the Notes will initially be 122.1225 shares per $1,000 principal amount, which is equivalent to an initial conversion price of approximately $8.19 per share of common stock, and is subject to adjustment under the terms of the Notes.

The 2020 Notes will mature on December 1, 2020, unless earlier repurchased or converted in accordance with their terms prior to such date. Prior to the close of business on the business day immediately preceding September 1, 2020, holders may convert all or a portion of their 2020 Notes only under the following circumstances: (1) during any fiscal quarter commencing after March 31, 2014, if, for at least 20 trading days (whether or not consecutive) during the 30 consecutive trading day period ending on the last trading day of the immediately preceding fiscal quarter, the last reported sale price of the Company's common stock on such trading day is greater than or equal to 130% of the applicable conversion price on such trading day; (2) during the five consecutive business day period immediately following any ten consecutive trading day period (the "measurement period") in which, for each trading day of that measurement period, the trading price per $1,000 principal amount of notes for such trading day was less than 98% of the product of the last reported sale price of the Company's common stock on such trading day and the applicable conversion rate on such trading day, or (3) upon the occurrence of specified corporate transactions. On and after September 1, 2020 until the close of business on the business day immediately preceding the maturity date, holders may convert all or a portion of their 2020 Notes at any time, regardless of the foregoing circumstances. Holders of the Notes will have the right to require the Company to repurchase all or some of their Notes at 100% of their principal amount, plus any accrued and unpaid interest, upon the occurrence of certain events.

The Company pays 2.75% interest per annum on the principal amount of the 2020 Notes semi-annually in arrears in cash on June 1 and December 1 of each year, beginning on June 1, 2014. If a designated event, as defined in the indenture for the 2020 Notes, including, but not limited to, a change in control, certain mergers or liquidation, occurs prior to the maturity date, subject to certain limitations, holders of the Notes may require the Company to repurchase all or a portion of their 2020 Notes for cash at a repurchase price equal to 100% of the principal amount of the 2020 Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the repurchase date.

The Company accounts separately for the liability and equity components of the 2020 Notes in accordance with authoritative guidance for convertible debt instruments that may be settled in cash upon conversion. The guidance requires the carrying amount of the liability component to be estimated by measuring the fair value of a similar liability that does not have an associated conversion feature. Because the Company has no outstanding non-convertible public debt, the Company determined that senior, unsecured corporate bonds traded on the market represent a similar liability to the 2020 Notes without the conversion option. The Company estimated the implied interest rate of its 2020 Notes to be 8.69%, assuming no conversion option. Assumptions used in the estimate represent what market participants would use in pricing the liability component, including market interest rates, credit standing, and yield curves, all of which are defined as Level 2 observable inputs. The estimated implied interest rate was applied to the 2020 Notes, which resulted in a fair value of the liability component of $79.7 million upon issuance, calculated as the present value of implied future payments based on the $115.0 million in aggregate principal amount. The $31.3 million difference between the cash proceeds of $111.0 million and the estimated fair value of the liability component was recorded in additional paid-in capital as the 2020 Notes were not considered redeemable.

A summary of the liability and equity components of the 2020 Notes is as follows at December 31, 2014 and December 31, 2013 (in thousands):

	December 31,	
	2014	2013
Principal amount of senior convertible notes outstanding	$115,000	$115,000
Unamortized discount of liability component	(31,092)	(34,969)
Long term convertible debt	$ 83,908	$ 80,031
Carrying value of equity component, net of issuance costs	$ 31,178	$ 31,178
Remaining amortization period of discount on the liability component	6 years	7 years

Operating Leases

In December 2007, the Company entered into an operating lease agreement for office facilities (corporate headquarters) in San Diego, California. The term of the lease began in April 2008 and was for an initial term of 64 months. In February 2013, the Company entered into an amendment to extend its lease to September 2017. The monthly rental payments are adjusted on an annual basis. As security for the lease, the landlord required a letter of credit, which is collateralized by a certificate of deposit of $177,000, which is included in restricted cash in the accompanying balance sheet at December 31, 2014. Rent expense is being recorded on a straight-line basis over the life of the lease.

In September 2008, the Company amended the lease to expand the office space at this location for a term of 52 months. In March 2012, the Company entered into a Partial Lease Termination Agreement with its landlord pursuant to which the Company decreased the total leased space at its corporate headquarters. The Agreement provided for, among other things, a one-time payment of $190,849 by the Company to the landlord and termination of the Company's payment obligations with respect to the terminated premises.

Future minimum payments under the operating leases as of December 31, 2014 are as follows (in thousands):

Years Ending December 31,	
2015	$1,053
2016	1,085
2017	742
2018	—
2019	—
	$2,880

Total rent expense for each of the years ended December 31, 2014, 2013 and 2012 was approximately $911,000, $1.1 million and $1.4 million, respectively.

Technology and License Agreements

Takeda Pharmaceutical Company Limited

In September 2010, the Company entered into a collaboration agreement with Takeda to develop and commercialize Contrave in the United States, Canada and Mexico. Effective in September 2013, the Company and Takeda entered into an amendment to the collaboration agreement pursuant to which Takeda assumed from the Company the responsibility to package Contrave for commercial sale in the United States, Canada and Mexico. Under the terms of the collaboration agreement, the Company received a nonrefundable upfront cash payment of $50.0 million from Takeda and is eligible to receive additional payments of over $1.0 billion upon achieving certain anniversary, regulatory/development and sales-based milestones, including $100.0 million that can be achieved between the execution of the collaboration agreement and the first commercial sale of Contrave in the United States. Of the remaining eligible payments of over $900 million, $45 million is related to anniversary payments of equal amounts over a three year period ending on the third anniversary of the first commercial launch of Contrave, and the remaining payments are primarily related to payments to be made upon the achievement of sales-based milestones of Contrave. The Company is also eligible to receive tiered royalty payments ranging from a minimum of 20% to a maximum of 35%, subject to customary reductions, on increasing levels of net sales in the United States, Canada and Mexico. In accordance with the Company's continuing performance obligation of the collaboration, the upfront payment of $50.0 million is being deferred and recognized over 14.5 years, the estimated term of the agreement. In addition to the upfront payment, the Company earned milestones of $30.0 million from Takeda for the FDA approval of Contrave and for delivery of launch supplies to Takeda in 2014. Also in October 2014, the Company earned and was paid a $70.0 million milestone from Takeda for the shipment of Contrave to pharmacy wholesalers in preparation for the commercial launch. This milestone payment was determined to not meet the definition of a substantive milestone. As a result, the Company recognized $20.8 million in 2014 with $49.2 million deferred which will be recognized over the remaining estimated life of the agreement. Additionally, the Company recognized $1.3 million in royalties earned for the sale of Contrave by Takeda in 2014.

For the years ended December 31, 2014, 2013 and 2012, the Company recognized revenues under this agreement of $55.5 million, $3.4 million and $3.4 million, respectively. At December 31, 2014 and 2013, deferred revenue under this agreement totaled $84.3 million and $38.6 million, respectively. Also the Company recorded receivables at December 31, 2014 and 2013 for approximately $2.6 million and $77,000, respectively, for reimbursement by Takeda for royalty revenue earned on the sales of Contrave by Takeda and certain manufacturing and patent costs permitted under the collaboration agreement prior to FDA approval which were accounted for as a reduction of the expenses reimbursed. Total reimbursements of manufacturing expenses from Takeda was $7.6 million and $0 in 2014 and 2013, respectively.

The Company has assessed milestones under the revised authoritative guidance for research and development milestones and determined that two regulatory/development milestone payments, $20.0 million due

to the Company upon regulatory approval in the United States and $10.0 million due to the Company upon the delivery of launch supplies to Takeda, meet the definition of a milestone as: (1) they are events that can only be achieved in part on the Company's performance or upon the occurrence of a specific outcome resulting in the Company's performance, (2) there was substantive uncertainty at the date the agreement was entered into that the event will be achieved, and (3) they result in additional payments being due to the Company. These milestones were achieved during the three months ended September 30, 2014. The third regulatory/development milestone payment, $70.0 million due to the Company upon the first commercial sale in the United States, does not meet the definition of a milestone as Takeda is responsible for the commercialization of Contrave. Sales-based milestone payments currently do not meet these criteria and will not be classified as milestones as their achievement is solely based on the performance of Takeda. The Company has determined that the anniversary milestones do not meet the definition of a milestone as these payments are contingent solely upon the passage of time. The milestone payments related to the first commercial sale and anniversary payments will be included with the upfront payment as additional consideration paid under the agreement. The Company will record revenue for the proportion of the payment that has been earned from the inception of the agreement to the date the payment is earned. The remainder will be recorded over the remainder of the term of the agreement. The sales-based milestone payments and royalties will be recorded when earned.

In September 2014, the Company and Takeda entered into a non-binding term sheet to address certain amendments and revisions to the collaboration agreement. Discussions between the Company and Takeda are ongoing and to date no definitive revised collaboration agreement has been executed by the parties.

In September 2014, the Company and Takeda entered into a manufacturing services agreement in accordance with the collaboration agreement. Pursuant to the manufacturing services agreement, among other things, the Company will supply to Takeda, and Takeda will, subject to certain exceptions as set forth in the collaboration and manufacturing services agreements, exclusively purchase from the Company, at our cost, all of Takeda's requirements of Contrave for commercialization in the United States, Canada and Mexico during the term of the collaboration agreement. At any time during the term of the collaboration agreement, Takeda may elect, subject to certain terms and conditions, to transfer and assume the right and responsibility to manufacture Contrave in the United States, Canada and Mexico. The Company has evaluated the terms of the manufacturing services agreement and concluded that it is not the principal in the transaction and is acting as an agent. As a result, the Company will record payments for purchases of Contrave by Takeda pursuant to this agreement on a net basis such that no revenue or costs is expected to be recognized in the statement of operations. Cost of inventory will be capitalized until such time that product is received by Takeda. All material costs of product sold to Takeda post FDA approval was previously expensed as research and development.

In October 2014, the Company transferred the responsibility for conducting the Light Study to Takeda pursuant to the terms of the collaboration agreement, as amended. At December 31, 2014, the Company had a payable to Takeda of $6.5 million related to the clinical study.

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 that the Company filed, which formed the basis for the Company's subsequently issued patents. This license agreement was amended in November 2003, December 2006 and December 2007. 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. The Company is also obligated to pay a royalty to OHSU on net sales for Contrave and any other products covered by the assigned patent rights. At December 31, 2014, the Company recorded a royalty payable of $65,000 under this agreement. The Company is also responsible for all prosecution and maintenance (including all costs associated with the enforcement) of any patent applications, that stem from these assigned rights, and for any patents that have or may issue with respect thereto.

OHSU has also licensed to the Company, on an exclusive basis, the issued patent underlying the *in vitro* model that the Company has used for screening combination therapies for impact on neuronal activity. With

respect to these rights, the Company was required to make a payment of $20,000 upon receipt of a pair of mice and is required to pay an additional $20,000 upon receipt of any additional pair of mice. OHSU is solely responsible for the prosecution, maintenance and enforcement (including all costs associated therewith) of this patent; however the Company is required to pay 100% of expenses incurred by OHSU in the maintenance and prosecution of this patent. As of December 31, 2014, the Company has paid a total of approximately $118,000 in connection with the maintenance and prosecution of this patent. 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 the Company 60 days' prior written notice and, in response, the Company may elect at its sole cost to pursue these actions. The Company's rights to this patent extend through the expiration of the patent, which is expected to occur in 2024.

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. In February 2015, the Company terminated the license agreement with Duke. The Company does not expect to pay Duke any royalties on Contrave.

9. Stockholders' Equity

Common Stock and Common Stock Warrants

In December 2011, the Company completed a public offering of 5,646,173 units. Each unit consists of one share of common stock and a warrant to purchase ten shares of common stock, at a price to the public of $1.45 per share of common stock and $1.449 per warrant to purchase each share of common stock, which together comprise the purchase price of $15.94 per unit. Net cash proceeds from the public offering were $86.9 million, after deducting underwriting discounts and commissions and offering expenses. The warrants issued in the transaction have an exercise price equal to $0.001 per share. Each warrant is exercisable in whole or in part for a period of 10 years commencing on December 22, 2011. A holder of a warrant will not have the right to exercise any portion of the warrant if such holder (together with its affiliates) would beneficially own in excess of 9.99% of the number of shares of the Company's common stock outstanding immediately after giving effect to the exercise of such warrant. These warrants may only be exercised pursuant to a cashless net exercise, whereby the exercise price of the warrants is satisfied through the reduction in shares issued upon exercise equal in value to the exercise price. There are no provisions in the warrant agreement which would require the Company to settle the warrants through the distribution of cash. The initial warrants provided for the purchase of up to 56,461,730 shares. A total of 17,294,521, 19,895,061 and 11,130,548 shares were issued upon warrant exercises in 2014, 2013 and 2012, respectively. Warrants to purchase an aggregate of up to 572,040, 17,869,618 and 37,767,900 shares were outstanding as of December 31, 2014, 2013 and 2012, respectively.

In October 2012, the Company completed a public offering of 11,000,000 shares of its common stock at a public offering price of $5.50 per share. Net cash proceeds from the public offering were approximately $56.5 million, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

Stock Options

During 2004, the Company adopted the 2004 Stock Plan (the "2004 Plan") under which, as amended, 3,159,275 shares of common stock are reserved for issuance to employees, directors and consultants of the Company. 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, 2014, no stock options are outstanding 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. Effective January 1, 2009, 2010 and 2011, the Company's Board of Directors increased the shares available for issuance under the 2007 Plan by 1,721,666, 2,000,000 and 2,000,000 shares, respectively, in accordance with an "evergreen" provision. 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. The 2007 Plan was amended in October 2009 and February 2010 to provide for the reservation of 500,000 and 2,000,000 shares, respectively, of the Company's common stock to be used exclusively for the grant of awards to individuals not previously an employee or non-employee director of the Company (or following a bona fide period of non-employment with the Company), as an inducement material to the individual's entering into employment with the Company within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules. In June 2011, the 2007 Plan was amended to, among other things, add an additional 10,000,000 shares to the number of shares of common stock authorized for issuance under the 2007 Plan, increase the number of shares to be added to the 2007 Plan automatically each January 1, starting with January 1, 2012, to the least of (i) 15% of the Company's outstanding common stock on the applicable January 1, (ii) 6,000,000 shares of common stock and (iii) a lesser number of shares of the Company's common stock determined by the Company's board of directors, and increase the limitation on the number of shares that may be granted pursuant to the exercise of incentive stock option to 40,000,000 shares. At December 31, 2014, options to purchase 17,958,969 shares have been granted and are outstanding under the 2007 Plan.

In June 2011, to provide incentive to the employees of the Company to continue their employment, the Company announced an option exchange program. Under the exchange program, eligible optionholders had an opportunity to exchange eligible stock options for a new stock option issued under the Company's 2007 equity incentive award plan. The exercise price of the new option was $1.66 per share, which was the closing price of the Company's common stock as reported by the Nasdaq Global Market on the first business day after the expiration date of the exchange offer. New options granted to employees vest over four years, with the shares vesting in equal monthly installments over 48 months. On July 22, 2011, the eligible optionholders exchanged options exercisable for an aggregate of 7,407,634 shares of common stock in the program. On July 25, 2011, the Company issued new stock options exercisable for an aggregate of 7,407,634 shares of common stock with an exercise price of $1.66 per share. As a result of the option exchange program, the Company is recognizing additional stock-based compensation expense of $2.7 million over the four year vesting period of the new stock options.

In March 2011, to provide incentive to the employees of the Company to continue their employment while its management and Board worked to update the Company's corporate strategy, the Compensation Committee of the Company's Board of Directors approved an amendment to certain outstanding option grants to provide for a one-time repricing of the exercise price of such options to purchase shares of the Company's common stock held by employees (the "Repricing"). The Repricing affected an aggregate of 1,443,150 shares of the Company's common stock subject to outstanding option grants (the "Affected Grants"). An aggregate of 492,357 shares subject to the Affected Grants had an original exercise price of $5.89 (the "September 2010 Grants") and the remaining 950,793 shares had an exercise price of $9.31 (the "January 2011 Grants"). The vesting commencement date for both the September 2010 Grants and the January 2011 Grants was January 18, 2011. The Compensation Committee chose to amend the September 2010 Grants and the January 2011 Grants because they believed that the amendment of these grants would achieve the desired retentive affect for the Company's employees given the circumstances around the Company's recent corporate realignment. The exercise price of all Affected Grants was amended in the Repricing to $2.94, the closing price of the Company's common stock on March 2, 2011. As a result of the Repricing, the Company is recognizing additional stock-based compensation expense of $819,000 over the four year vesting period of the Affected Grants.

The following table summarizes stock option activity for the 2004 and 2007 Plans:

	Number of Options	Weighted Average Exercise Price
Outstanding at December 31, 2011	10,586,379	$ 1.92
Granted	4,268,125	3.10
Exercised	(997,608)	1.74
Forfeited	(18,002)	3.44
Outstanding at December 31, 2012	13,838,894	$ 2.29
Granted	4,069,507	5.77
Exercised	(616,184)	1.78
Forfeited/Cancelled	(390,070)	4.38
Outstanding at December 31, 2013	16,902,147	$ 3.10
Granted	3,194,512	6.22
Exercised	(1,111,552)	2.07
Forfeited	(1,026,138)	5.35
Outstanding at December 31, 2014	17,958,969	$ 3.59

The following table summarizes information about stock options outstanding under the 2007 Plan at December 31, 2014:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number of Options	Weighted Average Remaining Contractual Life (In Years)	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price
$1.61 - $1.66	5,261,871	6.6	$ 1.66	4,210,658	$ 1.66
$1.70 - $2.58	4,559,386	6.7	$ 2.21	3,585,808	$ 2.18
$3.12 - $5.69	4,537,814	7.1	$ 5.08	2,746,256	$ 4.84
$5.73 - $8.18	3,599,898	8.6	$ 6.29	1,296,225	$ 6.38
$1.61 - $8.18	17,958,969	7.2	$ 3.59	11,838,947	$ 3.07

As of December 31, 2014, the aggregate intrinsic value of options outstanding and exercisable was approximately $45.3 million and $35.8 million, respectively. The aggregate intrinsic value of options exercised was $ 3.6 million, $3.1 million and $4.6 million during the year ended December 31, 2014, 2013 and 2012, respectively. At December 31, 2014, the weighted average remaining contractual term for options exercisable was 6.7 years.

Employee Stock Purchase Plan

In June 2013, the Company's stockholders approved the Company's ESPP, which permits the Company's eligible employees to purchase shares of common stock, at semi-annual intervals, through periodic payroll deductions. Payroll deductions may not exceed 15% of the participant's cash compensation subject to certain limitations, and the purchase price will not be less than 85% of the lower of the fair market value of the stock at either the beginning of the applicable "Offering Period" or the Purchase Date. Each Offering Period is 24 months, with new Offering Periods commencing every six months on the dates of June 1 and December 1 of each year. Each Offering Period consists of four (4) six month purchase periods (each a "Purchase Period") during which payroll deductions of the participants are accumulated under the ESPP. The last business day of each Purchase Period is referred to as the "Purchase Date." Purchase Dates are every six months on the last business day of May and November.

The assumptions used for the years ended December 31, 2014 and 2013 and the resulting estimates of weighted-average fair value per share for stock purchased under the ESPP during 2014 and 2013 are as follows:

	Years Ended December 31,	
	2014	2013
Expected term (in years)	0.49 – 2.00	0.45 – 1.95
Expected volatility	49.1 – 72.9%	46.6 – 72.8%
Risk-free interest rate	0.06 – 0.49%	0.07 – 0.26%
Expected dividend yield	0.0%	0.0%

At December 31, 2014, total unrecognized estimated stock-based compensation expense related to the ESPP was approximately $326,000, which is expected to be recognized over a weighted-average period of approximately 9 months. A total of 6,000,000 shares of the Company's common stock have been reserved for issuance under the ESPP plan. 84,325 and 45,285 shares were issued under the ESPP during the years ended December 31, 2014 and 2013, respectively.

Common stock reserved for future issuance consists of the following at December 31, 2014:

Common stock warrants	572,040
Available for future issuance under ESPP	5,870,390
Stock options issued and outstanding	17,958,969
Authorized for future option grants	7,769,668
	32,171,067

10. Income Taxes

The Company did not recognize federal or state income tax expense or benefit for the years ended December 31, 2012, 2013, or 2014.

A reconciliation of income taxes to the amount computed by applying the statutory federal income tax rate to the net loss is summarized as follows:

	December 31,		
(In thousands)	2014	2013	2012
Income tax expense (benefit) at statutory rates	$(13,133)	$(27,184)	$(31,532)
State income tax, net of federal benefit	(422)	(4,242)	(5,073)
Permanent items	2,157	804	379
Uncertain tax positions	843	2,629	69
Research and development credits	(2,041)	(5,492)	(344)
Stock-based compensation	751	760	447
Change in rate	(2,624)	—	(20)
Change in valuation allowance	14,469	32,725	36,074
Income tax expense (benefit)	$ —	$ —	$ —

Significant components of the Company's deferred tax assets as of December 31, 2014 and 2013 are shown below. A valuation allowance has been recognized to offset the net deferred tax assets as realization of such deferred tax assets has not met the more likely than not threshold.

(In thousands)	December 31, 2014	2013
Deferred tax assets:		
Net operating loss carryforwards	$ 55,035	$ 63,794
Research and development credits	5,988	4,752
Capitalized research and development expenditures	2,439	2,859
Deferred revenue	34,205	15,716
Stock-based compensation	10,911	8,919
Other, net	2,409	1,884
Total deferred tax assets	110,987	97,924
Valuation allowance for deferred tax assets	(99,807)	(85,330)
Deferred tax assets, net of valuation allowance	11,180	12,594
Deferred tax liabilities:		
Convertible debt	(11,180)	(12,594)
Total deferred tax liabilities	(11,180)	(12,594)
	$ —	$ —

At December 31, 2014, the Company has federal and state net operating loss carryforwards of approximately $398.1 million and $390.9 million, respectively, not considering the IRC Section 382 annual limitation discussed below. The federal loss carryforwards begin to expire in 2024, unless previously utilized. At December 31, 2014, the Company has federal and state research and development tax credits of $18.5 million and $5.5 million, respectively. The federal research and development tax credits begin to expire in 2024 unless previously utilized. The state research and development tax credits carry forward indefinitely.

The California net operating loss carry forwards are scheduled to expire as follows (in thousands):

Year	Amount
2015	$ 4,557
2016	20,936
2017	49,842
2018	3,841
2028 and beyond	311,309

Approximately $11.4 million of the net operating loss carryforwards relate to excess tax deductions for stock compensation, the income tax benefit of which will be recorded as additional paid-in-capital if and when realized.

Additionally, the utilization of the net operating loss and research and development tax credit carryforwards is subject to an annual limitation under Section 382 and 383 of the Internal Revenue Code of 1986, and similar state tax provisions due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes limit the amount of the 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 Section 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. The Company has completed an ownership change analysis in accordance with Section 382 from inception through December 31, 2014. As a result of the analysis, it was determined that the Company experienced several ownership changes during this period with the last one

occurring in December 2014. The analysis to determine the limitation of NOLs and credits as a result of the ownership changes has not been finalized. Based on our preliminary analysis of the limitation of our net operating losses and federal credits, the Company has removed deferred tax assets for net operating losses of $254.1 million and $231.1 million for federal and state, respectively, and federal research and development credits of $9.6 million from its deferred tax asset schedule and has recorded a corresponding decrease to its valuation allowance. When this analysis is finalized, the Company will reassess the amount of net operating losses and federal credits subject to limitation under Section 382. Due to the existence of the valuation allowance, future changes in the deferred tax assets related to these tax attributes will not impact the Company's effective tax rate.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits at the beginning and end of the years ended December 31, 2014, 2013 and 2012 (in thousands):

	December 31,		
	2014	2013	2012
Gross unrecognized tax benefits at the beginning of the year	$6,396	$3,239	$3,134
Increases related to current year tax positions	960	1,167	105
Decreases related to prior year tax positions	(35)	1,990	—
Expiration of unrecognized tax benefits	(12)	—	—
Gross unrecognized tax benefits at the end of the year	$7,309	$6,396	$3,239

Due to the valuation allowance, none of the unrecognized tax benefits as of December 31, 2014, if recognized, would reduce the Company's annual effective tax rate. The Company expects approximately $115,600 of unrecognized tax benefits will reverse over the next 12 months.

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, 2014, the Company had no interest or penalties accrued for uncertain tax positions.

11. Litigation

In May 2013, the Company received a shareholder demand alleging that certain option grants to the Company's President and Chief Executive Officer, Michael A. Narachi, the Company's Chief Business Officer and acting-Chief Financial Officer, Joseph P. Hagan, and the Company's Senior Vice President, General Counsel and Secretary, Heather D. Turner, in 2011 were granted in excess of the 1,500,000 share limit set forth in Section 3.3 of the 2007 Plan as to the number of shares of the Company's common stock with respect to which one or more stock awards may be granted to any one eligible participant during any of the Company's fiscal years. The Company refers to this limit as the 162(m) Award Limit. The Company's board of directors established a demand review committee composed of independent directors to conduct an investigation with respect to the shareholder demand and to make recommendations to the Company's board of directors. The demand review committee engaged independent counsel as part of its investigation and evaluated (1) the terms of the 2007 Plan, (2) the initial issuance procedures for the option grants to Mr. Narachi, Mr. Hagan and Ms. Turner during 2011, (3) the authority available to the compensation committee of the Company's board of directors under its charter and the 2007 Plan, (4) the expectations of the award recipients and (5) the intent of the Company's board of directors and the compensation committee regarding the availability of an exemption from the deductibility limitations of Section 162(m) of the Internal Revenue Code for such option grants. Following its investigation, the demand review committee determined that the 162(m) Award Limit first became effective as of September 2, 2011, and that, therefore, awards granted under the 2007 Plan prior to September 2, 2011, did not count toward the 162(m) Award Limit. The demand review committee determined that the awards granted to Mr. Hagan between September 2, 2011 and December 31, 2011 did not exceed the 162(m) Award Limit. The demand review committee further determined that the options granted to Mr. Narachi and Ms. Turner, including

the portion of such awards in excess of the 162(m) Award Limit, were validly approved under the 2007 Plan, although the portion of those awards in excess of the 162(m) Award Limit does not qualify as performance-based compensation under Section 162(m). In September 2013, the compensation committee amended the 2007 Plan, with the approval of the Company's board of directors, to take the following actions: (1) to clarify that the 162(m) Award Limit only applies to awards or the portion thereof intended to qualify as performance-based compensation under Section 162(m); and (2) to confirm that the compensation committee has the authority to make awards in excess of the 162(m) Award Limit, which the Company refers to as the Plan Amendment. The Plan Amendment is deemed effective as of September 10, 2011, consistent with the authority of the compensation committee as administrator of the 2007 Plan as of that date. Any grants under the 2007 Plan in excess of the 162(m) Award Limit are not intended to qualify as performance-based compensation under Section 162(m).

On December 6, 2013, a plaintiff claiming to be a shareholder of ours filed a derivative lawsuit purportedly on behalf of us against certain of our officers and the members of our board of directors, in the Superior Court for the State of California, County of San Diego, captioned *Wilkin v. Narachi, et al*. On December 9, 2013, the same shareholder who made a demand on the board in May 2013 filed a derivative lawsuit purportedly on behalf of us against certain of our officers and current and former members of our board of directors in the United States District Court, for the Southern District of California, captioned *Turgeman v. Narachi, et al*. Both of the lawsuits assert claims for breach of fiduciary duty, waste and unjust enrichment based on, among other things, the alleged grant of stock options to certain officers in excess of the 162(m) Award Limit, repricing stock options allegedly in violation of our equity incentive plan, the board of directors' conduct in responding to the May 2013 shareholder demand, and making allegedly false and misleading statements. Both of the lawsuits seek, among other things, declaratory relief, corporate governance reforms, rescission of certain stock option awards, rescission of the Plan Amendment, injunctive relief, damages, restitution, disgorgement and attorney's fees. On July 23, 2014, we and the individual defendants filed a motion to dismiss the *Turgeman* complaint. The judge has not yet ruled on the motion. The Company and the individual defendants filed a motion to dismiss the *Wilkin* complaint on August 13, 2014. On October 24, 2014, the judge granted the motion to dismiss with leave to amend the complaint. The plaintiff did not file an amended complaint within the court-ordered deadline but filed a motion to stay the action. On January 29, 2015, the judge denied the motion to stay and dismissed the lawsuit with prejudice. On February 6, 2015, the parties filed a stipulation with the court in which plaintiff waived his right to appeal and the parties agreed to a judgment dismissing the lawsuit. The Company is awaiting the judge's signature on the final judgment. Although management believes that the claims lack merit and intends to defend against them vigorously, there are uncertainties inherent in any litigation and we cannot predict the outcome.

12. Employee Benefit Plan

The Company has a defined contribution 401(k) retirement 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 years ended December 31, 2014, 2013 and 2012, the Company's matching contributions to the plan were approximately $275,000, $262,000 and $153,000, respectively.

13. 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, 2014 and 2013 are as follows (in thousands, except per share amounts):

	Year Ended December 31, 2014			
	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
Selected quarterly financial data:				
Revenues	$ 857	$ 857	$ 30,857	$ 22,950
Total operating expenses	24,011	23,659	17,816	20,565
Net income (loss)	(24,898)	(24,507)	11,273	607
Net income (loss) per share-basic and diluted(1)	$ (0.23)	$ (0.21)	$ 0.09	$ 0.00

	Year Ended December 31, 2013			
	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
Selected quarterly financial data:				
Revenues	$ 857	$ 857	$ 857	$ 857
Total operating expenses	20,255	19,120	19,438	21,813
Net loss	(19,368)	(18,246)	(18,572)	(21,485)
Net loss per share-basic and diluted(1)	$ (0.21)	$ (0.19)	$ (0.19)	$ (0.21)

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly net loss per share will not necessarily equal the total for the year.

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

None.

Item 9A. 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.

Management's Report on Internal Control Over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting

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

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled "Internal Control—Integrated Framework" published by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2014, the end of our most recent fiscal year. Ernst & Young LLP, our independent registered public accounting firm, has issued a report on the effectiveness of our internal control over financial reporting, which is included below.

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

Report of Independent Registered Public Accounting Firm

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

We have audited Orexigen Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) (the COSO criteria). Orexigen Therapeutics, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, Orexigen Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Orexigen Therapeutics, Inc. as of December 31, 2014 and 2013, and the related statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2014 of Orexigen Therapeutics, Inc. and our report dated February 27, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California
February 27, 2015

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 2015 annual meeting of stockholders, or the Definitive Proxy Statement, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, 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 Definitive 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 our Definitive Proxy Statement, which will be filed with the SEC within 120 days after December 31, 2014.

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, which will be filed with the SEC within 120 days after December 31, 2014.

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, which will be filed with the SEC within 120 days after December 31, 2014.

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, which will be filed with the SEC within 120 days after December 31, 2014.

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, which will be filed with the SEC within 120 days after December 31, 2014.

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:

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(7)	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant
3.3(1)	Amended and Restated Bylaws of the Registrant
3.4(23)	Amendment to 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
4.4(13)	Form of Warrant to Purchase Common Stock
4.5(20)	Indenture dated as of December 6, 2013, by and between the Registrant and Wilmington Trust, National Association, as trustee
10.1(1)	Form of Director and Executive Officer Indemnification Agreement
10.2#(6)	Form of Executive Officer Employment Agreement
10.3#(1)	2004 Stock Plan and forms of option agreements thereunder
10.4#(7)	2007 Equity Incentive Award Plan, as amended, and forms of stock option grant notice and stock option agreement thereunder
10.5(21)	2013 Employee Stock Purchase Plan
10.6†(1)	License Agreement dated June 27, 2003 by and between the Registrant and Oregon Health & Science University
10.7†(1)	Amendment to License Agreement dated November 1, 2003 by and between the Registrant and Oregon Health & Science University
10.8†(1)	Letter Agreement Amendment to License Agreement dated December 6, 2006 by and between the Registrant and Oregon Health & Science University
10.9(3)	Amendment No. 3 to License Agreement dated December 7, 2007 by and between the Registrant and Oregon Health & Science University
10.10(3)	Office Lease dated December 11, 2007 by and between the Registrant and Mullrock 3 Torrey Pines, LLC
10.11(4)	First Amendment to Lease dated September 23, 2008 by and between the Registrant and Mullrock 3 Torrey Pines, LLC
10.12†(5)	Naltrexone Hydrochloride Supply Agreement dated January 5, 2009 by and between the Registrant and Cilag GmbH International
10.13#(6)	Form of Amended and Restated Employment Agreement by and between the Registrant and Michael A. Narachi
10.14(8)	Amended and Restated Master Agreement for Pharmaceutical Development Services dated March 12, 2010 by and between the Registrant and Patheon Pharmaceuticals, Inc.
10.15(8)	Manufacturing Services Agreement dated March 12, 2010 by and among the Registrant, Patheon Pharmaceuticals, Inc. and Patheon Inc.

Exhibit Number	Description
10.16†(9)	Collaboration Agreement dated September 1, 2010 by and between the Registrant and Takeda Pharmaceutical Company Limited
10.17#(10)	Orexigen Therapeutics, Inc. Key Executive Employee Retention Plan
10.18#(11)	Form of Second Amended and Restated Employment Agreement by and between the Registrant and Michael A. Narachi
10.19#(11)	Form of Amendment No. 1 to Employment Agreement between the Registrant and Mark Booth
10.20#(12)	Amendment No. 2 to Amended and Restated Employment Agreement between Mark Booth and the Registrant dated November 1, 2011
10.21#(14)	Amendment No. 3 to Amended and Restated Employment Agreement dated March 15, 2012 by and between the Registrant and Mark Booth
10.22(15)	Partial Lease Termination Agreement dated February 22, 2012 by and between the Registrant and Mullrock 3 Torrey Pines, LLC
10.23#(16)	Amended and Restated Independent Director Compensation Policy
10.24(17)	Second Amendment to Lease dated February 15, 2013 by and between the Registrant and Mullrock3 Torrey Pines, LLC
10.25#(18)	Amendment No. 4 to Amended and Restated Employment Agreement dated February 15, 2013 by and between the Registrant and Mark Booth
10.26#(18)	Amendment No. 1 to Amended and Restated Employment Agreement dated February 15, 2013 by and between the Registrant and each of Joseph P. Hagan, Preston Klassen, M.D. and Heather D. Turner
10.27#(18)	Amendment No. 1 to Second Amended and Restated Employment Agreement dated February 15, 2013 by and between the Registrant and Michael A. Narachi
10.28#(19)	Amendment to the Orexigen Therapeutics, Inc. 2007 Equity Incentive Award Plan
10.29†(25)	Amendment Number 1 to Collaboration Agreement dated September 26, 2013 by and between the Registrant and Takeda Pharmaceutical Company Limited
10.30†(8)	Amendment No. 1 to Manufacturing Services Agreement dated November 1, 2013 by and between the Registrant, Patheon Pharmaceuticals Inc. and Patheon Inc.
10.31#(22)	Form of Acknowledgment Orexigen Therapeutics, Inc. Recoupment Policy
10.32†(24)	Manufacturing Services Agreement dated September 2, 2014, by and between the Registrant and Takeda Pharmaceutical Company Limited
10.33	Amendment No. 2 to Manufacturing Services Agreement dated September 11, 2014 by and between the Registrant, Patheon Pharmaceuticals Inc. and Patheon Inc.
23.1	Consent of Independent Registered Public Accounting Firm
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
101	The following financial statements and footnotes from the Orexigen Therapeutics Inc. Annual Report on Form 10-K for the year ended December 31, 2014 formatted in eXtensible Business Reporting Language (XBRL): (i) Consolidated Balance Sheets; (ii) Consolidated Statements of Operations; (iii) Consolidated Statements of Comprehensive Loss; (iv) Consolidated Statements of Stockholders' Equity; (v) Consolidated Statements of Cash Flows; and (vi) the Notes to Condensed Consolidated Financial Statements.

(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 December 14, 2007.
(4) Filed with the Registrant's Quarterly Report on Form 10-Q on November 7, 2008.
(5) Filed with the Registrant's Annual Report on Form 10-K on March 13, 2009.
(6) Filed with the Registrant's Current Report on Form 8-K on January 28, 2010.
(7) Filed with the Registrant's Registration Statement on Form S-8 on June 22, 2011.
(8) Filed with the Registrant's Annual Report on Form 10-K/A on January 26, 2015.
(9) Filed with the Registrant's Quarterly Report on Form 10-Q on November 4, 2010.
(10) Filed with the Registrant's Current Report on Form 8-K on March 7, 2011.
(11) Filed with the Registrant's Current Report on Form 8-K on June 14, 2011.
(12) Filed with the Registrant's Current Report on Form 8-K on November 1, 2011.
(13) Filed with the Registrant's Current Report on Form 8-K on December 15, 2011.
(14) Filed with the Registrant's Current Report on Form 8-K on March 16, 2012.
(15) Filed with the Registrant's Quarterly Report on Form 10-Q on May 10, 2012.
(16) Filed with the Registrant's Quarterly Report on Form 10-Q on November 12, 2013.
(17) Filed with the Registrant's Quarterly Report on Form 10-Q on May 9, 2013.
(18) Filed with the Registrant's Quarterly Report on Form 10-Q on August 7, 2013.
(19) Filed with the Registrant's Current Report on Form 8-K on September 23, 2013.
(20) Filed with the Registrant's Current Report on Form 8-K on December 9, 2013.
(21) Filed with the Registrant's Registration Statement on Form S-8 on June 6, 2013.
(22) Filed with the Registrant's Current Report on Form 8-K on April 25, 2014.
(23) Filed with the Registrant's Current Report on Form 8-K on July 3, 2014.
(24) Filed with the Registrant's Quarterly Report on Form 10-Q on November 10, 2014.
(25) Filed with the Registrant's Annual Report on Form 10-K on March 13, 2014.
† Confidential treatment has been granted or requested, as applicable, for portions of this exhibit. These portions have been omitted from the exhibit 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/ MICHAEL A. NARACHI
Michael A Narachi
President and Chief Executive Officer

Dated: February 27, 2015

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/ MICHAEL A. NARACHI Michael A. Narachi	President and Chief Executive Officer Director (Principal Executive Officer)	February 27, 2015
/s/ JOSEPH P. HAGAN Joseph P. Hagan	Chief Business Officer (Principal Financial and Accounting Officer)	February 27, 2015
/s/ ECKARD WEBER Eckard Weber, M.D.	Chairman of the Board of Directors	February 27, 2015
/s/ LOUIS C. BOCK Louis C. Bock	Director	February 27, 2015
/s/ WENDY DIXON Wendy Dixon, Ph.D.	Director	February 27, 2015
/s/ BRIAN H. DOVEY Brian H. Dovey	Director	February 27, 2015
/s/ DAVID J. ENDICOTT David J. Endicott	Director	February 27, 2015
/s/ PETER K. HONIG Peter K. Honig, M.D.	Director	February 27, 2015
/s/ PATRICK MAHAFFY Patrick Mahaffy	Director	February 27, 2015
/s/ LOTA S. ZOTH Lota S. Zoth	Director	February 27, 2015

Exhibit 10.33

AMENDMENT NO. 2 TO MANUFACTURING SERVICES AGREEMENT

SEPTEMBER 11, 2014

This Amendment No. 2 is intended to modify the **MANUFACTURING SERVICES AGREEMENT** dated March 12, 2010, as amended, (the "***Agreement***") by and between **OREXIGEN THERAPEUTICS, INC.**, a corporation existing under the laws of the State of Delaware ("***Client***"), and Patheon Pharmaceuticals Inc., a corporation existing under the laws of the State of Delaware, and Patheon Inc., a corporation existing under the laws of Canada (collectively, "***Patheon***") effective as of October 6, 2014 (the "***Amendment No. 2 Effective Date***"). All capitalized terms used herein and not otherwise defined will have the meanings assigned to such terms in the Agreement.

The parties hereto, intending to be legally bound, agree to modify the Agreement as follows (the "***Amendment No. 2***"):

1. Any capitalized term that is not defined in this Amendment No. 2 will have the meaning set forth in the Agreement.

2. All references to "Confidentiality Agreement" in the Agreement shall mean that certain Amended and Restated Confidentiality Agreement between Patheon and Client dated as of September 11, 2014.

3. The following new Section 9.3(k) shall be added to the Agreement:

> "it will comply with all applicable laws throughout the term of this Agreement, including providing all required written certifications, representations, and disclosures. Specifically, Patheon represents and warrants that it will comply with applicable requirements of the following Federal Acquisition Regulation ("FAR") clauses, which are hereby incorporated by reference and made a part of this Agreement as if fully set forth herein: (i) FAR 52.203-13, Contractor Code of Business Ethics and Conduct (Apr. 2010); (ii) FAR 52.219-8, Utilization of Small Business Concerns (Dec. 2010) (15 U.S.C. § 637(d)(2) and (3)); (iii) FAR 52.222-26, Equal Opportunity (Mar. 2007) (Executive Order 11246); (iv) FAR 52.222-35, Equal Opportunity for Veterans (Sep. 2010) (38 U.S.C. § 4212); (v) FAR 52.222-36, Affirmative Action for Workers with Disabilities (Oct. 2010) (29 U.S.C. § 793); (vi) FAR 52.222-40, Notification of Employee Rights Under the National Labor Relations Act (Dec. 2010) (E.O. 13496); (vii) FAR 52.222-50 Combating Trafficking in Persons (Feb. 2009) (22 U.S.C. 7104(g)) and (viii) FAR 52.247-64, Preference for Privately Owned U.S.-Flag Commercial Vessels (Feb 2006). For greater clarity, subparagraphs (iii), (iv), (v) and (vi) shall not be applicable to Patheon Inc. BY ACCEPTANCE OF THIS AGREEMENT, PATHEON HEREBY CERTIFIES THAT NEITHER PATHEON NOR ANY OF PATHEON'S PRINCIPALS IS PRESENTLY DEBARRED, SUSPENDED, PROPOSED FOR DEBARMENT, DECLARED INELIGIBLE OR VOLUNTARILY EXCLUDED FOR THE AWARD OF CONTRACTS BY ANY U.S. FEDERAL AGENCY.

4. Except for the matters set forth in this Amendment No. 2, all other terms of the Agreement will remain unchanged and will continue in full force and effect. If there is any conflict between the terms of the Agreement and this Amendment No. 2, the terms of this Amendment No. 2 will govern.

5. The Agreement and this Amendment No. 2 represent the complete and entire understanding between the parties regarding the subject matter hereof and supersede all prior or contemporaneous negotiations, representations or agreements, either written or oral, regarding

this subject matter. The Agreement and this Amendment No. 2 cannot be modified or amended except in a writing signed by an appropriate officer of each of the parties hereto.

6. This Amendment No. 2 will be construed and enforced in accordance with the laws of the State of New York, excluding its conflicts of law provisions, and the laws of the United States of America applicable therein and subject to the exclusive jurisdiction of the courts thereof. The UN Convention on Contracts for the International Sale of Goods will not apply to this Amendment No. 2.

7. This Amendment No. 2 may be executed in multiple counterparts, each of which will be deemed an original, but both of which together will constitute one and the same instrument. A facsimile, PDF or any other type of copy of an executed version of this Agreement signed by a Party is binding upon the signing party to the same extent as the original of the signed Agreement, and may be delivered electronically.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties hereto have duly executed this Amendment No. 2 as of the Amendment No. 2 Effective Date.

PATHEON PHARMACEUTICALS INC.

By: /s/ Francis P. McCune
Name: Francis P. McCune
Title: Secretary

PATHEON INC.

By: /s/ Michael Fournier
Name: Michael Fournier
Title: VP Commercial Operations

OREXIGEN THERAPEUTICS, INC.

By: /s/ Philip Roberts
Name: Philip Roberts
Title: V.P. Tech Ops

OREXIGEN THERAPEUTICS, INC.

By: /s/ Joseph Hagan
Name: Joseph Hagan
Title: CBO

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 No. 333-183918) of Orexigen Therapeutics, Inc. and

(2) Registration Statements (Form S-8 Nos. 333-142405, 333-165442, 333-175071, 333-189120 and 333-194951) pertaining to the Orexigen Therapeutics, Inc. 2007 Equity Incentive Plan, 2004 Stock Plan and the Orexigen Therapeutics, Inc. 2013 Employee Stock Purchase Plan;

of our reports dated February 27, 2015, with respect to the financial statements of Orexigen Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Orexigen Therapeutics, Inc., included in this Annual Report (Form 10-K) of Orexigen Therapeutics, Inc. for the year ended December 31, 2014.

/s/ Ernst & Young LLP

San Diego, California
February 27, 2015

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael A. Narachi, certify that:

1. I have reviewed this annual report on Form 10-K of Orexigen Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2015

/s/ Michael A. Narachi
Michael A. Narachi
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Joseph P. Hagan, certify that:

1. I have reviewed this annual report on Form 10-K of Orexigen Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 27, 2015

/s/ Joseph P. Hagan
Joseph P. Hagan
Chief Business Officer

Exhibit 32.1

Certifications
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
(Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

In connection with the Annual Report of Orexigen Therapeutics, Inc., a Delaware corporation (the "Company"), on Form 10-K for the period ended December 31, 2014, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael A. Narachi, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 27, 2015

/s/ Michael A. Narachi
Michael A. Narachi
President and Chief Executive Officer
(principal executive officer of the registrant)

In connection with the Report, I, Joseph P. Hagan, Chief Business Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 27, 2015

/s/ Joseph P. Hagan
Joseph P. Hagan
Chief Business Officer
(principal financial and accounting officer of the registrant)

The foregoing certifications are being furnished solely to accompany the Report pursuant to 18 U.S.C. § 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 the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.