ARENA PHARMACEUTICALS INC
Form 10-K
March 15, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

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 000-31161

ARENA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	23-2908305
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
6154 Nancy Ridge Drive, San Diego, CA	92121
(Address of principal executive offices)	(Zip Code)

858.453.7200

(Registrant’s telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	The NASDAQ Global Select Market

Securities registered pursuant to 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 (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

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 Exchange Act). Yes No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $416.0 million as of June 30, 2016, based on the last sale price of the registrant's common stock as reported on the NASDAQ Global Select Market on such date. For purposes of this calculation, shares of the registrant's common stock held by directors and executive officers have been excluded. This number is provided only for purposes of this Annual Report on Form 10-K and does not represent an admission that any particular person or entity is an affiliate of the registrant.

As of March 10, 2017, there were 245,469,142 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of this Annual Report on Form 10-K is incorporated by reference from the Registrant's Definitive Proxy Statement for the Annual Meeting of Stockholders to be held in June 2017, which will be filed with the Securities and Exchange Commission on or before May 1, 2017.

ARENA PHARMACEUTICALS, INC.

FORM 10-K – ANNUAL REPORT

For the Fiscal Year Ended December 31, 2016

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INFORMATION RELATING TO FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, includes forward-looking statements, which involve a number of risks and uncertainties. These forward-looking statements can generally be identified as such because the context of the statement will include words such as “may,” “will,” “intend,” “plan,” “believe,” “anticipate,” “expect,” “estimate,” “predict “potential,” “continue,” “likely,” or “opportunity,” the negative of these words or other similar words. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects and other statements that are not historical facts are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in “Business” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this Annual Report. For such statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this Annual Report are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the time this Annual Report was filed with the Securities and Exchange Commission, or SEC. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. These risks and uncertainties include, without limitation, those discussed in “Risk Factors” and in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report. In addition, past financial or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to update publicly or revise our forward-looking statements to reflect events or circumstances that arise after the filing of this Annual Report or documents incorporated by reference herein that include forward-looking statements.

TRADEMARKS AND CERTAIN TERMS

Arena Pharmaceuticals ® and Arena ® are registered service marks of Arena. Any other brand names or trademarks appearing in this Annual Report are the property of their respective holders.

In this Annual Report, “Arena Pharmaceuticals,” “Arena,” “we,” “us” and “our” refer to Arena Pharmaceuticals, Inc., and our wholly owned subsidiaries on a consolidated basis, unless the context otherwise provides. “APD” is an abbreviation for Arena Pharmaceuticals Development.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on developing novel, small molecule drugs with optimized receptor pharmacology designed to deliver broad clinical utility across multiple therapeutic areas. Our proprietary pipeline includes potentially first or best in class programs for which we own global commercial rights.

Our three most advanced investigational clinical programs are etrasimod (formerly APD334) in Phase 2 evaluation for multiple inflammatory indications, ralinepag (formerly APD811) in Phase 2 evaluation for pulmonary arterial hypertension (PAH), and APD371 entering Phase 2 evaluation for the treatment of pain associated with Crohn's disease.

Additionally, we have collaborations with the following pharmaceutical companies: Eisai Inc. and Eisai Co., Ltd. (collectively, Eisai) (commercial stage), Axovant Sciences Ltd., or Axovant, (Phase 2 candidate), and Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, (preclinical candidate).

Our Strategy

The primary elements of our strategic focus over time are as follows:

- Develop etrasimod – a modulator of the sphingosine 1-phosphate, or S1P, receptor – across a broad range of autoimmune conditions
- Develop ralinepag – an agonist of the prostacyclin, or IP, receptor – for broad utility in PAH patients
- Develop APD371 – an agonist of the cannabinoid-2, or CB2, receptor – for a range of visceral pain conditions
- Pursue strategic collaborations for certain of our clinical and preclinical programs
- Manage our cash to efficiently reach major milestones, including results from ongoing and planned trials in 2017
- Continue to build a streamlined, high-performing and high-energy organization

Arena Pharmaceuticals, Inc., incorporated in the state of Delaware in April 1997, and is located in San Diego, California. Our clinical operations are located in San Diego and Zug, Switzerland. We also have manufacturing operations in Zofingen, Switzerland.

Pipeline of Development Programs and Commercial Products with High Value Potential

Below is a summary of our portfolio:

Program	Indication	Status	Rights
Etrasimod	Ulcerative colitis	P2b	Arena: worldwide
	Dermatologic extraintestinal manifestations in inflammatory bowel disease	P2a	
	Pyoderma gangrenosum	P2a	
	Primary biliary cholangitis	P2a	
Ralinepag	Pulmonary arterial hypertension	P2b	Arena: worldwide
APD371	Pain associated with Crohn's disease	P2a	Arena: worldwide

Partnered Program	Indication	Status	Rights
BELVIQ and BELVIQ XR	Weight loss	Approved	Eisai: worldwide
	Reduction of major cardiovascular events and progression to type 2 diabetes	Ongoing CVOT (cardiovascular outcomes trial)	
Nelotanserin	Visual hallucinations in Lewy body dementia	P2	Axovant: worldwide
	REM sleep behavior disorder in dementia with Lewy bodies	P2	
Undisclosed orphan GPCR	Central nervous system	Preclinical	Boehringer Ingelheim: worldwide

Etrasimod Program

Etrasimod, a potent orally available next generation S1P receptor modulator, is our internally discovered investigational drug candidate intended for the potential treatment of autoimmune diseases. Our strategy for etrasimod is to develop it for one or more indications, including ulcerative colitis, dermatologic extraintestinal manifestations in inflammatory bowel disease, pyoderma gangrenosum and primary biliary cholangitis.

Etrasimod selectively targets key S1P receptor subtypes to provide systemic and local immune cell modulation. Immune cells include white blood cells, or WBCs, which are involved in protecting the body against both infections and foreign invaders. One important type of WBC is a T lymphocyte, which either kills foreign cells on contact or helps the body release chemicals that assist in killing invaders. The S1P receptors are thought to be involved in several biological responses, including movement of T lymphocyte from lymph nodes to the peripheral blood and the site of injury. As a result of S1P receptor modulation, lymphocytes are sequestered in lymph nodes and fewer immune cells are available to affect inflammatory processes.

There are five subtypes of the S1P receptor – labeled 1-5. It has been demonstrated that S1P receptor subtypes 1, 4, and 5 modulate immune response. With the selective targeting of S1P receptor subtypes 1, 4, and 5, we have sought to optimize etrasimod to be a potent and selective small molecule S1P receptor modulator that reduces the severity of disease and potentially avoids the negative effects connected to the receptor subtypes 2 and 3, which may be associated with more serious, off-target cardiac, pulmonary, and cancer-related effects. Drugs in this class have been associated with certain side effects, including cardiovascular effects, respiratory effects, infection, macular edema and elevations in liver enzymes.

Our clinical hypothesis is that this selectivity may be associated with a better safety profile and broader clinical utility.

We are currently developing etrasimod for:

- Ulcerative Colitis
- Dermatologic Extraintestinal Manifestations in Inflammatory Bowel Disease
- Pyoderma Gangrenosum

We intend to explore development in additional indications, including:

- Primary Biliary Cholangitis

Ulcerative Colitis

Inflammatory bowel diseases, or IBD, like ulcerative colitis, or UC, and Crohn's disease, or CD, are chronic inflammatory conditions of the gastrointestinal tract that affect approximately 1.7 million people in the United States alone. The prevalence of UC and CD in the United States were 907,000 and 780,000 patients, respectively in 2014. The prevalence of IBD in European Union is estimated at 2.6M with 1.1 million persons with CD and 1.5 million persons with UC. Both conditions have a significant impact on the patient's quality of life and can in many cases be very aggressive and disabling.

UC is characterized by mucosal inflammation limited to the colon which involves the rectum in about 95% of cases and may extend to involve parts or all of the large intestine. In contrast, CD is characterized by full thickness inflammation that can occur anywhere in the gastrointestinal, or GI, tract but most typically involves the terminal ileum and colon; fistulation and scarring result. Symptoms for UC and CD can vary, depending on the location and severity of inflammation, but some of the most common are diarrhea, abdominal cramps, and rectal bleeding.

Important goals of therapy for UC are to induce and maintain remission while improving the patient's quality of life. Currently available treatment options have limitations in terms of long-term efficacy and side effects, have complicated administration regimens, and often fail to induce or maintain remission. Therefore, a significant unmet need remains for differentiated agents that are efficacious for induction and maintenance therapy with a favorable side effect profile. We believe that the oral once-daily dosing, selectivity, mechanism of action, and emerging clinical profile of etrasimod may represent a significant opportunity to provide patients with an effective treatment for UC with an improved safety and dosing profile over current therapies.

Dermatologic Extraintestinal Manifestation of IBD

Extraintestinal manifestations, or EIMs, of IBD are common in both UC and CD. Inflammatory manifestations of the skin, eyes, liver, and joints are considered the primary types of EIMs associated with IBD. Cutaneous disorders associated with IBD occur in up to 15% of patients. Erythema nodosum, pyoderma gangrenosum, and psoriasis are the most common skin manifestations of IBD, in total affecting up to 11% of the IBD population.

IBD and these major skin EIMs in IBD share some common pathogenic mechanisms including T lymphocyte infiltration. We believe S1P receptor modulation's ability to sequester lymphocytes should result in fewer immune cells available to affect these inflammatory processes. In addition to the potential anti-inflammatory benefits resulting from reducing systemic lymphocyte circulation, activity on S1P1 and SIP4 are known to exert anti-proliferative effects in human keratinocytes, the predominant type of cell found in the outer-most layer of the skin, and inhibit skin dendritic cell migration. Therefore, the potential role of S1P receptor modulation in skin EIMs of IBD might involve both systemic and local dermal mechanisms.

There are no therapies currently approved specifically for treatment of IBD-mediated dermatologic manifestations. Therefore, a significant unmet need remains and we believe that etrasimod may represent a significant opportunity to provide an effective treatment for patients with IBD experiencing dermatologic EIM.

Pyoderma Gangrenosum

Pyoderma gangrenosum, or PG, is a rare inflammatory skin disease characterized by painful recurrent ulcerations. Lesions may occur either in the absence of any apparent underlying disorder or in association with other diseases, such as UC, CD, and other conditions. Diagnosis of PG is based on the history of the underlying disease, typical clinical presentation, histopathology, and exclusion of other diseases that would lead to a similar clinical picture. The clinical course can be mild or malignant, and chronic or relapsing.

The etiology of PG has not yet been clearly determined, although it is suspected to be an autoimmune disease caused by dysregulation of the immune system. Approximately 50% of cases of PG are associated with other disorders, especially UC or CD.

Based upon the U.S. Department of Health and Human Services' National Institutes of Health's Office of Rare Disease Research, the incidence of PG each year in the United States has been estimated to be 1 person per 100,000 people.

Treatment is challenging and the prognosis of PG remains unpredictable. Current treatments involve wound care and the use of anti-inflammatory agents, including antibiotics, corticosteroids, immune-suppressants and biologics, and attempts to target a broad spectrum of immunologic mediators and inflammatory cells, including T-lymphocytes shown to be involved in PG. Reduction of lymphocytes by S1P receptor modulators such as etrasimod may represent a novel therapeutic approach in PG.

Primary Biliary Cholangitis

Primary biliary cholangitis, or PBC (previously referred to as primary biliary cirrhosis), is a chronic cholestatic liver disease which is classified as a rare disease. The prevalence in the US is approximately 40 cases per 100,000 inhabitants. The incidence and prevalence of PBC in European countries are similar to those seen in the US.

Progressive bile-duct injury from portal and periportal inflammation could result in progressive fibrosis, cholangitis and eventually cirrhosis. Evidence to date suggests that immunological and genetic factors might cause the disease. The treatment goal is to slow the progression rate of the disease and to alleviate the symptoms. Liver transplantation appears to be the only life-saving procedure for PBC patients.

Inflammation, the underlying cause of PBC, is believed to be T lymphocyte mediated. In research models with etrasimod, we have demonstrated modulation of the specific subtypes of T lymphocytes implicated in PBC.

Etrasimod Development

Ulcerative Colitis

We are conducting a dose finding 12-week randomized, double-blind, placebo-controlled multinational Phase 2 clinical trial of etrasimod in moderate to severe UC. The aim of the trial includes investigating a clear dose response and establishing a clinically meaningful signal for the active arm(s) from placebo. The trial is expected to evaluate the effects of etrasimod, 1mg and 2mg, versus placebo on multiple efficacy measures including total Mayo Score (TMS), clinical remission and clinical response in up to 160 patients. Subjects from this study have the possibility to continue after 12 weeks in an open label extension study for up to 46 weeks with the focus on safety and maintenance of therapeutic effect.

Dermatologic Extraintestinal Manifestations of IBD

In March 2017, we initiated a Phase 2a, proof of concept, open-label study evaluating the efficacy and safety of etrasimod in IBD patients with active dermatologic extraintestinal manifestations. The objective is to determine the treatment effect of etrasimod in IBD patients on the clinical improvement of active dermatologic extraintestinal manifestations and to determine the safety profile and tolerability of etrasimod over a 12-week treatment period. The study includes patients with IBD experiencing active dermatologic extraintestinal manifestations including psoriasis, erythema nodosum, and PG.

Pyoderma Gangrenosum

In March 2017, we initiated a Phase 2a, proof of concept, open-label study to determine the efficacy and safety of etrasimod in patients with PG. The objective is to evaluate the efficacy, safety and tolerability of etrasimod in patients with PG over a 12-week treatment period. The study includes patients with diagnosed PG independent of IBD as a

background disease.

Primary Biliary Cholangitis

In 2017, we plan to initiate a Phase 2a study to evaluate etrasimod in patients with PBC.

Prior Development

In January 2015, we announced top-line results from a Phase 1b multiple-ascending dose clinical trial for etrasimod. In the trial, etrasimod demonstrated a dose-dependent effect on lymphocyte count lowering in blood, with mean decreases from baseline of up to 69%. Lymphocyte counts, on average, recovered to baseline within one week of conclusion of dosing. There was a modest impact on heart rate, but none of the changes were classified by the investigator as clinically significant. There were also no findings with respect to pulmonary function or liver enzyme tests that were classified by the investigator as clinically significant. The most common treatment-emergent adverse events were mild or moderate contact dermatitis, headache, constipation and diarrhea, with none being clearly drug related. There were no discontinuations for adverse events, and no serious adverse events were observed.

The randomized, double-blind, placebo-controlled Phase 1b clinical trial evaluated the safety, tolerability, pharmacodynamics and pharmacokinetics of multiple-ascending doses of etrasimod. In five different dosing cohorts, 50 healthy volunteers received etrasimod and 10 healthy volunteers received placebo for 21 days.

Prior to commencing the Phase 1b multiple-ascending dose clinical trial for etrasimod, we completed a Phase 1 single-ascending dose clinical trial of the compound. This randomized, double-blind and placebo-controlled trial evaluated the safety, tolerability and pharmacokinetics of single-ascending doses of etrasimod in 40 healthy adult volunteers. In the trial, etrasimod demonstrated favorable pharmacokinetic and pharmacodynamic effects, a dose-responsive reduction in blood lymphocyte count and a slowing of heart rate that appears comparable to other S1P receptor modulators. The terminal half-life was approximately 35 hours.

Etrasimod intellectual property

As of March 1, 2017, we owned issued patents that cover compositions of matter for etrasimod and related compounds, methods of treatment utilizing etrasimod and related compounds, and various salts of etrasimod and crystalline forms thereof in 57 jurisdictions, including the United States, China, Japan, Germany, France, Spain, Italy, the United Kingdom, Australia and Russia, and had applications pending in five other jurisdictions, of which the largest pharmaceutical markets were Brazil, India, Canada and South Korea. Based on sales statistics provided by IMS Health, the jurisdictions where etrasimod patents have been issued accounted for more than 83% of global pharmaceutical sales in 2015, while other jurisdictions where etrasimod patents remain pending accounted for more than 9% of global pharmaceutical sales in that same year. The patents on etrasimod issued by the US Patent and Trademark Office have serial numbers US 8,580,841 and US 9,126,932, while the corresponding patent granted by the European Patent Office has serial number EP 2326621 B2. Other of our etrasimod pending patent applications, including those directed to dosage regimens for etrasimod and synthetic routes and intermediates useful in the manufacturing of etrasimod, have all been filed in a lesser number of commercially important jurisdictions. The earliest priority date for the patents on etrasimod is 2008. The terms of these patents are capable of continuing into 2029 in most jurisdictions without taking into account any patent term adjustment or extension regimes of any country or any additional term of exclusivity we might obtain by virtue of the later filed patent applications.

Ralinepag Program

Ralinepag, an oral, selective IP receptor agonist targeting the prostacyclin pathway, is our internally discovered investigational drug candidate intended for the treatment of PAH. In September 2014, ralinepag was granted orphan drug status for the treatment of PAH by the US Food and Drug Administration, or FDA.

PAH is a progressive, life-threatening disorder characterized by increased pressure in the pulmonary arteries that carry blood from the heart to the lungs. PAH occurs when the pulmonary arteries thicken or grow rigid. This makes blood flow more difficult. The heart has to work harder to push blood through the arteries, and the arteries are unable to carry adequate blood to the lungs. PAH will continue to worsen over time, even with proper treatment. The increased pressure strains the heart, which can limit physical activity, result in heart failure and reduce life expectancy. Based on data from the Registry to EValuate Early And Long-term PAH disease management (REVEAL) of patients in the United States, there is an estimated five-year survival rate of 57% from diagnosis. The reported prevalence of PAH varies widely. One estimate is 15-50 cases/million with a higher female preponderance (approximately 3:1). More recently, the prevalence of PAH in the US among the privately insured (under age 65) and Medicare (over age 65) populations was estimated using administrative claims data in accordance with the current clinical classification of PH. This analysis suggests PAH prevalence was 109 (71–146) case/million among the <65 population, and 451 (384–519) cases/million for >65 or Medicare patients. Another estimate is that PAH affects about 500,000 individuals worldwide. A recent report characterizes the global market sales of PAH therapies as $5.8 billion in 2015 and are expected to increase to $6.7 billion by 2025.

PAH involves several interrelated mechanisms, with prostacyclin and thromboxane A2 playing a major role in maintaining pulmonary vascular tone through their balanced activity. Prostacyclin, released by endothelial cells, promotes vasodilation and inhibits platelet aggregation. Prostacyclin also has antiproliferative effects on vascular smooth muscle.

Current treatment of PAH falls within four distinct therapeutic classes: endothelin receptor antagonists (ERAs), phosphodiesterase-5 (PDE-5) inhibitors, prostacyclin analogues and soluble guanylate cyclase (SGc) stimulators. Traditionally, physicians typically prescribed ERAs, PDE-5 and SGc oral therapies to less-severe PAH patients while reserving parenteral prostacyclin therapy for severe patients. Treatment with prostacyclin receptor (IP) agonists, which can slow disease progression and improve exercise tolerance in PAH patients, is considered standard of care for advanced PAH – particularly intravenous dosing has been shown to improve mortality in PAH patients. Multiple attempts at developing prostanoid IP receptor agonists for oral administration have been limited by molecules with less than ideal pharmacokinetic properties resulting in inconsistent therapeutic drug levels in the blood. However, the launch of novel oral agents in the prostacyclin class and the increasing use of combination therapy to manage disease progression may result in a new PAH treatment paradigm.

With ralinepag, we sought to design a novel, non-prostanoid, small molecule agonist of the human IP receptor that could be dosed orally with significantly improved pharmacokinetic properties compared to current oral therapies. We also sought to engineer optimized IP receptor potency and selectivity to trigger targeted benefits in the blood and vessels of the lungs of PAH patients and minimize possible off-target side effects.

Ralinepag Development

In January 2015, we initiated patient dosing in a 22-week, randomized, double-blind, placebo-controlled Phase 2 trial evaluating the effectiveness in reducing pulmonary vascular resistance, improving exercise capacity, tolerability and safety of ralinepag. The study completed enrollment of approximately 60 patients at sites globally in December 2016.

In 2013, we announced top-line results from a multiple-dose, randomized, double-blind and placebo-controlled Phase 1 clinical trial evaluating multiple-ascending doses of ralinepag in healthy volunteers. In this trial, 40 healthy volunteers received ralinepag and 15 received placebo. The safety profile of ralinepag was characteristic of IP receptor agonists: the most frequent treatment-emergent adverse events were headache, nausea and jaw pain. One serious adverse event, transient atrial fibrillation, occurred in a single subject, and the study investigator considered it to be possibly treatment related. The subject had cardiac abnormalities prior to study start.

In 2011, we announced top-line results of a Phase 1 clinical trial to evaluate the safety, tolerability and pharmacokinetics of single-ascending doses of ralinepag. The randomized, double-blind and placebo-controlled trial evaluated 32 healthy volunteers in four cohorts of eight participants each, with six randomized to ralinepag and two to placebo. Ralinepag was rapidly absorbed and demonstrated dose-proportional pharmacokinetic exposure over the tested dose range. Consistent with the expected pharmacology of ralinepag, the most common adverse events were headache, vomiting, nausea, jaw pain and flushing.

Ralinepag intellectual property

As of March 1, 2017, we owned issued patents covering compositions of matter for ralinepag and related compounds and methods of treatment utilizing ralinepag and related compounds, synthetic routes, and various solid state forms of ralinepag, in 60 jurisdictions, including the United States, China, Japan, Germany, France, Spain, Italy, the United Kingdom, Australia, South Korea and Russia, and we had applications pending in four other jurisdictions, of which the ones with the largest pharmaceutical markets were Brazil, India and Canada. Based on sales statistics provided by IMS Health, the jurisdictions where ralinepag patents have been issued accounted for more than 85% of global pharmaceutical sales in 2015, while other jurisdictions where ralinepag patents remain pending accounted for more than 8% of global pharmaceutical sales in that same year. The patent on ralinepag issued by the US Patent and Trademark Office has serial number US 8,895,776, while the corresponding patent granted by the European Patent Office has serial number EP 2280696 B2. Other of our ralinepag patent applications, including those directed to synthetic processes and dosage regimens of ralinepag, have been filed. The earliest priority date for the patents on ralinepag is 2008. The terms of these patents are capable of continuing into 2029 in most jurisdictions without taking into account any patent term adjustment or extension regimes of any country or any additional term of exclusivity we might obtain by virtue of the later filed patent applications.

APD371 Program

APD371, an orally available, potent, peripherally restricted, highly selective, full agonist of the CB2 receptor, is an internally discovered investigational drug candidate we are exploring for the treatment of visceral pain, specifically pain associated with CD.

Visceral pain is defined as pain that originates within muscle, pleura, connective tissue, nervous system or solid organs within the abdomen or peritoneum. It is distinct from somatic or neuropathic pain, and is perceived as stretching, pulling and distention, rather than by cutting, crushing, or burning more commonly associated with neuropathic pain. Visceral pain is one of the most common types of pain. For example, abdominal pain affects approximately 20% of the general population. Visceral pain may be caused by a diverse set of organic causes, such as inflammation (e.g., IBD (including CD and UC), pancreatitis, prostatitis, and vaginitis), obstruction (e.g., bowel obstruction, and nephrolithiasis), ischemia, and malignancy, among others. Visceral pain may also be caused by functional disorders such as interstitial cystitis, dyspepsia, irritable bowel syndrome (IBS), and vulvodynia.

A specific type of visceral pain, pain associated with CD, affects a significant portion of patients with underlying CD. CD affects approximately 780,000 patients in the U.S., and 20% of patients suffer from residual pain even while in remission.

Common treatments for visceral pain range from non-invasive, conservative approaches (e.g., physical therapy or acupuncture), to pharmacologic (e.g., tricyclic antidepressants acting as neurotransmitter reuptake inhibitors), and invasive interventions (e.g., bowel resection). Potent analgesics, such as opioids, can adversely affect GI function. Other commonly prescribed analgesics are often not

potent enough, and may lead to other GI side effects such as bleeding. Apart from linaclotide and lubiprostone, prescribed for IBS, no visceral-specific analgesics are available. Approximately one in eight CD patients is chronically treated with opioids.

The CB2 receptor is expressed in the GI nervous system, and in many tissues and organs of the abdomen. CB2 receptors are found peripherally on immune cells but also on microglia, terminal neurons, dorsal root ganglia, and on visceral sensory neurons. We believe selectively targeting the CB2 receptor may provide therapeutic benefit for visceral pain without the potential for dependence, abuse, and GI and cardiovascular side effects associated with opiates or nonsteroidal anti-inflammatory drugs, or NSAIDs, which are among the most common pain relievers. In addition to analgesic effects, APD371 may have anti-inflammatory properties.

APD371 is designed to be a peripherally restricted and selective CB2 receptor agonist, which is intended to provide pain relief without the unwanted side effects associated with CB1 receptor activation.

APD371 Development

In the first part of 2017, we intend to commence a Phase 2 clinical trial to evaluate APD371 in pain associated with CD.

In April 2016, we announced favorable results from a Phase 1b multiple-ascending dose clinical trial of APD371. This randomized, double-blind, placebo-controlled Phase 1b clinical trial enrolled 36 healthy adults to evaluate the safety, tolerability and pharmacokinetics of multiple-ascending doses of APD371. Cohorts of 12 subjects (9 active, 3 placebo) were administered doses of 50 mg, 100 mg, or 200 mg of APD371 or placebo three times daily for 10 days and, in connection with the pharmacokinetic evaluation, one time on the 11th day. The most common adverse events were headache and nausea. All adverse events were classified as mild, and there were no serious adverse events reported. There was one discontinuation in the high-dose group due to an adverse event of mild thirst and somnolence. Reductions in blood pressure and heart rate were observed, but none were symptomatic or resulted in an adverse event. Drug levels at all doses tested in the trial, including the lowest dose, were well above those believed to be needed to stimulate the CB2 receptor.

In April 2015, we announced favorable top-line results from a Phase 1 single-ascending dose clinical trial of APD371. The randomized, double-blind and placebo-controlled trial enrolled 56 healthy adults to evaluate the safety, tolerability and pharmacokinetics of single-ascending doses of APD371. Dose-responsive exposure was observed over the explored dose range of 10-400 mg with good tolerability at all doses administered.

APD371 intellectual property

As of March 1, 2017, we owned issued patents covering compositions of matter for APD371 and related compounds in 19 jurisdictions, including the United States, China, Japan, Australia and Russia, and we had applications pending in 13 other jurisdictions, of which the ones with the largest pharmaceutical markets were Europe, Brazil, India, Canada and South Korea. Based on sales statistics provided by IMS Health, the jurisdictions where APD371 patents have been issued accounted for more than 59% of global pharmaceutical sales in 2015, while other jurisdictions where APD371 patents remain pending accounted for more than 36% of global pharmaceutical sales in that same year. The patent on APD371 issued by the US Patent and Trademark Office has serial number US 8,778,950. Other of our APD371 patent applications, including those directed to various solid state forms of APD371, have all been filed in a similar number of commercially important jurisdictions. The earliest priority date for the patents on APD371 is 2009. The terms of these patents are capable of continuing into 2030 in most jurisdictions without taking into account any patent term adjustment or extension regimes of any country or any additional term of exclusivity we might obtain by virtue of the later filed patent applications.

Additional Internal Preclinical and Clinical Programs

We have additional clinical and preclinical assets, including temanogrel and APD597, which we are evaluating for future development.

Partnered Programs

In addition to our clinical pipeline, we have three partnered programs – BELVIQ (lorcaserin) with Eisai, nelotanserin with Axovant and an orphan G protein-coupled receptor, or GPCR, research collaboration with Boehringer Ingelheim.

BELVIQ (lorcaserin)

Lorcaserin is approved for marketing in the United States, South Korea, Brazil, Mexico and Israel for the indication of weight management, and is being commercialized in the United States and South Korea under the brand name BELVIQ®. BELVIQ was

made available by prescription in the United States in June 2013 and in South Korea in February 2015. Eisai also has launched of a once-daily formulation of lorcaserin in the United States, which is marketed under the brand name BELVIQ XR®. Lorcaserin has not yet been launched in Brazil, Mexico or Israel, and CY Biotech is awaiting commercialization approval in Taiwan.

BELVIQ Collaboration

In December 2016, we replaced our marketing and supply agreement with Eisai, by entering into a Transaction Agreement and a Supply Agreement with Eisai.

Transaction Agreement

Pursuant to the Transaction Agreement, our wholly owned subsidiary, 356 Royalty Inc., or 356 Royalty, granted Eisai an exclusive, royalty-bearing license, or transferred intellectual property, to develop, manufacture and commercialize lorcaserin in all countries and territories of the world (collectively, the Territory). In consideration for the rights granted to Eisai under the Transaction Agreement, Eisai has agreed to make tiered royalty payments to 356 Royalty on the net sales of lorcaserin in the Territory. The royalty rates range from 9.5% on annual global net sales less than or equal to $175 million, 13.5% on annual global net sales greater than $175 million but less than or equal to $500 million and 18.5% on annual global net sales greater than $500 million.

356 Royalty is eligible to receive a milestone payment of $25.0 million upon the achievement of global net sales of lorcaserin for a calendar year first exceeding $250.0 million.

Eisai is solely responsible for all costs and expenses in connection with the development of lorcaserin, and our wholly owned subsidiary, Arena GmbH, was relieved of its obligation under the replaced marketing and supply agreement to pay for its share of development costs for lorcaserin. Eisai has the exclusive right and responsibility to plan and implement all research and development of lorcaserin at its own cost and expense, including conducting all regulatory activities and all clinical and development activities. Additionally, Eisai has agreed to (a) conduct all studies required by the FDA as a condition of obtaining and maintaining regulatory approval of lorcaserin in the United States (otherwise known as the cardiovascular outcomes trial, or CVOT), (b) continue the current study assessing whether lorcaserin reduces the incidence of major cardiovascular events, (c) continue the current study assessing whether lorcaserin reduces the incidence of conversion to Type 2 diabetes mellitus, and (d) use commercially reasonable efforts to develop and seek regulatory approval of lorcaserin in each of China, Japan and the European Union.

Eisai is solely responsible, and has the exclusive rights, for commercializing lorcaserin in the Territory and is responsible for manufacturing lorcaserin, except for any manufacturing to be conducted by Arena GmbH under the Supply Agreement. Eisai will be responsible for using commercially reasonable efforts to commercialize lorcaserin products in the United States, the European Union, China and Japan (collectively, the Major Markets) after regulatory approval in the applicable market.

356 Royalty and Eisai will each bear 50% of all expenses and losses arising from any product liability claim during a specified period after the date of the Transaction Agreement. Thereafter, 356 Royalty and Eisai will each bear 50% of all expenses and losses arising from any alleged defective manufacturing of lorcaserin by Arena GmbH under the Supply Agreement, and Eisai will be solely responsible for any expenses and losses associated with other product liability claims.

Eisai has agreed to certain standstill provisions, pursuant to which Eisai is obligated to refrain from taking certain actions with respect to Arena’s common stock during the term of the Transaction Agreement and for two years thereafter.

The Transaction Agreement will remain in effect until terminated by 356 Royalty or Eisai with respect to all countries in the Territory. 356 Royalty may terminate the Transaction Agreement with respect to a Major Market if Eisai permanently ceases development and commercialization of lorcaserin products in such Major Market, or in its entirety if Eisai permanently ceases development and commercialization of lorcaserin products in the Territory. 356 Royalty may also terminate the Transaction Agreement if Eisai challenges any patent controlled by 356 Royalty related to lorcaserin as of the effective date of the Transaction Agreement, or Licensed Patents, if Eisai is debarred under the United States Federal Food, Drug, and Cosmetic Act, or if Eisai is in material breach of the standstill provisions. Eisai may terminate the Transaction Agreement if as a result of its change of control, it would be in breach of certain competition restrictions.

In the event the Transaction Agreement is terminated by 356 Royalty due to Eisai's failure to develop and commercialize lorcaserin products, Eisai's challenging of any of the Licensed Patents or Eisai's debarment or material breach of the standstill provisions, or by Eisai after a change of control that would result in Eisai being in breach of certain competition restrictions, Eisai will grant Arena an exclusive, royalty-free license to certain patent rights and know-how necessary or useful for the development and commercialization of lorcaserin products in the Territory, re-assign the assets purchased by Eisai under the Transaction Agreement and Supply Agreement, and provide certain other transition assistance.

Supply Agreement

Under the Supply Agreement, Arena GmbH has agreed to manufacture and supply, and Eisai has agreed to purchase, all of Eisai's requirements (or specified minimum quantities if such quantities are greater than Eisai's requirements), subject to certain exceptions, for BELVIQ and BELVIQ XR for the development and commercial use of such products in the Territory for an initial two-year period, which initial period may be extended by Eisai for an additional six months upon payment of an extension fee of CHF 2.0 million. Eisai will pay Arena GmbH agreed upon prices to deliver finished drug product during this time. Additionally, Eisai has agreed to pay up to CHF 13.0 million in payments to Arena GmbH to support the maintenance of Arena GmbH's manufacturing facility in Switzerland during the initial two-year period supply period, and up to CHF 6 million during the six-month extension period, if any.

Pursuant to the Supply Agreement, Arena GmbH will transfer to Eisai all know-how and materials necessary for Eisai to manufacture BELVIQ at the facility in accordance with Arena GmbH's manufacturing processes used at the effective date of the Supply Agreement or 24 months prior. Arena GmbH also assigned its agreements with distributors in South Korea, Taiwan and Israel to Eisai, and Eisai agreed to assume responsibilities under such agreements.

On the effective date of the Supply Agreement, Eisai purchased Arena GmbH's entire inventory of the precursor materials for manufacturing lorcaserin then in Arena GmbH's possession. In exchange for these materials Eisai made a one-time payment to Arena GmbH of $10.0 million.

Absent early termination, the Supply Agreement will remain in effect until (a) the last day of the initial two-year supply period, or the last day of the six-month extension period (if any), or up to two weeks thereafter if so requested by Eisai, or (b) in the event of an acquisition of Arena or Arena GmbH by a third party, or of an assignment of the Supply Agreement by Arena GmbH to a third party, five years after the effective date of the Supply Agreement. After the initial two-year period of the Supply Agreement, either Arena GmbH or Eisai may terminate the Supply Agreement upon the other party's material breach that remains uncured 60 days after receiving written notice thereof. The Supply Agreement will also terminate automatically upon termination of the Transaction Agreement.

Nelotanserin Program

Nelotanserin, an orally available potent and selective inverse agonist of the 5-HT2A receptor, is an investigational drug candidate that has been implicated in the pathophysiology underlying psychosis. Nelotanserin was discovered by Arena, and we previously completed Phase 1 trials in healthy volunteers and Phase 2 trials in subjects with insomnia before development was discontinued for that indication.

Nelotanserin development

Under our Development, Marketing and Supply Agreement, Axovant is currently conducting multiple phase 2 studies. Axovant is conducting a phase 2, multi-center, double-blind, placebo-controlled crossover study evaluating nelotanserin in patients with Lewy body dementia (LBD) suffering from visual hallucinations. Axovant is also conducting a phase 2, multi-center, double-blind, placebo-controlled study evaluating nelotanserin in patients with dementia with Lewy bodies (DLB) experiencing rapid eye movement (REM) sleep behavior disorder (RBD).

We believe nelotanserin has the potential to be a best-in-class, once-daily, orally administered, potent and highly selective inverse agonist of the 5HT2A receptor. The 5HT2A receptor has been linked to neuropsychiatric disturbances including visual hallucinations – a common occurrence in people living with Lewy body dementia. We expect Axovant will seek to develop nelotanserin to address multiple aspects of Lewy body dementia. Axovant will be responsible for funding the development and commercialization of nelotanserin.

Nelotanserin collaboration

In May 2015, we entered into a Development, Marketing and Supply Agreement with Roivant Sciences Ltd., or Roivant, for nelotanserin. Roivant subsequently assigned all of its rights to develop and commercialize nelotanserin to its subsidiary, Axovant. Under our collaboration, Axovant has exclusive worldwide rights to develop and commercialize nelotanserin, and Arena will manufacture clinical supply and commercial product to sell to Axovant. We received a $4.0 million upfront payment and are eligible to receive $41.5 million in regulatory and development milestone payments. We are also eligible to receive 15% of net sales of nelotanserin in exchange for the manufacture and supply of finished commercial drug product, and up to a total of $60.0 million in one-time purchase price adjustment payments tied to certain commercial sales milestones.

Axovant will indemnify us for losses resulting from certain third-party claims, including for (a) Axovant's negligence, willful misconduct or violation of law, (b) Axovant's breach of the development, marketing and supply agreement or related agreements, (c) any product liability claim, (d) certain uses or misuses of nelotanserin, (e) certain infringement of intellectual property rights, and (f) product manufactured according to the product warranty. Arena GmbH will indemnify Axovant for losses resulting from certain third-party claims, including for (i) Arena GmbH's negligence, willful misconduct or violation of law, and (ii) Arena GmbH's breach of the development, marketing and supply agreement or related agreements.

Axovant has the right to terminate the agreement on a compound-by-compound basis or in its entirety upon 90 days' prior written notice to Arena GmbH. Arena GmbH has the right to terminate the agreement upon certain intellectual property concerns. Either party has the right to terminate the agreement early in certain circumstances, including if the other party is in material breach.

Nelotanserin intellectual property

As of March 1, 2017, we owned issued patents that cover compositions of matter for nelotanserin and related compounds and methods of treatment utilizing nelotanserin and related compounds in 77 jurisdictions, including the United States, China, Japan, Germany, France, Spain, India, Italy, the United Kingdom, Canada, Australia and Russia, and had applications pending in four other jurisdictions, of which the one with the largest pharmaceutical market was Brazil. Based on sales statistics provided by IMS Health, the jurisdictions where nelotanserin patents have been issued accounted for more than 91% of global pharmaceutical sales in 2015, while jurisdictions where nelotanserin patents remain pending accounted for more than 5% of global pharmaceutical sales in that same year. The patents on nelotanserin issued by the US Patent and Trademark Office have serial numbers US 8,754,238 and US 8,871,797, while the corresponding patent granted by the European Patent Office has serial number EP 1558582 B1. The earliest priority date for the patents on nelotanserin is 2003. The terms of these patents are capable of continuing into 2024 in most jurisdictions without taking into account any patent term adjustment or extension regimes of any country or any additional term of exclusivity we might obtain by virtue of the later filed patent applications.

Orphan GPCR Program

In December 2015, we entered into an exclusive agreement with Boehringer Ingelheim, to conduct joint research to identify drug candidates targeting a GPCR that belongs to the group of orphan central nervous system, or CNS, receptors. An "orphan receptor" is structurally related to a family of proteins that are known to act as functional cell-surface receptors but whose ligand has not yet been identified.

We will provide Boehringer Ingelheim exclusive rights to our internally discovered, novel compounds and intellectual property for the orphan CNS receptor. The agreement provides that the companies will jointly conduct research to identify additional drug candidates that are suitable for continued research and development as therapeutic compounds for various disease indications, with the initial focus expected to be psychiatric diseases such as schizophrenia. The agreement grants Boehringer Ingelheim exclusive worldwide rights to develop, manufacture and commercialize products resulting from the collaboration.

Under the terms of the agreement, in addition to the $7.5 million upfront payment, we are eligible to receive certain payments up to an aggregate of $254 million in research funding and success milestones in case of full commercial success of multiple drug products. In addition, we are eligible to receive tiered royalties on future sales of products that arise from the collaboration.

Boehringer Ingelheim will indemnify us for losses resulting from certain third-party claims, including for (a) Boehringer Ingelheim's default under the collaboration and license agreement, (b) Boehringer Ingelheim's gross

negligence or willful misconduct, (c) Boehringer Ingelheim's conduct of the research program, or (d) the development, manufacture or commercialization of any compound or product under the agreement. We will indemnify Boehringer Ingelheim for losses resulting from certain third-party claims, including for (i) our default under the agreement, (ii) our gross negligence or willful misconduct, or (iii) our conduct of the research program or use of any compound under the agreement.

Unless terminated earlier, the collaboration and license agreement will continue in effect until the later of the expiration of certain issued patents relating to a compound under the agreement and 10 years after the first commercial sale in all applicable countries. Either party has the right to terminate the agreement early in certain circumstances, including if the other party defaults under the collaboration and license agreement. In the case of our default, Boehringer Ingelheim has the option to terminate just a portion of agreement instead of the entire agreement. Boehringer Ingelheim has the right to terminate the agreement with 90 days' notice during the research term or with 30 days' notice thereafter. Boehringer Ingelheim also has the right after the research term to terminate development or commercialization with respect to any product under the agreement. We can terminate the agreement for certain development by Boehringer Ingelheim outside of the agreement.

We contracted with Beacon Discovery, Inc., or Beacon, to perform our research obligations under the Boehringer Ingelheim collaboration. In exchange, we agreed to share limited near term milestones with Beacon as well as the FTE funding paid to us by Boehringer Ingelheim. We have retained the longer term success milestones and all royalties.

Beacon Discovery and Services Agreement

On September 1, 2016, we also entered into a series of agreements with Beacon. Beacon was founded and is owned by several of our former employees.

We entered into a License and Collaboration Agreement with Beacon, pursuant to which we granted Beacon a non-exclusive, non-assignable and non-sublicensable license to certain database information relating to compounds, receptors and pharmacology, and transferred certain equipment to Beacon. Beacon will seek to engage global partners to facilitate discovery and development. Beacon has agreed to assign to us any intellectual property relating to our existing research and development programs developed in the course of performing research for us, and grant us a non-exclusive license to any intellectual property developed outside the course of performing work for us that is reasonably necessary or useful for developing or commercializing the products under our research and development programs. We are also entitled to rights of negotiation and rights of first refusal to potentially obtain licenses to compounds discovered and developed by Beacon. In addition, we are entitled to receive (i) a percentage of any revenue received by Beacon on or after the second anniversary of the effective date of the agreement from any third party pursuant to a third-party license, including upfront payments, milestone payments and royalties; (ii) single-digit royalties on the aggregate net sales of any related products sold by Beacon and its affiliates; and (iii) in the event that Beacon is sold, a percentage of the consideration for such sale transaction.

We entered a Master Services Agreement with Beacon, pursuant to which Beacon will perform certain research services for us relating to our proprietary pipeline, as well as a services agreement to support our research obligations under our collaboration with Boehringer Ingelheim.

Intellectual Property

Our success depends in large part on our ability to protect our compounds and information, and to operate without infringing the proprietary rights of third parties. We rely on a combination of patent, trade secret, copyright, and trademark laws, as well as confidentiality, licensing and other agreements, to establish and protect our proprietary rights. We seek patent protection for our key inventions, including drug candidates we identify, routes for chemical synthesis, pharmaceutical formulations and methods of treatment.

There is no assurance that any of our patent applications will issue, or that any of the patents will be enforceable or will cover a drug or other commercially significant product or method. In addition, we regularly review our patent portfolio to identify patents and patent applications for potential abandonment that we deem to have relatively low value to our ongoing business operations. There is also no assurance that we will correctly identify which of our patents and patent applications should be maintained and which should be abandoned. The term of most of our other current patents commenced, and most of our future patents, if any, will commence, on the date of issuance and terminate 20 years from the earliest effective filing date of the patent application. Because any marketing and regulatory approval for a drug often occurs several years after the related patent application is filed, the resulting market exclusivity afforded by any patent on our drug candidates will likely be substantially less than 20 years.

In the United States, patent term adjustment is available for certain delays in patent office proceedings. In addition, under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, the term of a patent that covers an FDA-approved drug may be eligible for patent term extension, or PTE. PTE permits patent term restoration of a US patent as compensation for the patent term lost during product development and the FDA

regulatory review process. The Hatch-Waxman Act permits a PTE of up to five years beyond the expiration of the patent. This period is generally one-half the time between the effective date of an Investigational New Drug, or IND (falling after issuance of the patent), and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, provided the sponsor acted with diligence. The Improving Regulatory Transparency for New Medical Therapies Act was signed into law in 2015 to prevent the loss of PTE (and market exclusivity) for drugs for which the FDA recommends scheduling under the Controlled Substances Act. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. The application for PTE is subject to approval by the PTO in conjunction with the FDA.

Outside of the United States, similar provisions may be available in the European Union, Japan, South Korea and some other jurisdictions to extend the term of a patent that covers an approved drug. The length of any such extension would vary by country. Our European patents may be eligible for supplemental protection certificates of up to five years in one or more countries.

Due to the specific requirements for obtaining these extensions, there is no assurance that our patents will be afforded extensions even if we encounter significant delays in patent office proceedings or marketing and regulatory approval.

In addition to patent protection, we rely on trade secrets, proprietary know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of our trade secrets and proprietary information, all of our employees are required to enter into and adhere to an employee confidentiality and invention assignment agreement, and invention disclosure procedures as a condition of employment. Additionally, our employee confidentiality and invention assignment agreements require that our employees not bring to us, or use without proper authorization, any third-party proprietary technology. We also generally require our consultants and collaborators that have access to proprietary property and information to execute confidentiality and invention rights agreements in our favor before beginning their relationship with us. While such arrangements are intended to enable us to better control the use and disclosure of our proprietary property and provide for our ownership of proprietary technology developed on our behalf, they may not provide us with meaningful protection for such property and technology in the event of unauthorized use or disclosure.

Competition

The biotechnology and pharmaceutical industries are highly competitive and are subject to rapid and significant change. We face significant competition from many organizations with drugs or drug candidates that do or may compete drug candidates we are developing. We may not be able to compete successfully against these organizations, which include many large, well-financed and experienced pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies. Developments by others may render our drug candidates obsolete or noncompetitive, and we or our collaborators may not be successful in developing either first or best in class drugs.

Many of our existing and potential competitors have substantially greater drug development capabilities and financial, scientific and marketing resources than we do. Additional consolidation in the pharmaceutical industry may result in even more resources being concentrated with our competitors. As a result, our competitors may be able to devote greater resources than we can to the research, development, marketing and promotion of therapeutic products or drug discovery techniques, or to adapt more readily to technological advances than we can. Accordingly, our competitors may succeed in obtaining patent protection, receiving regulatory approval or commercializing drugs before we do.

We expect to encounter significant competition in the therapeutic areas targeted by our principal drug candidates. Companies that complete clinical trials, obtain regulatory approvals and commence commercial sales of their drug candidates before us may achieve a significant competitive advantage. Furthermore, we may be competing against companies with substantially greater manufacturing, marketing, distribution and selling capabilities, and any drug candidate that we successfully develop may compete with existing therapies that have longer histories of safe and effective use.

We may rely on collaborators for support of development programs and for the manufacturing and marketing of drug candidates. Such collaborators may be conducting multiple drug development efforts within the same disease areas that are the subject of their agreements with us, which may negatively impact the development of drugs that are subject to our agreements. In addition, we face and will continue to face intense competition from other companies for such collaboration arrangements, and technological and other developments by others may make it more difficult for us to establish such relationships.

Government Regulation

We and our collaborators are subject to significant governmental regulation. The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the preclinical and clinical development, pre-market approval, manufacture, import, export, marketing and distribution of pharmaceutical products. These agencies and other regulatory agencies regulate research and development activities and the testing, approval, manufacture, quality control, safety, effectiveness, labeling, storage, tracking, recordkeeping, advertising, pricing and promotion of drug candidates and commercialized drugs. Failure to comply with applicable FDA or other regulatory requirements may result in inspectional notices of violation, warning letters, civil or criminal penalties, suspension or delays in clinical development, recall or seizure of products, partial or total suspension of production, withdrawal of a product from the market or other negative consequences.

In the United States

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and its implementing regulations. The process required by the FDA before drug candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and preclinical animal studies, many of which are required to be performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin and be updated annually;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of a New Drug Application, or NDA, after completion of adequate and well-controlled human clinical trials, generally accompanied by payment of a substantial user fee to the FDA;
- a determination by the FDA within 60 days of its receipt of the NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the active pharmaceutical ingredient and finished drug product are produced and tested to assess compliance with Current Good Manufacturing Practices, or cGMP, regulations;
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States; and
- Prior to commercialization, centrally acting drugs may be subject to review and potential scheduling by the DEA.

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

The results of preclinical tests (which include laboratory evaluation as well as GLP studies to evaluate toxicity in animals) for a particular drug candidate, together with related manufacturing information and analytical data, are submitted as part of an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA. During the 30-day time period the FDA may require additional information. The FDA may institute a clinical hold at the 30-day time period if any questions are not fully addressed or because of other concerns about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may place an IND on partial or full clinical hold at any time during a product candidate's development. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the study until completed. The FDA, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, regulations and regulations for informed consent and privacy of individually identifiable information.

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

- Phase 1 clinical trials. Studies are initially conducted in a limited population to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion, typically in healthy volunteers, but in some cases in patients.
- Phase 2 clinical trials. Studies are generally conducted in a limited patient population to identify possible adverse effects and safety risks, explore the initial efficacy of the product for specific targeted indications and to determine dose range or pharmacodynamics. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain

information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3 clinical trials. These are commonly referred to as pivotal studies or adequate and well-controlled studies. When Phase 2 evaluations demonstrate that a dose range of the product is effective and has an acceptable safety profile, Phase 3 clinical trials are undertaken in large patient populations to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial centers.
- Phase 4 clinical trials. The FDA may approve an NDA for a drug candidate, but require that the sponsor conduct additional clinical trials to further assess the drug after NDA approval under a post-approval commitment. In addition, a

sponsor may decide to conduct additional clinical trials after the FDA has approved an NDA. Post-approval trials are typically referred to as Phase 4 clinical trials.

New drug applications. The results of drug development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs also must contain extensive chemistry, manufacturing and control, or CMC, information. An NDA is usually accompanied by a significant user fee. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing, which occurs, if at all, 60 days after submission by the NDA sponsor. Once the submission has been accepted for filing, the FDA's goal is to review applications within 10 months from its acceptance of the filing or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months from its acceptance of the filing. The review process can be significantly extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. The FDA may deny approval of an NDA by issuing a Complete Response Letter, or CRL, if the applicable regulatory criteria are not satisfied. A CRL may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Data are not always conclusive and the FDA may interpret data differently than we or our collaborators interpret data. Approval may occur with Risk Evaluation and Mitigation Strategies, or REMS, that may limit the labeling, distribution or promotion of a drug product. Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase 4 clinical trials, and surveillance programs to monitor the safety effects of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these postmarketing programs or other information.

Other US regulatory requirements. Products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including recordkeeping, annual product quality review and reporting requirements. Adverse event experience with the product must be reported to the FDA in a timely fashion and pharmacovigilance programs to proactively look for these adverse events are mandated by the FDA. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic inspections (which may be unannounced) by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Following such inspections, the FDA may issue notices on Form FDA 483 and warning letters that could cause us to modify certain activities. A Form FDA 483 notice, if issued at the conclusion of an FDA inspection or after the appropriate FDA office review of the Establishment Inspection Report prepared by the investigator, can list conditions the FDA believes may have violated cGMP or other FDA regulations. FDA guidelines specify that a warning letter be issued for violations of "regulatory significance," also known as Official Action Indicated, or OAI. Failure to adequately and promptly correct the observation(s) can result in regulatory action. In addition to Form FDA 483 notices and warning letters, failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as suspension of manufacturing, recall of product, seizure of product, injunctive action or possible civil or criminal penalties.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for healthcare professional marketing activities and materials, direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for their approved indications and in accordance with the provisions of the confines of the pivotal studies and the approved label. Further, we may be required to develop additional data or conduct additional preclinical studies and clinical trials, and we may be required to submit and obtain FDA approval of a new or supplemental NDA for changes to, among other things, the indications, labeling, or manufacturing processes or facilities of a drug. Failure to comply with these requirements can subject a manufacturer to possible

legal or regulatory action, such as warning letters, corrective advertising, suspension of manufacturing, seizure of product, injunctive action or potential civil and criminal penalties.

Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA, if in their professional medical judgment, the physicians deem such use to be appropriate. Such off-label uses are common across certain medical specialties. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

To distribute products commercially, we or our collaborators, as applicable, must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution.

Drug Enforcement Administration regulation. The DEA regulates drugs that are controlled substances. Controlled substances are those drugs that appear on one of the five schedules promulgated and administered by the DEA under the Controlled Substances Act, or CSA. The CSA governs, among other things, the inventory, distribution, recordkeeping, handling, security and disposal of controlled substances. Any drug that acts on the central nervous system has the potential to become a controlled substance based on an evaluation of its abuse potential, and scheduling by the DEA is a separate process that may delay the commercial launch of a drug even after FDA approval of the NDA. Companies with a scheduled drug 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. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation or a denial of renewal of any DEA registration, injunctions, or civil or criminal penalties.

Outside of the United States

Outside of the United States, the ability to market a product is contingent upon obtaining marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical studies or marketing and sale of the product in those countries. Approval in the United States does not guarantee approval in other countries and vice-versa.

Hatch-Waxman Exclusivity. Market exclusivity provisions of the Hatch-Waxman Act can delay the submission or approval of applications seeking to rely upon the FDA's findings of safety and effectiveness for a previously approved NDA. A new chemical entity, or NCE, subject to an NDA is entitled to a five-year period of non-patent marketing exclusivity in the United States. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement of patents listed with the FDA by the NDA holder. The Hatch-Waxman Act also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active ingredient. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan drug designation and exclusivity. Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the

product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication or the same product for the same indication if demonstrated to be clinically superior. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Drug product manufacturing. Our Swiss subsidiary, Arena GmbH operates a drug product manufacturing facility in Zofingen, Switzerland. Swissmedic, a public service organization of the Swiss federal government, is the central Swiss agency for the authorization and supervision of therapeutic products. Our Swiss manufacturing facility has been inspected by the competent regional authorities (Regionales Heilmittelinspektorat der Nordwestschweiz, Basel, Switzerland), acting on behalf of Swissmedic, which issued GMP and production licenses to Arena GmbH for the production of drugs. The FDA conducted a pre-approval inspection of this facility for BELVIQ in July 2010, a subsequent inspection in 2014, and a pre-approval inspection for BELVIQ XR in March 2016, which resulted in No Actions Indicated, and classified this facility as acceptable. The FDA generally performs routine inspections about every two years, but the FDA may inspect a facility at any time.

Prescription drug reimbursement. In the United States and markets in other countries, sales of prescription drug products depend in part on the availability of reimbursement from third-party payers. Third-party payers include government health administrative authorities, managed care organizations, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies to demonstrate the cost-effectiveness of our products. A payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payers to reimburse all or part of the costs associated with their prescription drugs. Patients are less likely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement are important to new product acceptance.

If a drug is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 as well as the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, or VHCA, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the VHCA, drug companies are required to offer certain drugs at a reduced price to a number of federal agencies including US Department of Veterans Affairs and US Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs including Medicare and Medicaid. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as entry into government procurement contracts governed by the Federal Acquisition Regulations.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was enacted in the United States in March 2010 and contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. There have been judicial and Congressional challenges to certain aspects of the ACA. In March 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, which, if enacted, would amend or repeal significant portions of the ACA. Among other changes, the American Health Care Act would repeal the annual fee on certain brand prescription drugs and biologics imposed on manufacturers and importers, eliminate penalties on individuals and employers that fail to maintain or provide minimum essential coverage, create refundable tax credits to assist individuals in buying health insurance, and modify federal funding of Medicaid and certain eligibility requirements. While it is uncertain when or if the provisions in the American Health Care Act will become law, or the extent to which any changes may impact our business, it is clear that concrete steps are being taken to repeal and replace certain aspects of the ACA. Even if favorable coverage and reimbursement status is attained for our products, less favorable coverage policies and reimbursement rates may be implemented in the future. In the case of BELVIQ, Medicare explicitly excludes coverage of drugs for weight loss.

In countries outside the United States, pricing of pharmaceutical products may be subject to governmental control. Evaluation criteria used by many government agencies for the purposes of pricing and reimbursement typically focus on a product's degree of innovation and its ability to meet a clinical need unfulfilled by currently available therapies. Some countries operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

Healthcare fraud and abuse. Pharmaceutical companies are subject to various federal and state laws pertaining to healthcare fraud and abuse, including, but not limited to, anti-kickback and false claims laws.

The Federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer, or a party acting on its behalf, to knowingly and willfully solicit, offer, receive or provide any remuneration, directly or indirectly, in exchange for, or to induce, the referral of business, including the purchase, order, lease of any good, facility, service or item, including

the prescription of a particular drug, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. Some of the state prohibitions are broader in scope and apply to referral of patients for healthcare services reimbursed by any source, not only the Medicare and Medicaid programs.

In the course of practicing medicine, physicians may legally prescribe FDA-approved drugs for an indication that has not been approved by the FDA and which, therefore, is not described in the product's approved labeling, so-called "off-label use" or "the practice of medicine," if deemed appropriate in the physicians' professional medical judgment. The FDA does not ordinarily regulate the behavior of physicians in their choice of treatments. The FDA and other government agencies do, however, restrict communications on the subject of off-label use by a manufacturer or those acting on behalf of a manufacturer. Companies may not promote FDA-approved drugs for off-label uses. The FDA and other governmental agencies do permit a manufacturer (and those acting on its behalf) to engage in some limited, non-misleading, non-promotional exchanges of scientific information regarding unapproved indications.

There are numerous federal false claims laws and civil monetary penalty laws that forbid, among other things, anyone from knowingly presenting, or causing to be presented for payment to third-party payers (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary items or services.

Violations of fraud and abuse laws may be punishable by criminal, civil and/or administrative sanctions, including individual imprisonment, disgorgement, criminal fines and civil monetary penalties, as well as possible exclusion from federal healthcare programs (including Medicare and Medicaid). In addition, under certain healthcare fraud and abuse laws, there is an ability for private individuals to bring similar actions. Additionally, many states have analogous fraud and abuse laws, some of which may be broader in scope. Further, there are an increasing number of state laws that require pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, or register their sales representatives, as well as prohibiting certain other sales and marketing practices. The federal transparency requirements under the ACA require certain manufacturers of drugs, devices, biologics and medical supplies to annually report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests. Additionally, recent federal legislation imposes additional obligations on certain pharmaceutical manufacturers, among others, regarding drug product tracking and tracing.

Our activities are also potentially subject to federal and state consumer protection and unfair competition laws. We are also subject to the US Foreign Corrupt Practices Act, or the FCPA, which prohibits companies and individuals from engaging in specified activities to obtain or retain business or to influence a person working in an official capacity. Under the FCPA, it is illegal to pay, offer to pay, or authorize the payment of anything of value to any foreign government official, governmental staff members, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Healthcare privacy and security laws. The Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. In addition, many state laws apply to the use and disclosure of health information. We may be subject to, or our collaborators' marketing activities may be limited by, HIPAA and its implementing regulations.

Manufacturing, Revenues from External Customers, Sources and Availability of Materials, and Long-Lived Assets

In January 2008, we acquired from Siegfried AG (formerly Siegfried Ltd, and referred to collectively in this document as Siegfried) certain drug product facility assets, including manufacturing facility production licenses, fixtures, equipment, other personal property and real estate assets in Zofingen, Switzerland. We are using this facility to manufacture and package BELVIQ as well as for toll manufacturing of certain drug products for Siegfried, which is also located in Zofingen. From time to time, we may also use this facility to manufacture and package tablets and capsules for other of our programs or for other entities.

BELVIQ was made available to patients by prescription in the United States by Eisai in June 2013 and in South Korea by Ildong Pharmaceutical Co., Ltd., or Ildong, in February 2015. Through December 31, 2016, there have been no commercial sales of BELVIQ in any other territories.

Our revenues of $124.0 million for the year ended December 31, 2016, included (i) $98.9 million, or 79.8%, from Eisai, (ii) $11.4 million, or 9.2%, from Ildong and (iii) $3.6 million, or 2.9%, from Siegfried. Our revenues of $38.3 million for the year ended December 31, 2015, included (i) $23.7 million, or 61.9%, from Eisai, (ii) $8.9 million, or 23.2%, from Ildong and (iii) $3.5 million, or 9.0%, from Siegfried. Our revenues of $37.0 million for the year ended December 31, 2014, included $34.6 million, or 93.6%, from Eisai and $1.5 million, or 4.0%, from Siegfried.

We purchase raw materials, starting materials, intermediates, API, excipients and other materials from commercial sources. To decrease the risk of an interruption to our supply, when we believe it is reasonable for us to do so, we source these materials from multiple suppliers so that, in general, the loss of any one source of supply would not have a material adverse effect on commercial production. However, currently we have only one or a limited number of suppliers for some of these materials. The loss of a primary source of supply would potentially delay our production. Our facility in Zofingen, Switzerland is currently the only manufacturer of finished drug product for BELVIQ. Eisai maintains a safety stock of BELVIQ to help mitigate risks related to having only one manufacturer of finished drug product.

The carrying value of long-lived assets located in the United States and Switzerland were $35.1 million and $11.1 million, respectively, at December 31, 2016. The carrying value of long-lived assets located in the United States and Switzerland were $41.5 million and $38.1 million, respectively, at December 31, 2015. The carrying value of long-lived assets located in the United States and Switzerland were $49.0 million and $42.4 million, respectively, at December 31, 2014.

Compliance with Environmental Regulations

Our research and development programs involve the controlled use of hazardous materials, chemicals, biological materials and various radioactive compounds. In the United States, we are subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the US Environmental Protection Agency, the California Environmental Protection Agency, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, the CSA and other federal, state or local regulations.

With regard to Arena GmbH’s drug product manufacturing facility, Arena GmbH has contracted with Siegfried to provide certain safety, health and environmental services. Arena GmbH is subject to regulation under the Environmental Protection Act (Umweltschutzgesetz, USG), the Chemicals Act (Chemikaliengesetz, ChemG), and the Federal Act on the Protection of Waters (Gewässerschutzgesetz, GSchG), which refer to several ordinances such as the Ordinance on Air Pollution Control (Luftreinhalte-Verordnung, LRV), the Ordinance on Incentive Taxes on Volatile Organic Compounds (Verordnung über die Lenkungsabgabe auf flüchtigen organischen Verbindungen, VOCV), the Water Protection Ordinance (Gewässerschutzverordnung, GSchV), the Ordinance of the Handling of Wastes (Verordnung über den Verkehr mit Abfällen, VeVA), the Chemicals Ordinance (Chemikalienverordnung, ChemV), the Chemical Risk Reduction Ordinance (Chemikalien-Risikoreduktions-Verordnung, ChemRRV) and the Ordinance on Protection against Major Accidents (Störfallverordnung, StFV). The competent authorities in Switzerland for the implementation of environmental regulations are BAFU (Bundesamt für Umwelt / Federal Office for the Environment), which is the Swiss federal agency for the environment, and the respective authorities of the Canton of Aargau (Abteilung für Umwelt, AfU). Furthermore, the BAFU and the BAG (Bundesamt für Gesundheit / Federal Office of Public Health) share authorities with regard to the implementation and, together with the respective authority of the Canton of Aargau (Amt für Verbraucherschutz), the supervision of compliance with the laws and regulations related to chemicals. Occupational health and safety is regulated, in particular, by the EKAS (Eidgenössische Koordinationskommission für Arbeitssicherheit) guideline No. 6508 (ASA), governing the evaluation of worker safety and the reporting to the relevant authorities. The competent authority for the implementation of occupational health and safety regulations is the Canton of Aargau (Amt für Wirtschaft und Arbeit), whereby exposure limits are set by SUVA (Schweizerische Unfallversicherungsanstalt), which is the Swiss Accident Insurance Fund.

We may be subject to further such regulations in the future. Although we believe that our operations comply in all material respects with the applicable environmental laws and regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any damages that result, and the extent of that liability could exceed our resources. Our compliance with these laws and

regulations has not had, and is not expected to have, a material effect upon our capital expenditures, results of operations or competitive position.

Research and Development Expenses

Research and development activities are the primary source of our expenses. Our research and development expenses include personnel costs, research supplies, facility and equipment costs, clinical and preclinical study fees, and manufacturing costs for non-commercial products. Such expenses totaled $66.4 million, $88.4 million, and $100.3 million for the years ended December 31, 2016, 2015, and 2014, respectively. For research and development sponsored by collaborators for which we initially incur the costs, we record the costs within research and development expenses and record the reimbursements we receive from the collaborators for these costs within revenues; these expenses and revenues totaled $4.1 million, $2.1 million, and $10.0 million for the years ended December 31, 2016, 2015, and 2014, respectively.

Employees

As of March 10, 2017, we had a total of 106 employees, including 79 in research, development and manufacturing and 27 in administration, which includes finance, legal, facilities, information technology and other general support areas.

Available Information

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, or the Exchange Act, are available free of charge on our website (www.arenapharm.com) as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC.

Item 1A. Risk Factors

Investment in our stock involves a high degree of risk. You should consider carefully the risks described below, together with other information in this Annual Report on Form 10-K and other public filings, before making investment decisions regarding our stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. Moreover, the risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, operating results, prospects or financial condition.

Risks Relating to Our Business

We will need to obtain additional funds or enter into collaboration agreements to execute on our corporate strategy, and we may not be able to do so at all or on terms you view as favorable; your ownership may be substantially diluted if we do obtain additional funds; you may not agree with the manner in which we allocate our available resources; and we may not be profitable.

It takes many years and potentially hundreds of millions of dollars to successfully develop a compound into a marketed drug. We have accumulated a large deficit that has primarily resulted from the significant expenditures we have made in research and development since our inception. We expect that our losses and operating expenses will continue to be substantial.

All of our current active development programs are in Phase 2 or an earlier development stage, and we currently do not have, and we may not have in the future, adequate funds to develop any of our compounds into marketed drugs.

We may enter into collaboration or other agreements with other entities to continue to develop and, if successful, commercialize one or more of our drug candidates. We may not be able to enter into any such agreement on terms that we or third parties, including investors or analysts, view as favorable, if at all. Our ability to enter into any such agreement for any of our programs or drug candidates depends on many factors, potentially including the outcomes of additional testing (including clinical trial results) or regulatory applications for marketing approval, and we do not control these outcomes.

We may seek to obtain additional funding through the capital markets or other financing sources, or we may eliminate, scale back or delay some or all of our research and development programs. Any such additional funding may dilute or otherwise negatively impact your ownership interest, and any such reductions or failure to apply our resources effectively may narrow, slow or otherwise adversely impact the development and commercialization of one or more of our drug candidates, which we believe may reduce our opportunities for success and have a material adverse effect on our business and prospects.

We may allocate our resources in ways that do not improve our results of operations or enhance the value of our assets, and our stockholders and others may also not agree with the manner in which we choose to allocate our resources or obtain additional funding. Any failure to apply our resources effectively or obtain additional funding could have a material adverse effect on our business or the development of our drug candidates and cause the market price of our common stock to decline.

In addition, we cannot assure you that we will be profitable or, if we are profitable for any particular time period, that we will be profitable in the future.

We are executing a revised strategy, and we may not be successful in transitioning from a company with a broad research and development focus and a commercial stage drug to a company focused on developing its clinical-stage pipeline.

In June 2016, we initiated a strategic shifting of priorities to emphasize our proprietary clinical-stage pipeline, and the implementation of cost reductions that included a substantial reduction of our workforce, primarily in areas of research, manufacturing and general and administrative. In January 2017, we announced we had amended our agreements relating to lorcaserin, a drug we had internally discovered and developed and that is being marketed for weight management under the tradenames BELVIQ and BELVIQ XR, in an effort to further reduce our expenses. In order to execute our revised strategy, we are also hiring new personnel, primarily to support development of our pipeline, and revising our systems, processes and vendors. We cannot guarantee that we will be able to

realize any cost savings or other anticipated benefits from the actions we have taken to date or may take in the future, or that our efforts will not interfere with our ability to achieve our business objectives or have other negative consequences.

Drug development programs are expensive, time consuming, uncertain and susceptible to change, interruption, delay or termination.

Drug development programs are very expensive, time consuming and difficult to design and implement. Our drug candidates are in various stages of clinical and preclinical development and are prone to the risks of failure inherent in research and development. Clinical trials and preclinical studies are needed to demonstrate that drug candidates are safe and effective to the satisfaction of the US Food and Drug Administration, or FDA, and similar non-US regulatory authorities, and the FDA or other regulatory authority may require us to, or we or others may decide to, conduct additional research and development even after a drug is approved. The commencement or completion of our clinical trials or preclinical studies could be substantially delayed or prevented by several factors, including the following:

- limited number of, and competition for, suitable patients required for enrollment in our clinical trials or animals to conduct our preclinical studies;
- limited number of, and competition for, suitable sites to conduct our clinical trials or preclinical studies;
- delay or failure to obtain approval or agreement from the applicable regulatory authority to commence a clinical trial or approval of a study protocol;
- delay or failure to obtain sufficient supplies of drug candidates, drugs or other materials for the trial or study;
- delay or failure to reach agreement on acceptable agreement terms or protocols; and
- delay or failure to obtain institutional review board, or IRB, approval to conduct a clinical trial at a prospective site.

For example, recruitment for ulcerative colitis studies is competitive and challenging, and led us to make changes to our internal staffing, external vendors and trial design relating to our etrasimod program. It is not known how such changes, or any future changes we may implement, will impact clinical trials for our drug candidates, and it is difficult to predict when ongoing trials will be fully enrolled or when data will be available. Recruitment for trials for other indications, such as our ralinepag for pulmonary arterial hypertension, or PAH, can also be competitive and challenging.

In addition, the FDA, other regulatory authorities, collaborators, or we may suspend, delay or terminate our development programs at any time for various reasons, including those listed above affecting the commencement or completion of trials and the following:

- lack of effectiveness of any drug candidate during clinical trials;
- side effects experienced by study participants or other safety issues;
- slower than expected rates of patient recruitment and enrollment or lower than expected patient retention rates;
- inadequacy of or changes in our manufacturing process or compound formulation;
- delays in obtaining regulatory approvals to commence a study, or “clinical holds,” or delays requiring suspension or termination of a study by a regulatory authority, such as the FDA, after a study is commenced;
- changes in applicable regulatory policies and regulations;
- delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;
- uncertainty regarding proper dosing;
- unfavorable results from ongoing clinical trials or preclinical studies;
- failure of our clinical research organizations to comply with all regulatory and contractual requirements or otherwise perform their services in a timely or acceptable manner;
- scheduling conflicts with participating clinicians and clinical institutions;
- failure to design appropriate clinical trial protocols;
- insufficient data to support regulatory approval;

- termination of clinical trials at one or more clinical trial sites;
- inability or unwillingness of medical investigators to follow our clinical protocols;

- difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data;
- lack of sufficient funding to continue clinical trials or preclinical studies; or
- changes in business priorities or perceptions of the value of the program.

There is typically a high rate of attrition from the failure of drug candidates proceeding through clinical trials, and many companies have experienced significant setbacks in advanced development programs even after promising results in earlier studies or trials. We have experienced setbacks in our internal and partnered development programs and expect to experience additional setbacks from time to time in the future. In addition, even if the earlier-stage results of our development programs are favorable, these programs may take significantly longer than expected to complete or may not be completed at all. If we or our collaborators abandon or are delayed in our development efforts related to any drug or drug candidate, we may not be able to generate sufficient revenues to continue our operations at the current level or be profitable, our reputation in the industry and in the investment community would likely be significantly damaged, additional funding may not be available to us or may not be available on terms we or others believe are favorable, and our stock price may decrease significantly.

We may not be successful in initiating or completing our studies or trials or advancing our programs on our projected timetable, if at all. Any failure to initiate or delays in our studies, trials or development programs, or unfavorable results or decisions or negative perceptions regarding any of our programs, could cause our stock price to decline significantly. This is particularly the case with respect to our clinical programs.

Our efforts will be seriously jeopardized if we are unable to retain and attract key and other employees.

Our success depends on the continued contributions of our principal management, development and scientific personnel, and the ability to hire and retain key and other personnel. We face competition for such personnel, and we believe that risks and uncertainties related to our business may impact our ability to hire and retain key and other personnel. If we do not recruit and retain effective management and other key employees, particularly our executive officers, our operations, ability to generate or raise additional capital, and our business in general may be adversely impacted. For example, to execute our clinical programs, our strategy is to maintain a sufficient and robust clinical expertise and program management function. We are in the process of modifying and building this function, and we may not be able to establish the function we believe necessary to support our clinical goals and meet our corporate objectives.

Our business may be negatively impacted based on the clinical trials and preclinical studies of, and decisions affecting, one or more of our drug candidates.

The results and timing of clinical trials and preclinical studies, as well as related decisions by us, collaborators and regulators, can affect our stock price. Results of clinical trials and preclinical studies are uncertain and subject to different interpretations by regulatory agencies, us or others. The design of these trials and studies (which may change significantly and be more expensive than anticipated depending on results and regulatory decisions), as well as related analyses of such results, including adverse effects, may not be viewed favorably by us or third parties, including investors, analysts, current or potential collaborators, the academic and medical communities, and regulators, which could adversely impact the development and opportunities for regulatory approval of drug candidates and commercialization (and even result in withdrawal from the market) of approved drugs. The same may be true of decisions regarding the focus and prioritization of our research and development efforts. Stock prices of companies in our industry have declined significantly when such results and decisions were unfavorable or perceived negatively or when a drug candidate or product did not otherwise meet expectations.

The development, approval or commercialization of any of our drug candidates could be negatively affected by circumstances related to other drug candidates or approved products.

Information on our drug candidates in clinical development is preliminary and incomplete, and for such drug candidates, particularly in the earlier stages of development, information on approved products in the same or related drug classes may indicate potential risks related to the development of our drug candidates. For example, etrasimod is an orally available modulator of the S1P receptors. An approved drug that is also an orally available modulator of the S1P receptors, Gilenya, is associated with risks such as adverse cardiovascular effects, including lowering of the heart rate and heart blocks, infection, macular edema, respiratory effects, fetal risk, a rare brain infection, and elevations in liver enzymes. These adverse reactions and risks may be associated with S1P receptor modulation and could be found to be associated with the use of etrasimod. Such adverse reactions and risks, either actual or perceived, could negatively impact its development, approval or commercialization, or our ability to enter into a collaboration on acceptable terms.

Top-line data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose top-line or interim data from time to time, which is based on a preliminary analysis of then-available efficacy and safety data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and others, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or drug and our company in general. In addition, the information we may publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business.

Our hypothesis that selectively targeting receptors can lead to more efficacious or safer drugs may not be correct.

In general, we have designed and optimized our drug candidates (including etrasimod, ralinepag and APD371) to selectively target certain receptors found on cells in humans. Our hypothesis is that selectivity may allow our drug candidates to address diseases more efficaciously or without some of the negative effects associated with less selective drugs. In certain cases, we believe early research and, if available, early clinical testing, provides preliminary support for our hypothesis. However, our hypothesis may not be correct, early research and early phase clinical testing may not be predictive of efficacy or safety in later trials, and our drug candidates may not be approved or, if approved, have the desired efficacy or safety profile.

The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and our current drug candidates or any approved drugs may not be further developed or have favorable results in later studies or trials.

Preclinical studies and Phase 1 and Phase 2 clinical trials are not primarily designed to test the efficacy of a drug candidate, but rather to test safety, to study pharmacokinetics and pharmacodynamics, and to understand the drug candidate’s side effects at various doses and schedules. Favorable results in early studies or trials may not be confirmed in later studies or trials, including preclinical studies that continue or that are initiated after earlier clinical trials and large-scale clinical trials, and our drug candidates or drugs in subsequent trials or studies may fail to show desired safety and efficacy despite having progressed through earlier-stage trials. Unfavorable results from clinical trials or preclinical studies could result in delays, modifications or abandonment of ongoing or future clinical trials, or abandonment of a program. Clinical and preclinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals or commercialization. Negative or inconclusive results or adverse medical events during such trials or studies could cause a clinical trial to be delayed, repeated or terminated; a program to be abandoned; or negatively impact a related marketed drug, which could have a material adverse effect on our business, financial condition and results of operations.

Drug discovery and development is intensely competitive in the therapeutic areas on which we focus. If the number of our competitors increase or they develop treatments that are approved faster, marketed better, less expensive or demonstrated to be more effective or safer than our drugs or drug candidates, our commercial opportunities will be reduced or eliminated.

Many of the drugs we or our collaborators are attempting or may attempt to discover and develop may compete with existing therapies in the United States and other territories. In addition, many companies are pursuing the development

of new drugs that target the same diseases and conditions that we target.

For example, with regard to etrasimod, there are other drugs that have a similar mechanism of action already in Phase 3 clinical development for the same indications that we are pursuing, such as ulcerative colitis. By way of another example, with regard to ralinepag, a competitor with the same mechanism of action, selexipag is already currently approved in the United States, Europe and other countries. Our competitors, particularly large pharmaceutical companies, may have substantially greater research, development and marketing and sales capabilities and greater financial, scientific and human resources than we do. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before we do for the same indication may achieve a significant competitive advantage, including certain patent and marketing exclusivity rights. In addition, our competitors' drugs may have fewer side effects, more desirable characteristics (such as efficacy, route of administration or frequency of dosing), or be viewed more favorably by patients, healthcare providers, healthcare payers, the medical community, the media or others than our drug candidates or drugs, if any, for the same indication. Our competitors may also market generic or other drugs that compete with our drugs at a lower price than our drugs, which may negatively impact our drug sales, if any. Any results from our research and development efforts, or from our joint efforts with our existing or any future collaborators, may not compete successfully with existing or newly discovered products or therapies.

Our revenues in the future will be substantially dependent on the success of our or our collaborators marketing of drugs we have discovered or developed. To the extent such drugs are not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.

We believe our revenues will be substantially dependent on the success of the drugs we or our collaborators successfully develop. We do not know whether or when such drug candidates will be approved by regulatory authorities for sale or commercialized. Even if approved and commercialization begins, we do not know if such commercialization will be successful or otherwise meet our, your, analysts' or others' expectations, and the market price of our common stock could decline significantly. For example, sales of lorcaserin to date have been less than we and others initially anticipated, and, because lorcaserin is the only approved and marketed drug in which we have a financial interest, our revenue for the near-term is substantially dependent on our licensing agreement with Eisai and sales of lorcaserin.

We cannot guarantee future product sales or achievement of any other milestones. In addition, our licensing agreement with Eisai for lorcaserin, and any of our other collaborations, may be terminated early in certain circumstances, which may result in us not receiving additional milestone or other payments under the terminated agreement.

The degree of market acceptance and commercial success of a drug will depend on a number of factors, including the following, as well as risks identified in other risk factors:

- the number of patients treated with the drug and their results;
- market acceptance and use of the drug, which may depend on the public's view of the drug, economic changes, national and world events, potentially seasonal and other fluctuations in demand, the timing and impact of current or new competition, and the drug's perceived advantages or disadvantages over alternative treatments (including relative convenience, ease of administration, and prevalence and severity of any adverse events, including any unexpected adverse events);
- the actual and perceived safety and efficacy of the drug on both a short- and long-term basis among actual or potential patients, healthcare providers and others in the medical community, regulatory agencies and insurers and other payers, including related decisions by any such entity or individual;
- incidence and severity of any side effects, including as a result of off-label use or in combination with one or more drugs;
- new data relating to the drug, including as a result of additional studies, trials or analyses of the drug or related drugs or drug candidates;
- the willingness of physicians to prescribe and of patients to use the drug;
- the claims, limitations, warnings and other information in the drug's current or future labeling;
- any current or future scheduling designation for the drug by the US Drug Enforcement Administration, or DEA, or any comparable foreign authorities;
- our or our collaborators' maintenance of an effective sales force, marketing team, strategy and program, and medical affairs group and related functions, as well as its sales, marketing and other representatives accurately describing the drug consistent with its approved labeling;
- the price and perceived cost-effectiveness of the drug, including as compared to possible alternatives;
- the ability of patients and physicians and other providers to obtain and maintain coverage and adequate reimbursement, if any, by third-party payers, including government payers;
- the ability and desire of group purchasing organizations, or GPOs, including distributors and other network providers, to sell the drug to their constituencies;
- introduction of counterfeit or unauthorized versions of the drug;
- to the extent the drug is approved and marketed in a jurisdiction with a significantly lower price than in another jurisdiction, the impact of the lower pricing in the higher-priced territory, including on the pricing of reimbursement,

if available, and by the diversion of lower-priced of the drug into the higher-priced territory; and

- the availability of adequate commercial manufacturing and supply chain for the drug.

Our drugs may not be commercially successful if not widely covered and adequately reimbursed by third-party payers, and we may depend on others to obtain and maintain third-party payer access; inadequate third-party coverage and reimbursement could make entering into agreements with pharmaceutical companies to collaborate or commercialize our drugs more difficult and diminish our revenues.

Our and our collaborators' ability to successfully commercialize any of our drugs that have been or may be approved will depend, in part, on government regulation and the availability of coverage and adequate reimbursement from third-party payers, including private health insurers and government payers, such as the Medicaid and Medicare programs, increases in government-run, single-payer health insurance plans and compulsory licenses of drugs. We expect government and third-party payers will continue their efforts to contain healthcare costs by limiting coverage and reimbursement levels for new drugs. In addition, many countries outside of the United States have nationalized healthcare systems in which the government pays for all such products and services and must approve product pricing. A government or third-party payer decision not to approve pricing, or provide adequate coverage and reimbursements, for our drugs, if any, could limit market acceptance of and demand for our drugs.

It is increasingly difficult to obtain coverage and adequate reimbursement levels from third-party payers, and significant uncertainty exists as to the coverage and reimbursement of newly approved prescription drug products. We or our collaborators also face competition in negotiating for coverage from pharmaceutical companies and others with competitive drugs or other treatment, and these competitors may have significantly more negotiating leverage or success with respect to individual payers than we or our collaborators may have.

We expect that the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, its potential repeal, as well as other federal and state healthcare reform measures that have been or may be implemented in the future, may result in more rigorous coverage criteria, more limited coverage and downward pressure on the price that we may receive for any approved product, which could seriously decrease our future revenues. Any reduction in reimbursement from Medicare, Medicaid or other government programs may result in a similar reduction in payments from private payers. For example, reimbursement has been challenging for BELVIQ, including because Medicare explicitly excludes coverage for drugs for weight loss. The implementation of cost containment measures or other healthcare reforms may also limit our commercial opportunities by reducing the amount a potential collaborator is willing to pay to license our programs or drug candidates in the future, which may prevent us from being able to generate revenue, attain profitability, commercialize our products or establish and maintain collaborations.

Forecasting potential sales for drugs will be difficult, and if our projections are inaccurate, our business may be harmed and our stock price may be adversely affected.

Our business planning requires us to forecast or make assumptions regarding demand and revenues for our drugs if they are approved despite numerous uncertainties. These uncertainties may be increased if we rely on our collaborators to conduct commercial activities and provide us with accurate and timely information. Actual results may deviate materially from projected results for various reasons, including the following, as well as risks identified in other risk factors:

- the rate of adoption in the particular market, including fluctuations in demand for various reasons, such as fluctuations related to economic changes, national and world events, holidays and seasonal changes;
- pricing (including discounting or other promotions), reimbursement, product returns or recalls, competition, labeling, DEA scheduling, adverse events and others items that impact commercialization;
- lack of patient and physician familiarity with the drug;
- lack of patient use and physician prescribing history;
- lack of commercialization experience with the drug;

- actual sales to patients may significantly differ from expectations based on sales to wholesalers; and
- uncertainty relating to when the drug may become commercially available to patients and rate of adoption in other territories.

We expect that our revenues from drug sales will continue to be based in part on estimates, judgment and accounting policies, and incorrect estimates or regulators' or others' disagreement regarding such estimates or accounting policies may result in changes to guidance, projections or previously reported results. Expected and actual product sales and quarterly and other results may greatly fluctuate, including in the near-term, and such fluctuations can adversely affect the market price of our common stock, perceptions of our ability to forecast demand and revenues, and our ability to maintain and fund our operations.

Data generated or analyzed with respect to product use in the market or required postmarketing or other studies or trials may result in decreased demand, lower sales, product recall, regulatory action or litigation.

A New Drug Application, or NDA, holder (or the equivalent outside the United States) is responsible for assessing and monitoring the safety of a drug that has been approved for marketing, including reviewing reports of adverse safety events. In addition, NDA holders often conduct additional studies or trials or analyze new or previous data related to an approved drug, including with respect to required postmarketing studies and in connection with seeking additional regulatory approvals in new territories.

For example, as a condition to obtaining FDA approval of lorcaserin, the FDA required the conduct of postmarketing studies, including evaluation of the effect of long-term treatment with lorcaserin on the incidence of major adverse cardiovascular events, or MACE (non-fatal myocardial infarction, non-fatal stroke and cardiovascular death), in overweight and obese subjects with cardiovascular disease or multiple cardiovascular risk factors (otherwise known as the cardiovascular outcomes trial, or CVOT). The FDA-required portion of the trial is designed to evaluate lorcaserin's effect on the incidence of major adverse cardiovascular events compared to placebo, with a non-inferiority margin for the hazard ratio of 1.4. The trial also includes FDA-required echocardiographic assessments. Along with the FDA-required portion of the trial, we expect that the trial will include the non-FDA required evaluation of whether lorcaserin reduces the incidence of conversion to type 2 diabetes in patients without type 2 diabetes at baseline and the incidence of MACE+ (MACE or hospitalization for unstable angina or heart failure, or any coronary revascularization), both as compared to placebo. We expect that the trial (including the non-FDA required portion) will run for up to several more years, but the duration could be longer or shorter depending on the actual number of events observed. New data relating to lorcaserin, including from adverse event reports or required postmarketing, registration or other studies or trials, may result in label changes, may adversely affect sales or development, result in withdrawal of lorcaserin from the market, or result in litigation. In addition, analyses of previous data can have similar risks. We expect Eisai to continue to generate data from new studies and trials, as well as to continue analyzing existing data from previously conducted studies and trials, including for potential use in applications for the marketing approval of lorcaserin. Regulatory agencies may consider the new data or analyses in reviewing marketing applications for lorcaserin in their territories or impose post-approval requirements that require significant additional expenditures. Furthermore, the discovery of significant problems with a product or class of products similar to lorcaserin could have an adverse effect on the lorcaserin program, including commercialization.

The commercialization and continuing development of lorcaserin may be adversely impacted by cardiovascular side effects associated with drugs used for the treatment of obesity.

We developed lorcaserin to more selectively stimulate the serotonin 2C receptor than did fenfluramine or dexfenfluramine because we believe this may avoid the cardiovascular side effects associated with fenfluramine and dexfenfluramine (often used in combination with phentermine, the combination of which was commonly referred to as "fen-phen"). These two drugs were serotonin-releasing agents and non-selective serotonin receptor agonists, and were withdrawn from the market in 1997 after reported incidences of heart valve disease and pulmonary hypertension associated with their usage. In in vitro studies examining affinity, activity and serotonin receptor subtype specificity, lorcaserin demonstrated affinity for, and activity at, serotonin 2A, 2B and 2C receptors, but demonstrated greater affinity, activity and selectivity for the serotonin 2C receptor than for the serotonin 2A and 2B receptors. Activation of the latter two receptors has been associated with undesirable effects. Activation of the 2A receptor has been associated with central nervous system, or CNS, effects, including altered perception, mood and abuse potential, and activation of the 2B receptor has been associated with cardiac valvulopathy.

We may not be correct in our belief that more selectively stimulating the serotonin 2C receptor will avoid these undesired side effects, or lorcaserin's selectivity profile may not be adequate to avoid these side effects. Lorcaserin's selectivity profile and the potential relationship between the activity of lorcaserin and the activity of fenfluramine and

dexfenfluramine may result in increased regulatory scrutiny of the safety of lorcaserin, may raise potential adverse publicity and may affect product sales or result in litigation.

If we license or otherwise partner our drugs, our failure to maintain such agreements or poor performance under such agreements could negatively impact our business.

Our collaborators may have primary responsibility for the regulatory approval and, ultimately, marketing and distribution of our drug candidate in the territory or territories under the applicable collaboration. We may have limited or no control over the amount and timing of resources that any of these collaborators will dedicate to such activities. This is the case with lorcaserin and our license agreement with Eisai.

When we enter collaboration agreements, we are subject to a number of other risks, including:

- our collaborators may not comply with applicable regulatory guidelines, which could adversely impact the commercialization or development of the drug candidate;
- there could be disagreements regarding the agreements or the study or development that delay or terminate the commercialization, research, study or development, delay or eliminate potential payments under the agreements or increase our costs under or outside of the agreements;
- our collaborators may not effectively allocate adequate resources or may have limited experience in a particular territory; and
- our collaborators may not perform as expected, including with regard to making any required payments, and the agreements may not provide adequate protection or may not be effectively enforced.

We or our collaborators might terminate our agreements in certain circumstances or amend the terms of our agreement, and investors and analysts may not view any termination or amendments as favorable.

We are responsible for manufacturing lorcaserin and certain other drugs. We also rely on other companies, including third-party manufacturers and sole-source suppliers, and we or such other companies may encounter failures or difficulties or not receive or provide adequate supply, which could adversely affect development or commercialization.

Our drug product manufacturing facility in Switzerland is currently the only source for finished drug product of lorcaserin.

In addition, we do not own or operate manufacturing facilities that can produce active pharmaceutical ingredient, or API, intermediates and other material required to make our drug candidates or lorcaserin. Instead, we currently contract with other companies to supply API, intermediates and other materials. Certain of these materials are available from only one or a small number of suppliers, and using a new supplier, if available, could result in substantial delay and greater cost. Our dependence on single or limited sources of materials may adversely affect our ability to develop and deliver drug products on a timely and competitive basis, or at all.

Any performance failure on the part of us or a third-party manufacturer could result in a product recall or seizure, delay or otherwise adversely affect sales of an approved product or the clinical development or regulatory approval of lorcaserin or one or more of our other drug candidates. We or third-party manufacturers may encounter difficulties involving production yields, regulatory compliance, lot release, quality control and quality assurance, as well as shortages of qualified personnel. For example, in December 2014, Eisai and we discovered that a small number of bottles of lorcaserin in a limited number of lots had a missing or incomplete label, and, as a precautionary measure, Eisai voluntarily initiated a recall from wholesalers of the involved lots for inspection.

The ability to adequately and timely manufacture and supply drug product is dependent on the uninterrupted and efficient operation of the manufacturing facilities, which is impacted by many manufacturing variables, including:

- availability or contamination of raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier;
- capacity of our facilities or those of our contract manufacturers;
- having the ability to adjust to changes in actual or anticipated use of the facility, including with respect to having sufficient capacity and a sufficient number of qualified personnel;
- facility contamination by microorganisms or viruses or cross contamination;
- compliance with regulatory requirements, including inspectional notices of violation and warning letters;
- maintenance and renewal of any required licenses or certifications;
- changes in actual or forecasted demand;

- timing and number of production runs;
- production success rates and bulk drug yields; and
- timing and outcome of product quality testing.

In addition, we or our third-party manufacturers may encounter delays and problems in manufacturing our drug candidates or drugs for a variety of reasons, including accidents during operation, failure of equipment, delays in receiving materials, natural or

other disasters, political or governmental unrest or changes, social unrest, intentional misconduct or other factors inherent in operating complex manufacturing facilities. Commercially available starting materials, reagents and excipients may be or become scarce or more expensive to procure, and we may not be able to obtain favorable terms in agreements with subcontractors. We or our third-party manufacturers may not be able to operate our respective manufacturing facilities in a cost-effective manner or in a time frame that is consistent with our expected future manufacturing needs. If we or our third-party manufacturers cease or interrupt production or if our third-party manufacturers and other service providers fail to supply materials, products or services to us for any reason, such interruption could delay progress on our programs, or interrupt the commercial supply, with the potential for additional costs and lost revenues. If this were to occur, we may also need to seek alternative means to fulfill our manufacturing needs.

We may not be able to enter into or maintain agreements with manufacturers whose facilities and procedures comply with applicable law. Manufacturers are subject to ongoing periodic inspection (which may be unannounced) by the FDA, the DEA, corresponding state and foreign authorities and other regulatory authorities to ensure strict compliance with Current Good Manufacturing Practices, or cGMPs, regulations and other applicable government regulations and corresponding foreign standards. We do not have control over a third-party manufacturer's compliance with these regulations and standards. In addition, we have contracted with Siegfried to provide to us certain business and technical services, including safety, health and environmental services. We are, therefore, relying at least in part on Siegfried's judgment, experience and expertise. We intend to reduce or eliminate our dependence on Siegfried for such business and technical services, and any changes may result in increased cost, additional risk or otherwise negatively impact our operations. If we or one of our manufacturers or other company in the supply chain fail to maintain compliance or otherwise experience setbacks, we or they could be subject to civil or criminal penalties, the production of one or more of our drug candidates or lorcaserin could be interrupted or suspended, or our product could be recalled or withdrawn, resulting in delays, additional costs and potentially lost revenues.

Our drug candidates are subject to extensive regulation, and we may not receive required regulatory approvals, or timely approvals, for any of our drug candidates.

Preclinical and clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, marketing and distribution, and other activities relating to developing and manufacturing drugs are subject to extensive regulation by the FDA and other regulatory agencies. We are subject to periodic inspections (which may be unannounced) by the FDA, the DEA and other regulatory agencies, including inspections at our Swiss manufacturing facility. Failure to comply with applicable regulatory requirements may, either before or after product approval, subject us to administrative or judicially imposed sanctions that may negatively impact research and development or commercialization, or otherwise negatively impact our business. Regulatory agencies have in the past inspected certain aspects of our business in the United States and Switzerland, and we were provided with observations of objectionable conditions or practices with respect to our business in the United States. There is no assurance that regulatory agencies will not provide us with observations in future inspections or that we satisfactorily addressed observations provided to us in past inspections.

Regulatory approval of a drug candidate is not guaranteed, and our business and reputation may be harmed by any failure or significant delay in receiving regulatory approval. The number and types of preclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to target and the regulations applicable to any particular drug candidate. Despite the time and expense exerted in preclinical and clinical studies, failure can occur at any stage, and we could encounter problems that cause us to abandon clinical trials or to repeat or perform additional preclinical studies and clinical trials.

We cannot predict when or whether, or assure you that, our collaborators' or our past or any future regulatory submissions or responses will be sufficient to the applicable regulatory authority or others, that the applicable regulatory authority or others will consider data or our analyses, interpretations or procedures related to any of our drug candidates as sufficient or persuasive, or that any regulatory authority will ever approve any of our drug candidates in the future.

To market any drugs outside of the United States, we and our current or future collaborators must comply with numerous and varying regulatory requirements of other countries. 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 associated with FDA approval as well as additional risks, some of which may be unanticipated. The approval by the FDA or any other regulatory authority does not assure or predict with any certainty that any other regulatory authority will approve the drug.

In addition, existing regulatory policies and laws may change. We cannot predict the likelihood, nature or extent of new government regulation, either in the United States or in other countries, or the impact on our drug candidates or drugs. For example, new FDA regulation could delay or prevent marketing approvals, increase the cost of research and development, and result in narrower product labeling and expensive post-marketing requirements.

Our activities and drugs will still be subject to extensive postmarketing regulation if approved.

Following regulatory approval of any of our drug candidates, we and our collaborators will be subject to ongoing obligations and continued regulatory review from the FDA and other applicable regulatory agencies, such as continued adverse event reporting requirements. There may also be additional postmarketing obligations imposed by the FDA or other regulatory agencies. These obligations may result in significant expense and limit the ability to commercialize such drugs.

The FDA or other regulatory agencies may also require that the sponsor of the NDA or foreign equivalent, as applicable, conduct additional clinical trials to further assess approved drugs after approval under a post-approval commitment. Such additional studies may be costly and may impact the commercialization of the drug. For example, as part of the approval of BELVIQ, the FDA required the conduct of the CVOT described above as well as postmarketing studies to assess the safety and efficacy of BELVIQ for weight management in obese pediatric and adolescent patients. Along with being costly and time consuming, a delay or unfavorable results from these trials could negatively impact market acceptance of BELVIQ; limit the revenues we generate from sales; result in BELVIQ's withdrawal from the market; negatively impact the potential approval of lorcaserin in other territories for weight management, for other indications, in combination with other agents or using different formulations; and result in litigation.

The FDA or other regulatory agencies may also impose significant restrictions on the indicated uses for which a drug may be marketed. Additionally, the FDA may require a Risk Evaluation and Mitigation Strategies, or REMS, study, including in connection with a drug's approval, to help ensure that the benefits of the drug outweigh its risks. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, requirements that patients enroll in a registry or undergo certain health evaluations or other measures that the FDA deems necessary to ensure the safe use of the drug.

With regard to any of drug that receives regulatory approval, the labeling, packaging, adverse event reporting, storage, advertising and promotion for the drug will be subject to extensive regulatory requirements. We and the manufacturers of our products are also required to comply with cGMP regulations, which include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation. Further, regulatory agencies must approve these manufacturing facilities before they can be used to manufacture our products, and these facilities are subject to ongoing regulatory inspections. In addition, regulatory agencies subject a drug, its manufacturer and the manufacturer's facilities to continual review and inspections. The subsequent discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured, may result in restrictions on the marketing of that drug, up to and including withdrawal of the drug from the market. In the United States, the DEA and comparable state-level agencies also heavily regulate the manufacturing, holding, processing, security, recordkeeping and distribution of drugs that are considered controlled substances, and the DEA periodically inspects facilities for compliance with its rules and regulations.

Our ability to generate revenues from any of our drugs that receive regulatory approval will be subject to a variety of risks, many of which are out of our control.

Any drug that may be approved for marketing may not gain market acceptance among patients, healthcare providers, healthcare payers or the medical community. We believe that the degree of market acceptance and our ability to generate revenues from such products will depend on a number of factors, including:

- timing of market introduction of our drugs and competitive drugs and alternative treatments;

- actual and perceived efficacy and safety of our drugs;
- incidence and severity of any side effects;
- potential or perceived advantages or disadvantages as compared to alternative treatments;
- effectiveness of sales, marketing and distribution support;
- price of our future products, both in absolute terms and relative to alternative treatments;
- the general marketplace for the particular drug;
- the effect of current and future healthcare laws on our drug candidates;
- availability of coverage and adequate reimbursement from government and other third-party payers; and
- product labeling or product insert requirements of the FDA or other regulatory authorities.

If our approved drugs fail to achieve market acceptance, we may not be able to generate significant revenues to be profitable.

Collaboration relationships may lead to disputes and delays in drug development and commercialization, and we may not realize the full commercial potential of our drug candidates or drugs.

We may have conflicts with our prospective, current or past collaborators, such as conflicts concerning rights and obligations under our agreements, the interpretation of preclinical or clinical data, the achievement of milestone or other payments, the ownership of intellectual property, or research and development, regulatory, commercialization or other strategy. Collaborators may stop supporting our drug candidates or drugs, including if they no longer view the program as in their best financial or other interests or they develop or obtain rights to competing drug candidates or drugs. In addition, collaborators may fail to effectively develop, obtain approval for or commercialize our drugs, which may result in us not realizing their full commercial potential. If any conflicts arise with any of our current, past or prospective collaborators, the other party may act in a manner that is adverse to our interests. Any such disagreement could result in one or more of the following, each of which could delay, or lead to termination of, development or commercialization of our drug candidates or drugs, and in turn prevent us from generating revenues:

- unwillingness on the part of a collaborator to pay for studies or other research, milestones, royalties or other payments that we believe are due to us under a collaboration;
- uncertainty regarding ownership of intellectual property rights arising from our collaboration activities, which could prevent us from entering into additional collaborations;
- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development, regulatory, commercialization, pharmacovigilance or other activities or to permit public disclosure of the results of those activities;
- slowing or cessation of a collaborator's research, development, regulatory or commercialization efforts with respect to our drug candidates or drugs; or
- litigation or arbitration.

We have obtained orphan drug designation from the FDA for ralinepag for the treatment of PAH, but we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a drug that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the drug is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the drug with orphan drug exclusivity or where the manufacturer is unable to assure sufficient drug quantity.

Even though ralinepag has been granted orphan drug status for the treatment of PAH, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the drug from competition because different drugs with different active moieties (which is the molecule or ion responsible for the action of the drug substance) can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Setbacks and consolidation in the pharmaceutical and biotechnology industries could make entering into agreements with pharmaceutical companies to collaborate or commercialize our drugs more difficult and diminish our revenues.

Setbacks in the pharmaceutical and biotechnology industries, such as those caused by safety concerns relating to drugs or drug candidates, as well as competition from generic drugs, litigation and industry consolidation, may have an adverse effect on us, including by making it more difficult to enter into agreements with pharmaceutical companies to collaborate or commercialize our drugs and diminishing our revenues. For example, the FDA may be more cautious in approving our drug candidates based on safety concerns relating to these or other drugs or drug candidates, or pharmaceutical companies may be less willing to enter into new collaborations or continue existing collaborations if they are integrating a new operation as a result of a merger or acquisition or if their therapeutic areas of focus change following a merger.

We and our collaborators may from time to time rely on third parties to conduct clinical trials and preclinical studies. If those parties do not comply with regulatory and contractual requirements, successfully carry out their contractual obligations or meet expected deadlines, our drug candidates may not advance in a timely manner or at all.

In the course of our discovery, preclinical testing and clinical trials, we and our collaborators may from time to time rely on third parties, including laboratories, investigators, clinical research organizations and manufacturers, to perform critical services. For example, we rely on third parties to conduct our clinical trials and many of our preclinical studies. Clinical research organizations are responsible for many aspects of the trials, including finding and enrolling subjects for testing and administering the trials. Although we rely on these third parties to conduct our clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its investigational plan and protocol. Moreover, the FDA and foreign regulatory authorities require us to comply with regulations and standards, commonly referred to as Good Clinical Practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. Our reliance on third parties does not relieve us of these responsibilities and requirements. These third parties may not be available when we need them or, if they are available, may not comply with all regulatory and contractual requirements or may not otherwise perform their services in a timely or acceptable manner, and we may need to enter into new arrangements with alternative third parties and our preclinical studies or clinical trials may be extended, delayed or terminated. These independent third parties may also have relationships with other commercial entities, some of which may compete with us. In addition, if such third parties fail to perform their obligations in compliance with regulatory requirements and our protocols, our preclinical studies or clinical trials may not meet regulatory requirements or may need to be repeated. As a result of our dependence on third parties, we may face delays or failures outside of our direct control. These risks also apply to the development activities of collaborators, and we do not control their research and development, clinical trial or regulatory activities.

We may participate in new strategic transactions that could impact our liquidity, increase our expenses, present significant distractions to our management and be viewed as unfavorable.

From time to time we consider strategic transactions, such as out-licensing or in-licensing of compounds or technologies, acquisitions of companies and asset purchases. Additional potential transactions we may consider include a variety of different business arrangements, such as strategic collaborations, joint ventures, spin-offs, restructurings, divestitures, business combinations and investments. In addition, another entity may pursue us as an acquisition target. Any such transaction may be viewed as unfavorable by our stockholders or others and may require us to incur non-recurring or other charges, may create potential liabilities, may increase our near- and long-term expenditures and may pose significant integration challenges, require additional expertise or disrupt our management or business, which could harm our operations and financial results.

As part of an effort to enter into significant transactions, we conduct business, legal and financial due diligence with the goal of identifying and evaluating material risks involved in the transaction. Despite our efforts, we ultimately may be unsuccessful in ascertaining or evaluating all such risks and, as a result, might not realize the intended advantages of the transaction. If we fail to realize the expected benefits from any transaction we may consummate, whether as a result of unidentified risks, integration difficulties, regulatory setbacks or other events, our business, results of operations and financial condition could be adversely affected.

We may incur substantial liabilities for any product liability claims or otherwise as a drug product manufacturer.

We develop, test, manufacture and expect to commercialize drugs for use by humans. We face an inherent risk of product liability exposure related to the testing of our drug candidates in clinical trials, and face an even greater risk with the commercialization of lorcaserin as well as any other drug that may be approved for marketing. In addition,

under our agreement with Eisai, Arena GmbH and Eisai will, for a limited period of time, in general share equally in losses resulting from third-party product liability claims relating to lorcaserin, with certain limited exceptions.

Whether or not we are ultimately successful in any product liability or related litigation, such litigation would consume substantial amounts of our financial and managerial resources, and might result in adverse publicity, all of which would impair our business. In addition, damages awarded in a product liability action could be substantial and could have a negative impact on our financial condition.

An individual may bring a liability claim against us if one of our drugs or drug candidates causes, or merely appears to have caused, an injury. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our drug;
- injury to our reputation;
- increased difficulty to attract, or withdrawal of, clinical trial subjects;

- costs of related litigation;
- substantial monetary awards to subjects or other claimants;
- loss of revenues; and
- the inability to commercialize our drug candidates.

We will have limited product liability insurance that covers our clinical trials and products. We may not be able to maintain or obtain insurance coverage at a reasonable cost, and we may not have insurance coverage that will be adequate to satisfy any liability that may arise, which could have an adverse effect on our results of operations and financial condition.

We expect that Arena GmbH will, from time to time, manufacture BELVIQ for commercialization and lorcaserin and other drug candidates for clinical trials or other studies and potentially commercialization. Arena GmbH will also, from time to time, manufacture certain drug products for other companies. Arena GmbH is subject to liability for non-performance, product recalls and breaches of the agreements with our collaborators and other third parties.

We have significant contractual obligations, which may adversely affect our cash flow, cash position and stock price.

We have long-term leases on real properties and other contractual obligations. If we are unable to generate cash from operations sufficient to meet our financial obligations, we will need to obtain additional funds from other sources, which may include one or more financings. However, we may be unable to obtain sufficient additional funds when we need them on favorable terms or at all. The sale of equity or convertible debt securities or other financing transaction in the future may be dilutive to our stockholders, and some financing arrangements may require us to enter into covenants that would further restrict certain business activities or our ability to incur additional indebtedness or conduct other financing transactions, and may contain other terms that are not favorable to our stockholders or us.

Also, if we are unable to generate cash from operations or obtain additional funds from other sources sufficient to meet our contractual obligations, or we need to use existing cash to fund our contractual obligations, we may have to delay or curtail some or all of our development and commercialization programs, sell or license some or all of our assets on terms that you or others may view as unfavorable, or default under our agreements. Our contractual obligations could have significant additional negative consequences, including, without limitation:

- increasing our vulnerability to general adverse economic conditions;
- limiting our ability to obtain additional funds;
- placing us at a possible competitive disadvantage to less leveraged competitors and competitors that have better access to capital resources; and
- litigation or other disagreements.

We may be subject, directly or indirectly, to federal and state healthcare laws, including but not limited to fraud and abuse and false claims laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties and prosecution.

In the United States, drug manufacturers and marketers are subject to various state and federal fraud and abuse laws, including, without limitation, the Federal Anti-Kickback Statute and Federal False Claims Act. There are similar laws in other countries. These laws may impact, among other things, the research, manufacturing, sales, marketing and education programs for our drugs.

The Federal Anti-Kickback Statute prohibits persons and entities from knowingly and willingly soliciting, offering, receiving or providing any remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the purchase, lease, order or the furnishing or arranging for, a good, item, facility or service, for which payment may be made, in whole or in part, under a federal healthcare program such as the Medicare and Medicaid programs. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an

arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The Federal Anti-Kickback Statute is broad and, despite a series of narrow statutory exceptions and regulatory safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Moreover, the ACA, among other things, amended the intent requirement of the Federal Anti-Kickback Statute and certain criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them. The ACA also provides that 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 Civil False Claims

Act. Many states have also adopted laws similar to the Federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The Federal Civil False Claims Act prohibits, among other things, persons or entities from knowingly presenting, or causing to be presented, a false claim to, or the knowing use of false statements to obtain payment from the federal government. Suits filed under the Federal Civil False Claims Act can be brought by any individual on behalf of the government, known as "qui tam" actions, and such individuals, commonly known as "whistleblowers," may share in any amounts paid by the entity to the government in fines or settlement. The filing of qui tam actions has caused a number of pharmaceutical, medical device and other healthcare companies to have to defend a Federal Civil False Claims Act action. When an entity is determined to have violated the Federal Civil False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim, in addition to other penalties that may apply. Various states have also enacted laws modeled after the Federal Civil False Claims Act, some of which are broader in scope and may apply regardless of payer.

The Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Additionally, the civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The Federal Physician Payment Sunshine Act, created under the ACA, and its implementing regulations requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the US Department of Health and Human Services, or HHS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

We may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information.

Additionally, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers will also be required to verify that purchasers of the manufacturers' products are appropriately licensed. Further, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

We are unable to predict whether we could be subject to actions under any of these fraud and abuse or other laws, or the impact of such actions. If we are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil, criminal and/or administrative penalties, damages, fines, individual imprisonment, disgorgement, possible exclusion from government healthcare reimbursement programs and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations.

We may not be able to effectively integrate, manage or maintain our international operations, and such difficulty could adversely affect our business operations, financial condition, results of operations and stock price.

The headquarters of our operations outside of the United States is in Switzerland. Activities conducted in Switzerland include clinical operations and regulatory, manufacturing, quality control, quality assurance, development of manufacturing processes, qualifying suppliers and otherwise managing aspects of the supply chain, regulatory compliance, distribution of finished products, alliance management, and strategic planning and development. We also have drug candidates in clinical trials outside of the United States. There are significant risks associated with foreign operations, including, but not limited to, compliance with local laws and regulations, the protection of our intellectual property, the ability to integrate our corporate culture with local customs and cultures, the distraction to our management, foreign currency exchange rates and the impact of shifts in the United States and local economies on

those rates, and integration of our policies and procedures, including disclosure controls and procedures and internal control over financial reporting, with our international operations.

With respect to local laws and regulations, the European Union, Switzerland and certain other foreign territories have restrictions on the transfer, use and maintenance of certain personal data, including providing that transfers of personal data outside of their territories may only take place if the country to which the personal data is transferred ensures an "adequate" level of privacy protection. The European Commission has previously found that the United States did not provide adequate levels of protection. Any restrictions on our data transfers may negatively impact our ability and increase our costs to maintain international operations, including our Swiss manufacturing facility and clinical trials and other studies.

In October 2015 and July 2016, we initiated measures to reduce our expenditures and streamline our operations in Switzerland, including changes with respect to the staffing, process, procedures and strategy relating our Swiss manufacturing facility and our ongoing Phase 2 clinical trials. These staffing and other changes may increase risks related to our international operations as well as our operations in general.

We use biological materials, hazardous materials, chemicals and radioactive compounds.

Our activities involve the use of potentially harmful biological materials, as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. These materials and various wastes resulting from their use are stored at our facility pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause:

- interruption of our development or manufacturing efforts;
- injury to our employees and others;
- environmental damage resulting in costly clean up; and
- liabilities under domestic or foreign laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

In such an event, we may be held liable for any resulting damages, and any such liability could exceed our resources. Although we carry insurance in amounts and type that we consider commercially reasonable, we cannot be certain that the coverage or coverage limits of our insurance policies will be adequate, and we do not have insurance coverage for losses relating to an interruption of our research and development efforts caused by contamination.

Our business and operations might be adversely affected by business disruptions and security breaches, including any cybersecurity incidents.

Our US operations are located in a business park in San Diego, and our clinical operations outside the US are located in single building in Zug, Switzerland. We also have a drug product manufacturing facility in Zofingen, Switzerland, and we expect that, at least for the near-term, this facility will be the sole location for the manufacturing of lorcaserin finished drug product. We depend on our facilities and on collaborators, contractors and vendors for the continued operation of our business, some of whom are located in Europe and Asia. Natural disasters or other catastrophic events, including interruptions in the supply of natural resources, political and governmental changes, disruption in transportation networks or delivery services, severe weather conditions, wildfires and other fires, explosions, actions of animal rights activists, terrorist attacks, earthquakes and wars could disrupt our operations or those of our collaborators, contractors and vendors.

We depend on the efficient and uninterrupted operation of our computer and communications systems, which we use for, among other things, sensitive company data, including our financial data, intellectual property and other proprietary business information.

While certain of our operations have business continuity and disaster recovery plans and other security measures intended to prevent and minimize the impact of IT-related interruptions, our IT infrastructure and the IT infrastructure of our current and any future collaborators, contractors and vendors are vulnerable to damage from cyberattacks, computer viruses, unauthorized access, electrical failures and natural disasters or other catastrophic events. We could experience failures in our information systems and computer servers, which could result in an interruption of our normal business operations and require substantial expenditure of financial and administrative resources to remedy. System failures, accidents or security breaches can cause interruptions in our operations and can result in a material disruption of our research and development programs, manufacturing or commercialization activities and other business operations. The loss of data from completed or future studies or clinical trials could result in delays in our research, development or regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Similarly, we rely on third parties to supply materials for the manufacture of our drug candidates and lorcaserin, conduct studies and clinical

trials of our drug candidates and warehouse, market and distribute lorcaserin, and similar events relating to their computer systems could also have a material adverse effect on our business. 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 liabilities and the development of any of our other drug candidates and the commercialization of drugs could be delayed or otherwise adversely affected.

Even though we believe we carry commercially reasonable business interruption and liability insurance, and our contractors may carry liability insurance that protect us in certain events, we might suffer losses as a result of business interruptions that exceed the coverage available under our and our contractors' insurance policies or for which we or our contractors do not have coverage. For example, we are not insured against a terrorist attack. Any natural disaster or catastrophic event could have a significant negative impact on our operations and financial results. Moreover, any such event could delay our research and development programs and adversely affect, which may include stopping, our commercial production.

We and certain of our current and former employees and directors have been named as defendants in litigation that could result in substantial costs and divert management's attention.

Beginning in September 2010, a number of lawsuits were filed against us and certain of our employees and directors on behalf of certain purchasers of our common stock. The lawsuits in general include allegations that we and certain of our employees and directors violated laws by making materially false and misleading statements regarding our BELVIQ trials, thereby artificially inflating the price of our common stock. The plaintiffs are seeking unspecified monetary damages and other relief.

There is no guarantee that we will be successful in defending these lawsuits. Also, our insurance coverage may be insufficient, our assets may be insufficient to cover any amounts that exceed our insurance coverage, and we may have to pay damage awards or otherwise may enter into settlement arrangements in connection with such claims. A settlement of any of these lawsuits could involve the issuance of common stock or other equity, which may dilute your ownership interest. Any payments or settlement arrangements could have material adverse effects on our business, operating results, financial condition or your ownership interest. Even if the plaintiffs' claims are not successful, this litigation could result in substantial costs and significantly and adversely impact our reputation and divert management's attention and resources, which could have a material adverse effect on our business, operating results or financial condition. In addition, such lawsuits may make it more difficult to finance our operations, obtain certain types of insurance (including directors' and officers' liability insurance), and attract and retain qualified executive officers, other employees and directors.

Our executive officers and directors may sell shares of their stock, and these sales could adversely affect our stock price.

Sales of our stock by our executive officers and directors, or the perception that such sales may occur, could adversely affect the market price of our stock. Our executive officers and directors may sell stock in the future, either as part, or outside, of trading plans under Rule 10b5-1 of the US Securities and Exchange Commission, or SEC.

Negative US and global economic conditions may pose challenges to our business strategy, which relies on funding from collaborators or the financial markets, and creates other financial risks for us.

Negative conditions in the US or global economy, including financial markets, may adversely affect our business and the business of our current and prospective collaborators, distributors and licensees, which we sometimes refer to generally as our collaborators, and others with which we do or may conduct business. The duration and severity of these conditions is uncertain. If negative economic conditions persist or worsen, we may be unable to secure funding

to sustain our operations or to find suitable collaborators to advance our internal programs, even if we achieve positive results from our research and development or business development efforts. Such negative conditions could also impact commercialization of BELVIQ or any other drugs we develop as well as our financial condition.

From time to time, we may maintain a portfolio of investments in marketable debt securities, which are recorded at fair value. Although we have established investment guidelines relative to diversification and maturity with the objectives of maintaining safety of principal and liquidity, we rely on credit rating agencies to help evaluate the riskiness of investments, and such agencies may not accurately predict such risk. In addition, such agencies may reduce the credit quality of our individual holdings, which could adversely affect their value. Lower credit quality and other market events, such as changes in interest rates and further deterioration in the credit markets, may have an adverse effect on the fair value of our investment holdings and cash position.

Currency fluctuations may negatively affect our financial condition.

We primarily spend and generate cash in US dollars, and present our consolidated financial statements in US dollars. However, a portion of our expected and potential payments and receipts under our agreements are in foreign currencies, including Swiss francs. For example, payments and receipts under our agreements with Siegfried are required to be paid in Swiss francs. A fluctuation of the exchange rates of foreign currencies versus the US dollar may, thus, adversely affect our financial results, including cash balances, expenses and revenues. We may in the future enter into hedging transactions to try to reduce our foreign currency exposure, but there is no assurance that such transactions will occur or be successful.

Laws, rules and regulations relating to public companies may be costly and impact our ability to attract and retain directors and executive officers; our disclosure controls and procedures and our internal control over financial reporting may not prevent potential errors and fraud.

Laws and regulations affecting public companies, including rules adopted by the SEC and by NASDAQ, as well as the laws and regulations of foreign governments, may result in increased costs to us, particularly as we continue to develop the required capabilities in the United States and abroad to commercialize our products. These laws, rules and regulations could make it more difficult or costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on our board committees or as executive officers. We cannot estimate accurately the amount or timing of additional costs we may incur to respond to these laws, rules and regulations.

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

Risks Relating to Our Intellectual Property

Our success is dependent on intellectual property rights held by us and third parties and our interest in these rights is complex and uncertain.

Our success will depend on our own and on current or future collaborators' abilities to obtain, maintain and defend patents. In particular, the patents directed to our drug candidates and drugs are important to developing and commercializing drugs and our revenue. We have numerous US and foreign patents issued and patent applications pending for our technologies. There is no assurance that any of our patent applications will issue, or that any of the patents will be enforceable or will cover a drug or other commercially significant technology or method, or that the patents will be held to be valid for their expected terms.

The procedures for obtaining a patent are complex. These procedures require an analysis of the scientific technology related to the invention and many sophisticated legal issues. Obtaining patent rights outside the United States often requires the translation of highly technical documents and an improper translation may jeopardize our patent protection. Ensuring adequate quality of translators and foreign patent attorneys is often very challenging.

Consequently, the process for having our pending patent applications issue as patents will be difficult, complex and time consuming. Our patent position is very uncertain and we do not know when, or if, we will obtain additional patents, or if the scope of the patents obtained will be sufficient to protect our drugs, or be considered sufficient by parties reviewing our patent positions pursuant to a potential marketing, licensing or financing transaction.

In addition, other entities may challenge the validity or enforceability of our patents in litigation or administrative proceedings. We cannot make assurances as to how much protection, if any, our patents will provide if we attempt to enforce them or they are challenged. It is possible that a competitor or a generic pharmaceutical provider may successfully challenge our patents and those challenges may result in reduction or elimination of our patent coverage.

We also rely on confidentiality agreements and trade secrets to protect our technologies. However, such information is difficult to protect. We require our employees to contractually agree not to improperly use our confidential information or disclose it to others, but we may be unable to determine if our employees have conformed or will conform to their legal obligations under these agreements. We also enter into confidentiality agreements with prospective collaborators, collaborators, service providers and consultants, but we may not be able to adequately protect our trade secrets or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of this information. Many of our employees and consultants were, and many of them may currently be, parties to confidentiality agreements with other pharmaceutical and biotechnology companies,

and the use of our technologies could violate these agreements. In addition, third parties may independently discover our trade secrets or other proprietary information.

Some of our research and development collaborators and scientific consultants have rights to publish data and information to which we have rights. We generally seek to prevent our collaborators and consultants from disclosing scientific discoveries before we have the opportunity to file patent applications on such discoveries. In some of our collaborations, we do not control our collaborators' ability to disclose their own discoveries under the collaboration and in some of our academic relationships we are limited to relatively short periods to review a proposed publication and file a patent application. If we cannot maintain confidentiality in connection with our collaborations and relationships, our ability to receive patent protection or protect our proprietary information will be impaired.

We believe that the United States is by far the largest single market for pharmaceuticals in the world. Because of the critical nature of patent rights to our industry, changes in US patent laws could have a profound effect on our future profits, if any. It is unknown which, if any, patent laws will change, how changes to the patent laws will ultimately be enforced by the courts and the impact on our business.

A dispute regarding the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be costly and result in delays or termination of our future research, development, manufacturing and sales activities.

Our commercial success depends upon our ability to develop and manufacture our drugs and drug candidates, market and sell drugs, and conduct our research and development activities without infringing or misappropriating the proprietary rights of others. There are many issued patents and pending patent applications owned by others relating to research and development programs that could be determined to be similar, identical or superior to ours or our licensors or collaborators. We may be exposed to future litigation by others based on claims that our drugs, drug candidates, technologies or activities infringe the intellectual property rights of others. Numerous issued patents and pending patent applications owned by others exist in the areas of our research and development, including some which purport to allow the patent holder to control the use of all drugs that modulate a particular drug target regardless of whether the infringing drug bears any structural resemblance to a chemical compound known to the patent holder at the time of patent filing. Numerous issued patents and pending patent applications owned by others also exist in the therapeutic areas in which we are developing drugs. There are also numerous issued patents and pending patent applications owned by others that are directed to chemical compounds or synthetic processes that may be necessary or useful to use in our research, development, manufacturing or commercialization activities. These could materially affect our ability to develop our drug candidates or manufacture, import or sell drugs, and our activities, or those of our licensors or collaborators, could be determined to infringe these patents. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our drugs, drug candidates or technologies may infringe. There also may be existing patents owned by others, of which we are not aware, that our drug candidates or technologies may infringe. Further, there may be issued patents or pending patent applications owned by others in fields relevant to our business, of which we are or may become aware, that we believe (i) are invalid, unenforceable, or we do not infringe; (ii) relate to immaterial portions of our overall research and development, manufacturing and commercialization efforts; or (iii) in the case of pending patent applications, the resulting patent would not be granted or, if granted, would not likely be enforced in a manner that would materially impact such efforts. We cannot assure you that others holding any of these patents or patent applications will not assert infringement claims against us and seek damages or enjoinment of our activities. We also cannot assure you that, in the event of litigation, we will be able to successfully assert non-infringement, unenforceability, invalidity or immateriality, or that any infringement claims will be resolved in our favor.

In addition, others may infringe or misappropriate our proprietary rights. We may have to institute costly legal action to protect our intellectual property rights, or may not be able to afford the costs of enforcing or defending our

intellectual property rights.

There could be significant litigation and other administrative proceedings in our industry that affect us regarding patent and other intellectual property rights. Any legal action or administrative action against us, or our collaborators, claiming damages or seeking to enjoin commercial activities relating to our research and development, manufacturing and commercialization activities could:

- require us, or our collaborators, to obtain a license which may not be available on commercially reasonable terms, if at all;
- prevent us from importing, making, using, selling or offering to sell the subject matter claimed in patents held by others and subject us to potential liability for damages;
- consume a substantial portion of our managerial, scientific and financial resources; or
- be costly, regardless of the outcome.

Furthermore, because of the substantial amount of pre-trial document and witness discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised. In addition, during the

course of intellectual property litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

We are aware of third-party patents, as well as third-party patent applications, that could adversely affect the potential commercialization of etrasimod. For example, we are aware of a third-party patent, as well as third-party patent applications, with broad claims to administering an S1P modulators by starting with a lower dose and then increasing to a higher, standard daily dose. While we do not believe that any such claims that would cover the potential commercialization of etrasimod are valid and enforceable, we may be incorrect in this belief. In addition, other patents may issue from third-party patent applications with respect to certain dosing regimens, which could also adversely affect the potential commercialization of etrasimod, if etrasimod is approved with a specific dosing regimen.

We have been contacted from time to time by third parties regarding their intellectual property rights, sometimes asserting that we may need a license to use their technologies. For example, a third party has communicated that it believes its issued US patents (one of which has subsequently expired) include patent claims that cover lorcaserin or its use. If we fail to obtain any required licenses or make any necessary changes to our technologies, we may become involved in expensive and time-consuming litigation or we may be unable to develop or commercialize some or all of our drugs or drug candidates.

We and Eisai have filed a patent infringement lawsuit against an ANDA filer relating to a “Paragraph IV certification.” While we intend to vigorously enforce our intellectual property rights relating to lorcaserin, we cannot predict the outcome of any litigation matter. For example, our existing patents could be invalidated, found unenforceable or found not to cover a generic form of lorcaserin. If an ANDA filer were to prevail in patent litigation and/or receive approval to sell a generic version of lorcaserin, lorcaserin would become subject to increased competition and our revenue would be adversely affected.

We cannot protect our intellectual property rights throughout the world.

Filing, prosecuting, defending and enforcing patents on all of our drug candidates throughout the world would be prohibitively expensive. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to “work” the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our drug candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which makes it difficult for us to stop the infringement of our patents. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Risks Relating to Our Securities

Our stock price will likely be volatile, and your investment in our stock could decline in value.

Our stock price has fluctuated historically. From January 1, 2015, to March 10, 2017, the market price of our stock was as low as $1.30 per share and as high as $6.28 per share.

Very few drug candidates being tested will ultimately receive regulatory approval, and companies in our industry sometimes experience significant volatility in their stock price. Our stock price may fluctuate significantly depending on a variety of factors, including:

- regulatory actions or decisions or legislation affecting drugs or drug candidates, including ours and those of our competitors;
- the commercial availability and success or failure of any of our drug candidates or lorcaserin;
- the development and implementation of our continuing development and research plans, including outcome studies for lorcaserin;
- the entrance into, or failure to enter into, a new collaboration or the modification or termination of an existing collaboration or other material transaction;

- the timing and receipt by us of milestone and other payments or failing to achieve and receive the same;
- fluctuation in prescriptions, sales or financial results (including with respect to revenue recognition) or inaccurate sales or cash forecasting;
- accounting restatements and changes;
- supply chain or manufacturing issues;
- discussions or recommendations affecting our drugs or drug candidates by FDA advisory committees or other reviewers of preclinical or clinical data or other information related to lorcaserin, drug candidates or other drugs;
- results or decisions affecting the development or commercialization of any of our drug candidates or lorcaserin, including the results of studies, trials and other analyses;
- the timing of the development of our drug candidates;
- changes in our research and development budget or the research and development budgets of our existing or potential collaborators;
- the introduction, development or withdrawal of drug candidates or drugs by others that target the same diseases and conditions that we or our collaborators target or the introduction of new drug discovery techniques;
- the success, failure or setbacks of our or a perceived competitor's drugs or drug candidates;
- expenses related to, and the results of, litigation, other disputes and other proceedings;
- financing strategy or decisions;
- the allocation of our resources;
- our ability, or the perception by investors of our ability, to continue to meet all applicable requirements for continued listing of our common stock on The NASDAQ Stock Market, and the possible delisting of our common stock if we are unable to do so;
- developments in intellectual property rights or related announcements; and
- capital market conditions.

We are not able to control many of these factors. If our financial or scientific results in a particular period do not meet stockholders' or analysts' expectations, our stock price may decline and such decline could be significant.

We may be unable to comply with the applicable continued listing requirements of the NASDAQ Global Select Market.

Our common stock is currently listed on the NASDAQ Global Select Market, or NASDAQ. In order to maintain this listing, we must satisfy minimum financial and other continued listing requirements and standards, including a minimum closing bid price requirement for our common stock of $1.00 per share. There can be no assurance that we will be able to comply with the applicable listing standards. For example, if we were to fail to meet the minimum bid price requirement for 30 consecutive business days, we could become subject to delisting. Although NASDAQ may provide us with a compliance period in which to regain compliance with the minimum bid price requirement, we cannot assure you that we would be able to regain compliance within the period provided by NASDAQ. In order to regain compliance with such requirement, the closing bid price of our common stock would need to meet or exceed $1.00 per share for at least 10 consecutive business days during the compliance period. If we were not able to regain compliance within the allotted compliance period for this requirement or any other applicable listing standard, including any extensions that may be granted by NASDAQ, our shares of common stock would be subject to delisting. In the event that our common stock is delisted from NASDAQ and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further.

Any future equity or debt issuances or other financing transactions may have dilutive or adverse effects on our existing stockholders.

We have been opportunistic in our efforts to obtain cash, and we expect to continue to evaluate various funding alternatives from time to time. We have primarily financed our operations, and we may continue to finance our operations, by issuing and selling our common stock or securities convertible into or exercisable for shares of our common stock. We may issue additional shares of

common stock or convertible securities that could dilute your ownership in our company and may include terms that give new investors rights that are superior to yours. We have an effective registration statement to sell shares of our common stock and certain other securities, and we may elect to sell shares pursuant to such registration from time to time, including pursuant to an Equity Distribution Agreement that we put in place in January 2017 with Citigroup Global Markets Inc. Through March 13, 2017, we had sold 2,017,301 shares for aggregate gross proceeds of $3.2 million under the Equity Distribution Agreement, which permits total sales of up to $50.0 million in the aggregate.

Moreover, any issuances by us of equity securities may be at or below the prevailing market price of our common stock and in any event may have a dilutive impact on your ownership interest, which could cause the market price of our common stock to decline. In addition, we may also raise additional funds through the incurrence of debt or other financing transaction, and the investors may have rights superior to your rights in the event we are not successful and are forced to seek the protection of bankruptcy laws or the transaction may otherwise adversely affect our business prospects and existing stockholders.

There are a substantial number of shares of our common stock that may become eligible for future sale in the public market, and the sale of our common stock could cause the market price of our common stock to fall.

As of March 10, 2017, there were (i) options to purchase 36,585,754 shares of our common stock outstanding under our equity incentive plans at a weighted-average exercise price of $2.33 per share, (ii) 502,974 restricted stock unit awards outstanding under our equity incentive plans, (iii) performance restricted stock unit awards outstanding under our equity incentive plans targeted at 358,194 shares (however, the actual number of shares that may be awarded ranges from 0% to 200% of such amount), (iv) 7,345,674 additional shares of common stock remaining issuable under our 2013 Long-Term Incentive Plan, as amended, and our 2009 Employee Stock Purchase Plan, as amended, and (v) 62,501 shares of common stock remaining issuable under our Deferred Compensation Plan.

Once issued, the shares described above will be available for immediate resale in the public market. The market price of our common stock could decline as a result of such resales due to the increased number of shares available for sale in the market. As of March 10, 2017, there were 245,469,142 shares of our common stock outstanding.

The holders of our common stock and other securities may take actions that are contrary to your interests, including selling their stock.

A small number of stockholders may hold or acquire a significant amount of our outstanding stock. From time to time, there is a large short interest in our stock. These holders of such stock or positions may seek control of us, support transactions that we or you do not believe are favorable, and have interests that are different from yours. In addition, sales of a large number of shares of our stock by these large stockholders or other stockholders within a short period of time could adversely affect our stock price.

We may also be involved in disagreements with the holders of our stock, warrants or other securities in the future. Such disagreements may lead to proxy contests or litigation, which may be expensive and consume management’s time, involve settlements, the terms of which may not be favorable to us, or result in other negative consequences to our business.

Certain of our agreements, provisions in our charter documents, possible future agreements and Delaware law could delay or prevent a change in management or a takeover attempt that you may consider to be in your best interests.

There is a standstill provision in our marketing and supply agreement with Eisai, and we may enter into agreements with similar provisions. In addition, we may in the future adopt a stockholders’ rights agreement, which would cause substantial dilution to any person who attempts to acquire us in a manner or on terms not approved by our board of

directors. These provisions or agreements, as well as other provisions in our certificate of incorporation and bylaws and under Delaware law, could delay or prevent the removal of directors and other management and could make more difficult a merger, tender offer or proxy contest involving us that you may consider to be in your best interests. For example, our charter provisions:

- allow our board of directors to issue preferred stock without stockholder approval;
- limit who can call a special meeting of stockholders;
- eliminate stockholder action by written consent; and
- establish advance notice requirements for nomination for election to the board of directors or for proposing matters to be acted upon at stockholders' meetings.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

As set forth in the table below, we lease approximately 336,000 square feet of research, development, warehouse and office space located at various addresses in the same business park in San Diego, California and own or lease approximately 153,000 square feet of laboratory, manufacturing, warehouse and office space located in the same business park in Zofingen, Switzerland.

Location	Own/ Lease	Description
6114 Nancy Ridge Drive, San Diego, California	Lease	This chemical development facility consists of approximately 40,000 square feet (which includes approximately 18,000 of internal square feet and approximately 22,000 square feet of integrated external space), of which approximately 5,000 square feet is office space. We sublease this facility to a third party.
6118 Nancy Ridge Drive, San Diego, California	Lease	This facility of approximately 30,000 square feet consists of approximately 30% laboratory space and 70% office space. We sublease approximately 15,000 square feet of this space to Beacon and the rest is substantially unoccupied.
6122-6124-6126 Nancy Ridge Drive, San Diego, California	Lease	This facility of approximately 68,000 square feet consists of approximately 28,500 square feet of laboratory space, 37,500 square feet of office space and 2,000 square feet of warehouse space, which is substantially unoccupied.
6138-6150 Nancy Ridge Drive, San Diego, California	Lease	This facility of approximately 55,000 square feet consists of approximately 33,000 square feet of laboratory space and 22,000 square feet of office space, which is substantially unoccupied.
6154 Nancy Ridge Drive, San Diego, California	Lease	This facility of approximately 143,000 square feet consists of approximately 131,000 square feet of office space and 12,000 square feet of warehouse space, which is partially unoccupied.
Zofingen, Switzerland	Own	This facility of approximately 134,000 square feet includes approximately 76,000 square feet we occupy of which 39,000 square feet is manufacturing space, 30,000 square feet is warehouse space and 7,000 square feet is office space. We lease the remaining 58,000 square feet of warehouse space to Siegfried.
Zofingen, Switzerland	Lease	We lease from Siegfried a total of approximately 19,000 square feet, consisting of approximately 11,000 square feet of office space, 5,000 square feet of warehouse space and 3,000 square feet of laboratory space, in various facilities.
Zug, Switzerland	Lease	We lease a total of approximately 4,500 square feet of office space.

We expect these facilities to be sufficient for our needs for at least the near term. We have significantly more space in San Diego than we expect to need for the foreseeable future, and we have subleased certain of our space and are exploring subleasing additional unused space to reduce our expenses.

Item 3. Legal Proceedings

Beginning on September 20, 2010, a number of complaints were filed in the US District Court for the Southern District of California, or District Court, against us and certain of our current and former employees and directors on behalf of certain purchasers of our common stock. The complaints were brought as purported stockholder class actions, and, in general, include allegations that we and certain of our current and former employees and directors violated federal securities laws by making materially false and misleading statements regarding our BELVIQ program, thereby artificially inflating the price of our common stock. The plaintiffs sought unspecified monetary damages and other relief. On August 8, 2011, the District Court consolidated the actions and appointed a lead plaintiff and lead counsel. On November 1, 2011, the lead plaintiff filed a consolidated amended complaint. On March 28, 2013, the District Court dismissed the consolidated amended complaint without prejudice. On May 13, 2013, the lead plaintiff filed a second consolidated amended complaint. On November 5, 2013, the District Court dismissed the second consolidated amended complaint without prejudice as to all parties except for Robert E. Hoffman, who was dismissed from the action with prejudice. On November 27, 2013, the lead plaintiff filed a motion for leave to amend the second consolidated amended complaint. On March 20, 2014, the District Court denied plaintiff's motion and dismissed the second consolidated amended complaint with prejudice. On April 18, 2014, the lead plaintiff filed a notice of appeal, and on August 27, 2014, the lead plaintiff filed his appellate brief in the US Court of Appeals for the

Ninth Circuit, or Ninth Circuit. On October 24, 2014, we filed our answering brief in response to the lead plaintiff's appeal. On December 5, 2014, the lead plaintiff filed his reply brief. A panel of the Ninth Circuit heard oral argument on the appeal on May 4, 2016. On October 26, 2016, the Ninth Circuit panel reversed the District Court's dismissal of the second consolidated amended complaint and remanded the case back to the District Court for further proceedings. On January 25, 2017, the District Court permitted us to submit a renewed motion to dismiss the second consolidated amended complaint. On February 2, 2017, we filed the renewed motion to dismiss. On February 23, 2017, the lead plaintiff filed his opposition, and on March 2, 2017, we filed our reply. Due to the stage of these proceedings, we are not able to predict or reasonably estimate the ultimate outcome or possible losses relating to these claims.

On September 30, 2016, we and Eisai Inc. filed a patent infringement lawsuit against Lupin Limited and Lupin Pharmaceuticals, Inc. (collectively, Lupin) in the U.S. District Court for the District of Delaware. The lawsuit relates to a "Paragraph IV certification" notification that we and Eisai Inc. received regarding an abbreviated new drug application, or ANDA, submitted to the FDA by Lupin requesting approval to engage in the commercial manufacture, use, importation, offer for sale or sale of a generic version of BELVIQ® (lorcaserin hydrochloride tablets, 10 mg). In its notification, Lupin alleged that no valid, enforceable claim of any of the patents that are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, or Orange Book, for BELVIQ® will be infringed by Lupin's manufacture, importation, use, sale or offer for sale of the product described in its ANDA. The lawsuit claims infringement of U.S. Patent Nos. 6,953,787; 7,514,422; 7,977,329; 8,207,158; 8,273,734; 8,546,379; 8,575,149; 8,999,970 and 9,169,213. In accordance with the Hatch-Waxman Act, as a result of filing a patent infringement lawsuit within 45 days of receipt of Lupin's notification, the FDA cannot approve the ANDA any earlier than 7.5 years from NDA approval unless a District Court finds that all of the asserted claims of the patents-in-suit are invalid, unenforceable or not infringed. On January 11, 2017, Lupin filed an answer, defenses and counterclaims to the September 30, 2016 complaint. We and Eisai Inc. filed an answer to Lupin's counterclaims on February 1, 2017. We and Eisai Inc. are seeking a determination from the court that, among other things, Lupin has infringed our patents, Lupin's ANDA should not be approved until the expiration date of our patents, and Lupin should be enjoined from commercializing a product that infringes our patents. Trial is currently scheduled for April 15, 2019. The parties are currently in the fact discovery phase of the case. We cannot predict the ultimate outcome of any proceeding.

On March 6, 2017, we and Eisai Inc. filed a patent infringement lawsuit against Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd. (collectively, Teva) in the U.S. District Court for the District of Delaware. The lawsuit also relates to a "Paragraph IV certification" notification that we and Eisai Inc. received regarding an ANDA submitted to the FDA by Teva requesting approval to engage in the commercial manufacture, use, importation, offer for sale or sale of a generic version of BELVIQ XR® (lorcaserin hydrochloride extended-release tablets, 20 mg). In its notification, Teva alleged that no valid, enforceable claim of any of the patents that are listed in the Orange Book for BELVIQ XR® will be infringed by Teva's manufacture, importation, use, sale or offer for sale of the product described in its ANDA. The lawsuit claims infringement of U.S. Patent Nos. 6,953,787; 7,514,422; 7,977,329; 8,207,158; 8,273,734; 8,546,379; 8,575,149; 8,999,970 and 9,169,213. In accordance with the Hatch-Waxman Act, as a result of filing a patent infringement lawsuit within 45 days of receipt of Teva's notification, the FDA cannot approve the ANDA any earlier than 7.5 years from NDA approval unless a District Court finds that all of the asserted claims of the patents-in-suit are invalid, unenforceable or not infringed. Teva has not yet filed an answer to the March 6, 2017 complaint. We and Eisai Inc. are seeking a determination from the court that, among other things, Teva has infringed our patents, Teva's ANDA should not be approved until the expiration date of our patents, and Teva should be enjoined from commercializing a product that infringes our patents. We cannot predict the ultimate outcome of any proceeding.

Item 4. Mine Safety Disclosures

Not applicable.

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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 listed on the NASDAQ Global Select Market under the symbol "ARNA." The following table sets forth, for the periods indicated, the high and low sale prices for our common stock as reported by the NASDAQ Global Select Market.

	High	Low
Year ended December 31, 2016		
First quarter	$1.97	$1.41
Second quarter	2.15	1.50
Third quarter	1.81	1.48
Fourth quarter	1.86	1.35

	High	Low
Year ended December 31, 2015		
First quarter	$6.28	$3.30
Second quarter	4.79	3.90
Third quarter	5.12	1.86
Fourth quarter	2.68	1.60

Holders

As of March 10, 2017, there were approximately 107 stockholders of record of our common stock, one of which is Cede & Co., a nominee for Depository Trust Company, or DTC. Shares of common stock that are held by financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC, and are considered to be held of record by Cede & Co. as one stockholder.

Dividends

We have never paid cash dividends on our capital stock. We anticipate that we will retain earnings, if any, to support operations and finance the growth and development of our business and, therefore, do not expect to pay cash dividends in the foreseeable future.

Securities authorized for issuance under equity compensation plans

Information on securities authorized for issuance under our equity compensation plans is set forth in Item 12 of Part III of this Annual Report on Form 10-K.

Performance graph

The graph below compares the cumulative five-year total return on our common stock from December 31, 2011, through December 31, 2016, to the cumulative total return over such period for (i) the NASDAQ Composite Index and (ii) the NASDAQ Biotechnology Index. The graph assumes the investment of $100 on December 31, 2011, with the reinvestment of dividends, although dividends have not been declared on our common stock, and is calculated according to the Securities and Exchange Commission's methodology. We caution that the stock price performance shown in the graph may not be indicative of future stock price performance. The graph, including each of the graph lines, was provided by Research Data Group, Inc.

This information, including the graph below, is not deemed to be “soliciting material” or to be “filed” with the Securities and Exchange Commission, or subject to the Securities and Exchange Commission’s proxy rules, other than as provided in such rules, or to the liabilities of Section 18 of the Securities Exchange Act of 1934, and shall not be deemed incorporated by reference into any prior or subsequent filing by us under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent that we specifically incorporate it by reference into any such filing.

Item 6. Selected Financial Data

The following Selected Financial Data should be read in conjunction with “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Item 8. Financial Statements and Supplementary Data” included below in this Annual Report on Form 10-K.

	Years ended December 31,				
	2016	2015	2014	2013	2012
	(In thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenues					
Net product sales	$26,349	$19,726	$15,983	$5,702	$—
Other Eisai collaboration revenue	79,701	9,505	18,611	72,416	23,617
Other collaboration revenue	13,796	4,845	879	586	153
Toll manufacturing	4,129	4,250	1,497	2,690	3,817
Total revenues	123,975	38,326	36,970	81,394	27,587
Operating Costs and Expenses					
Cost of product sales	9,297	8,590	6,369	1,803	—
Cost of toll manufacturing	6,044	4,585	1,390	4,377	3,671
Research and development	66,425	88,411	100,347	66,468	54,112
General and administrative	31,243	35,966	34,137	31,681	26,226
Restructuring charges	6,346	3,972	—	—	—
Impairment of long-lived assets	21,766	—	—	—	—
Amortization of intangibles	—	—	—	—	691
Total operating costs and expenses	141,121	141,524	142,243	104,329	84,700
Interest and other income (expense), net	(5,750)	(4,781)	44,765	3,500	(28,364)
Net loss	(22,896)	(107,979)	(60,508)	(19,435)	(85,477)
Less net loss attributable to noncontrolling interest in consolidated variable interest entity	380	—	—	—	—
Deemed dividends related to beneficial conversion feature of convertible preferred stock	—	—	—	—	(2,824)
Net loss allocable to common stockholders	$(22,516)	$(107,979)	$(60,508)	$(19,435)	$(88,301)
Net loss per share allocable to common stockholders, basic and diluted	$(0.09)	$(0.45)	$(0.28)	$(0.09)	$(0.45)
Shares used in calculating net loss per share allocable to common stockholders, basic and diluted	243,133	240,671	219,734	218,104	196,524

	As of December 31,				
	2016	2015	2014	2013	2012
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$90,712	$156,184	$163,209	$221,878	$156,091

Total assets	169,010	256,792	276,385	339,807	261,206
Total deferred revenues	37,455	109,042	108,302	139,190	62,735
Total lease financing obligations	65,266	68,245	70,737	72,794	74,458
Total derivative liabilities	—	—	474	4,892	15,042
Accumulated deficit	(1,398,736)	(1,376,220)	(1,268,241)	(1,207,733)	(1,188,298)
Total equity	40,395	53,542	47,345	91,857	98,639

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

You should read the following discussion and analysis in conjunction with "Item 8. Financial Statements and Supplementary Data" included below in this Annual Report on Form 10-K, or Annual Report. Operating results are not necessarily indicative of results that may occur in future periods.

This discussion and analysis contains forward-looking statements that involve a number of risks, uncertainties and assumptions. Actual events or results may differ materially from our expectations. Important factors that could cause actual results to differ materially from those stated or implied by our forward-looking statements include, but are not limited to, those set forth in "Item 1A.

Risk Factors" in this Annual Report. All forward-looking statements included in this Annual Report are based on information available to us as of the time we file this Annual Report and, except as required by law, we undertake no obligation to update publicly or revise any forward-looking statements.

OVERVIEW AND RECENT DEVELOPMENTS

We are a biopharmaceutical company focused on developing novel, small molecule drugs with optimized receptor pharmacology designed to deliver broad clinical utility across multiple therapeutic areas. Our proprietary pipeline includes potentially first or best in class programs for which we own global commercial rights.

Our three most advanced investigational clinical programs are etrasimod (formerly APD334) in Phase 2 evaluation for multiple inflammatory indications, ralinepag (formerly APD811) in Phase 2 evaluation for pulmonary arterial hypertension (PAH), and APD371 entering Phase 2 evaluation for the treatment of pain associated with Crohn's disease.

Additionally, we have collaborations with the following pharmaceutical companies: Eisai Inc. and Eisai Co., Ltd. (collectively, Eisai) (commercial stage), Axovant Sciences Ltd., or Axovant, (Phase 2 candidate), and Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, (preclinical candidate).

In 2016, we made significant changes to our operations, including:

- hiring a new chief executive officer, other executive management and new clinical operations team;
- appointment of three new independent directors;
- implementing a reduction in force; and
- restructuring our agreements with Eisai and other distributors relating to lorcaserin.

In May 2016, our Board of Directors appointed Amit Munshi as our President and Chief Executive Officer, and he joined our Board of Directors in June 2016 following our 2016 Annual Stockholders' Meeting. Harry F. Hixson, Jr., Ph.D., who served as our interim Chief Executive Officer from October 2015 to May 2016, continues to serve on our Board of Directors. In June 2016, our Board of Directors appointed Kevin R. Lind as our Executive Vice President and Chief Financial Officer. In August 2016, our Board of Directors appointed Vincent Aurentz as our Executive Vice President and Chief Business Officer.

In February 2017, Arena appointed Jayson Dallas, M.D., Oliver Fetzer, Ph.D., and Garry A. Neil, M.D. as independent directors to the company's Board of Directors.

In the second quarter of 2016, we committed to a reduction of our US workforce of approximately 73%, or approximately 100 employees, which we substantially completed in the third quarter of 2016. As a result of this workforce reduction, we recorded a restructuring charge in the second quarter of 2016 of $6.1 million for termination benefits, including severance and other benefits. Included within this amount is non-cash, share-based compensation expense of $1.0 million related to the accelerated vesting of stock options and the extension of the exercise period of vested options for employees impacted by the workforce reduction.

In the third quarter of 2016, we committed to a reduction of our Switzerland manufacturing workforce of approximately 23%, or approximately 15 employees, which we substantially completed by the end of January 2017. As a result of this workforce reduction, we recorded a restructuring charge in the third quarter of 2016 of $0.2 million for cash termination benefits.

On December 28, 2016, we amended and restated the terms of the marketing and supply agreement for lorcaserin with Eisai by entering into a new Transaction Agreement and a new Supply Agreement (collectively with the Transaction

Agreement, the Eisai Agreement) with Eisai. Under the Eisai Agreement, Eisai acquired global commercialization and manufacturing rights to lorcaserin, including in the territories retained by us under the prior agreement, with control over global development and commercialization decisions. Eisai is responsible for all lorcaserin development expenses going forward. We also assigned to Eisai our rights under the commercial lorcaserin distribution agreements with Ildong Pharmaceutical Co., Ltd., or Ildong, for South Korea; CY Biotech Company Limited, or CYB, for Taiwan; and Teva Pharmaceuticals Ltd.'s Israeli subsidiary, Abic Marketing Limited, or Teva, for Israel.

In general, developing drugs and obtaining marketing approval is a long, uncertain and expensive process, and our ability to execute on our plans and achieve our goals depends on numerous factors, many of which we do not control. To date, we have generated limited revenues. We expect to continue to incur substantial net losses for at least the short term as we advance our clinical development programs, support our collaborators, and manufacture lorcaserin for Eisai.

We plan to raise additional cash from outside sources in order to carry out our operational strategy and advance our clinical pipeline. There is no guarantee that adequate funds will be available when needed from additional debt or equity financing, development and commercialization partnerships or from other sources, or on terms acceptable to us. If our efforts to obtain sufficient additional funds are not successful, we would be required to delay, scale back, or eliminate some or all of our research or development, manufacturing operations, administrative operations, and clinical or regulatory activities, which could negatively affect our ability to achieve certain corporate goals. We believe our cash resources are sufficient to allow us to continue operations for the next twelve months.

Our clinical operations outside of the United States are located in Zug, Switzerland, where we maintain research and development operations for our pipeline programs. We also continue to manufacture for BELVIQ in Zofingen, Switzerland.

See the above “Business” section for a more complete discussion of our business.

RESULTS OF OPERATIONS

We are providing the following summary of our revenues, research and development expenses and general and administrative expenses to supplement the more detailed discussion below. The dollar values in the following tables are in millions.

Revenues

	Years ended December 31,			% change from	% change from
Source of revenue	2016	2015	2014	2015 to 2016	2014 to 2015
Revenue associated with upfront payments from Eisai	$66.0	$7.5	$7.6	*	(1.2)%
Arena’s portion of Eisai net product sales	19.2	14.2	16.0	34.9%	(10.9)%
Milestones earned from Eisai	12.0	0.0	0.5	—%	*
Arena’s portion of Ildong’s net product sales	7.2	5.5	0.0	30.3%	—%
Collaboration agreement with Boehringer Ingelheim	5.1	0.0	0.0	—%	—%
Toll manufacturing agreements	4.1	4.3	1.5	(2.9)%	*
Revenue associated with upfront payment from Ildong	3.9	0.4	0.4	*	—%
Reimbursement of development expenses and patent and trademark expenses from Eisai	1.7	2.0	10.5	(14.1)%	(81.3)%
Milestones earned from Ildong	0.3	3.0	0.0	(89.5)%	—%
Other collaboration agreements	4.5	1.4	0.5	*	*
Total revenues	$124.0	$38.3	$37.0	223.8%	3.7%

*The change is more than 100%.

Research and development expenses

Type of expense	Years ended December 31, 2016	2015	2014	% change from 2015 to 2016	% change from 2014 to 2015
External clinical and preclinical study fees and internal non-commercial manufacturing costs	$31.8	$34.1	$44.6	(6.7)%	(23.6)%
Salary and other personnel costs (excluding non-cash share-based compensation)	17.2	29.1	30.6	(40.9)%	(4.9)%
Facility and equipment costs	8.0	10.0	10.0	(20.6)%	0.1 %
Non-cash share-based compensation	5.6	7.6	7.1	(26.0)%	6.5 %
Research supply costs	2.3	6.2	5.5	(63.1)%	13.7 %
Other	1.5	1.4	2.5	10.3 %	(45.3)%
Total research and development expenses	$66.4	$88.4	$100.3	(24.9)%	(11.9)%

General and administrative expenses

Type of expense	Years ended December 31, 2016	2015	2014	% change from 2015 to 2016	% change from 2014 to 2015
Salary and other personnel costs (excluding non-cash share-based compensation)	$11.4	$14.5	$13.0	(21.5)%	10.9 %
Legal, accounting and other professional fees	9.0	8.0	8.4	13.2 %	(5.3)%
Facility and equipment costs	5.1	5.3	4.2	(5.0)%	25.9 %
Non-cash share-based compensation	4.4	6.7	6.4	(34.1)%	5.0 %
Other	1.3	1.5	2.1	(10.7)%	(27.3)%
Total general and administrative expenses	$31.2	$36.0	$34.1	(13.2)%	5.4 %

YEAR ENDED DECEMBER 31, 2016, COMPARED TO YEAR ENDED DECEMBER 31, 2015

Revenues. We recognized revenues of $124.0 million for the year ended December 31, 2016, compared to $38.3 million for the year ended December 31, 2015. This increase was primarily due to (i) $64.0 million of revenue resulting from the rights delivered by us to Eisai pursuant to the Eisai Agreement entered in December 2016, (ii) a total of $12.3 million of milestones from Eisai and Ildong that we earned during 2016 primarily from the approval of the once-daily formulation of lorcaserin in the United States (branded as BELVIQ XR), the approval of the twice-daily formulation of lorcaserin in Mexico (branded as VENESPRI), and the approval of BELVIQ in Brazil, (iii) an increase of $6.6 million in net product sales of BELVIQ, primarily due to recognition of deferred revenue discussed below, and (iv) $5.1 million earned in the year ended December 31, 2016, under our collaboration agreement with Boehringer Ingelheim, or Boehringer Ingelheim Agreement, which commenced in December 2015. These increases were partially offset by the $3.0 million milestone from Ildong that we earned in February 2015 for the approval of BELVIQ in South Korea.

Prior to the Eisai Agreement, we received from Eisai, Ildong, CYB and Teva total upfront payments of $122.5 million. Revenues from these upfront payments were previously deferred, as we determined that the exclusive rights did not have standalone value without our ongoing development and regulatory activities. Accordingly, these payments were recognized ratably as revenue over the periods in which we expected the services to be rendered. The Eisai Agreement eliminated our obligation to continue performing the development and regulatory activities required in the prior agreements. Therefore, on December 28, 2016, $64.0 million of deferred revenues from these upfront payments was allocated to the rights delivered by us to Eisai pursuant to the Eisai Agreement and recognized as revenue in 2016.

At December 31, 2016, we had a total of $37.5 million in deferred revenues. Under the Eisai Agreement, we have agreed to manufacture and supply, and Eisai has agreed to purchase from us, all of Eisai’s requirements (or specified minimum quantities if such quantities are greater than Eisai’s requirements), subject to certain exceptions, for lorcaserin for development and commercial use for an initial two-year period. The initial period may be extended by Eisai for an additional six months. Eisai will pay us agreed upon prices to deliver finished drug product during this time and also pay us manufacturing support payments. Of the $37.5 million in deferred revenues at December 31, 2016, we expect to recognize $30.8 million as revenue as we manufacture and supply lorcaserin to Eisai over this period. The remaining amount of revenues is primarily attributable to the upfront payments we received under our collaboration agreements with Axovant and Boehringer Ingelheim which we expect to recognize as the services are

performed under these agreements.

We previously deferred recognition of revenue and the related cost at the time we sold BELVIQ to Eisai and Ildong because we did not have the ability to estimate the amount of product that could have been returned to us and thus recognized revenues and the related costs from net product sales when Eisai and Ildong shipped BELVIQ to their distributors. In December 2016, primarily pursuant to a change in the terms of the Eisai Agreement, we determined that we now have the ability to reasonably estimate returns for product sold to Eisai and Ildong. Accordingly, we recognized revenues and the related costs in December 2016 on net product sales which had been previously deferred. The $6.6 million increase in net product sales of BELVIQ for the year ended December 31, 2016, compared to the year ended December 31, 2015, primarily related to (i) the recognition of revenue of $8.7 million which had been previously deferred and (ii) a $2.0 million sales price adjustment from Eisai for sales sold from Eisai to distributors from April 1, 2016, through December 28, 2016, which would have been otherwise due from us to Eisai under the prior agreement but will not be refunded by us to Eisai pursuant to the Eisai Agreement, partially offset by a decrease in the volume of BELVIQ tablets sold to distributors in the United States by Eisai and in South Korea by Ildong.

Absent any new collaborations, we expect our 2017 revenues will primarily consist of (i) product payments for manufacturing and supply of BELVIQ to Eisai, (ii) manufacturing support payments from Eisai (iii) royalty payments from Eisai based upon Eisai’s sales of BELVIQ to its distributors, (iv) toll manufacturing, (v) amortization of the upfront payments we have received from our collaborators and (vi) reimbursements from collaborators for research funding.

Revenues from royalties based on sales of BELVIQ are difficult to predict, and our overall revenues will likely vary from quarter to quarter and year to year. In the short term, we expect the amount of BELVIQ-related revenue we earn to decrease significantly due to the terms of the Eisai Agreement.

Cost of product sales. Cost of product sales consists primarily of direct and indirect costs related to manufacturing BELVIQ, including, among other costs, salaries, share-based compensation and other personnel costs, machinery depreciation costs and amortization expense related to our manufacturing facility production licenses. Cost of products sold increased to $9.3 million for the year ended December 31, 2016, from $8.6 million for the year ended December 31, 2015. This increase was primarily due to costs recognized in December 2016 of $2.6 million on net product sales which had been previously deferred, partially offset by a decrease in the volume of BELVIQ tablets sold to distributors in the United States by Eisai and in South Korea by Ildong.

Cost of toll manufacturing. Cost of toll manufacturing consists of direct and indirect costs associated with manufacturing drug products, primarily for Siegfried AG, or Siegfried, under toll manufacturing agreements, including related salaries, other personnel costs, machinery depreciation costs, amortization expense related to our manufacturing facility production licenses, and material costs. Cost of toll manufacturing increased by $1.4 million to $6.0 million for the year ended December 31, 2016, from $4.6 million for the year ended December 31, 2015, primarily due to increased costs incurred on toll manufacturing performed for Siegfried and from a toll manufacturing agreement that we entered into in April 2015 with a third party.

Research and development expenses. Research and development expenses, which account for the majority of our expenses, consist primarily of salaries and other personnel costs, clinical trial costs (including payments to contract research organizations, or CROs), preclinical study fees, manufacturing costs for non-commercial products, research supply costs and facility and equipment costs. We expense research and development costs as they are incurred when these expenditures have no alternative future uses. We generally do not track our earlier-stage, internal research and development expenses by project; rather, we track such expenses by the type of cost incurred.

Research and development expenses decreased by $22.0 million to $66.4 million for the year ended December 31, 2016, from $88.4 million for the year ended December 31, 2015. This decrease was primarily due to decreases of $11.9 million in salary and other personnel costs, $3.9 million in research supply costs, $2.0 million in non-cash, share-based compensation expense and $2.0 million in facility and equipment costs, primarily due to the recent reduction in the number of our research and development employees. This decrease was also due to a decrease of $2.3 million in external clinical and preclinical study fees and internal non-commercial manufacturing costs.

We expect to incur substantial research and development expenses in 2017 and for the aggregate amount in 2017 to be potentially greater than the amount incurred in 2016. While we expect our internal costs to be lower primarily due to our recent workforce reductions, we expect to incur higher external clinical trial costs. Our actual expenses may be higher or lower than anticipated due to various factors, including our focus, progress and results. For example, patient enrollment in our Phase 2 clinical trials for etrasimod is competitive and challenging and has taken longer than projected. This has resulted in our related external expenses being lower at this point than anticipated.

Included in the $31.8 million of total external clinical and preclinical study fees and internal non-commercial manufacturing costs noted in the table above in this section for the year ended December 31, 2016, were the following:

- $17.6 million related to etrasimod,
- $7.3 million related to lorcaserin and non-commercial manufacturing costs and
- $4.7 million related to ralinepag.

Included in the $34.1 million of total external clinical and preclinical study fees and internal non-commercial manufacturing costs noted in the table above in this section for the year ended December 31, 2015, were the following:

- $16.2 million related to lorcaserin and non-commercial manufacturing costs,
- $8.7 million related to etrasimod and
- $5.1 million related to ralinepag.

Cumulatively through December 31, 2016, we have recognized (i) external clinical and preclinical study fees of $307.7 million for lorcaserin, $43.8 million for nelotanserin, $33.5 million for etrasimod, $21.1 million for ralinepag and $7.5 million for APD371 and (ii) $52.6 million for non-commercial manufacturing and other development costs for lorcaserin and, to a lesser extent, nelotanserin.

While expenditures on current and future clinical development programs are expected to be substantial, they are subject to many uncertainties, including whether we have adequate funds and develop our drug candidates with one or more collaborators or independently. As a result of such uncertainties, we cannot predict with any significant degree of certainty the duration and completion costs of our research and development projects or whether, when and to what extent we will generate revenues from the commercialization and sale of any of our drug candidates. The duration and cost of clinical trials may vary significantly over the life of a project as a result of unanticipated events arising during clinical development and a variety of factors, including:

- the nature and number of trials and studies in a clinical program;
- the potential therapeutic indication;
- the number of patients who participate in the trials;
- the number and location of sites included in the trials;
- the rates of patient recruitment, enrollment and withdrawal;
- the duration of patient treatment and follow-up;
- the costs of manufacturing drug candidates; and
- the costs, requirements, timing of, and the ability to secure regulatory approvals.

General and administrative expenses. General and administrative expenses decreased by $4.8 million to $31.2 million for the year ended December 31, 2016, from $36.0 million for the year ended December 31, 2015. This decrease was primarily due to decreases of $3.1 million in salary and other personnel costs and $2.3 million in non-cash, share-based compensation expense, primarily due to the recent reduction in the number of our employees. This decrease was partially offset by an increase of $1.0 million in legal, accounting and other professional fees. We expect that our 2017 general and administrative expenses will be lower than in 2016, primarily due to the recent workforce reductions and other cost control initiatives.

Restructuring charges. We recognized $6.3 million of restructuring charges for the year ended December 31, 2016, in connection with employee termination costs, including severance and other benefits, related to the reduction of our US workforce to which we committed in June 2016 and the reduction of our manufacturing workforce in Zofingen, Switzerland to which we committed in July 2016. We recognized $4.0 million of restructuring charges for the year ended December 31, 2015, in connection with employee termination costs, including severance and other benefits, related to the workforce reductions to which we committed in the fourth quarter of 2015.

Impairment of long-lived assets. We recognized an impairment loss of $21.8 million for the year ended December 31, 2016. The Eisai Agreement entered on December 28, 2016, results in a significant change in our expected use of our Zofingen facility. We have agreed to manufacture and supply all of Eisai’s requirements (or specified minimum quantities if such quantities are greater than Eisai’s requirements), subject to certain exceptions, for BELVIQ for an initial two-year period. Eisai may extend this initial period for an additional six months upon payment of an exercise fee. Eisai will pay us agreed-upon prices to deliver BELVIQ during this period. Based on our estimate of future cash flows that are directly associated with our Zofingen facility, we determined that long-lived assets with a carrying amount of $32.9 million were no longer recoverable and were in fact impaired and wrote them down to $11.1 million, which was based on the estimated fair value of the Zofingen facility asset group.

Interest and other expense, net. Interest and other expense, net, increased by $1.0 million to $5.8 million for the year ended December 31, 2016, from $4.8 million for the year ended December 31, 2015. This increase was primarily due to (i) $0.9 million in foreign currency transaction gains, net for the year ended December 31, 2016, compared to $2.0 million in foreign currency transaction gains, net for the year ended December 31, 2015, and (ii) a $0.5 million gain from revaluation of our derivative liabilities related to our previously outstanding warrant for the year ended December 31, 2015, with no revaluation recorded for the year ended December 31, 2016, as the warrant expired in August 2015 according to its terms and (iii) a $0.2 million increase in fixed asset disposal losses, net. This increase

was partially offset by an increase of $0.4 million in rental income and a decrease of $0.3 million in interest expense.

YEAR ENDED DECEMBER 31, 2015, COMPARED TO YEAR ENDED DECEMBER 31, 2014

Revenues. We recognized revenues of $38.3 million for the year ended December 31, 2015, compared to $37.0 million for the year ended December 31, 2014. This increase was primarily due to (i) an increase of $3.7 million in net product sales of BELVIQ primarily due to sales of BELVIQ in South Korea commencing in February 2015, partially offset by a decrease in net product sales of BELVIQ in the United States, (ii) the $3.0 million milestone payment from Ildong, that we earned in February 2015 for the approval of BELVIQ in South Korea and (iii) an increase of $2.8 million in toll manufacturing revenue. These increases were partially offset by a decrease in revenues of $8.5 million from Eisai for reimbursements of our development expenses and patent and trademark expenses

primarily due to the completion of our Phase 2 smoking cessation trial in early 2015 and lower costs related to our once-daily formulation studies which were substantially completed in 2014.

Cost of product sales. Cost of products sold increased to $8.6 million for the year ended December 31, 2015, from $6.4 million for the year ended December 31, 2014. This increase was due to sales of BELVIQ commencing in February 2015 and an increase in the volume of BELVIQ tablets sold to distributors in the United States by Eisai, partially offset by a decrease in per tablet manufacturing costs.

Cost of toll manufacturing. Cost of toll manufacturing increased by $3.2 million to $4.6 million for the year ended December 31, 2015, from $1.4 million for the year ended December 31, 2014, primarily due to including costs of materials for drug products in both the sales price and cost of toll manufacturing for products manufactured for Siegfried (prior to 2015 materials for drug products were supplied by Siegfried at no cost to us), and to a lesser extent, from a new toll manufacturing agreement that we entered into with a third party in April 2015.

Research and development expenses. Research and development expenses decreased by $11.9 million to $88.4 million for the year ended December 31, 2015, from $100.3 million for the year ended December 31, 2014. This decrease was primarily due to a decrease of $10.5 million in external clinical and preclinical study fees and internal non-commercial manufacturing costs, primarily a result of completing the Phase 2 clinical trial evaluating lorcaserin for smoking cessation in 2014 and lower internal, non-commercial manufacturing costs related to BELVIQ XR. This decrease was partially offset by increases related to our Phase 2 programs for etrasimod and ralinepag.

Included in the $34.1 million of total external clinical and preclinical study fees and internal non-commercial manufacturing costs noted in the table above in this section for the year ended December 31, 2015, were the following:

- $16.2 million related to lorcaserin and non-commercial manufacturing costs,
- $8.7 million related to etrasimod and
- $5.1 million related to ralinepag.

Included in the $44.6 million of total external clinical and preclinical study fees and internal non-commercial manufacturing costs noted in the table above in this section for the year ended December 31, 2014, were the following:

- $35.3 million related to lorcaserin and non-commercial manufacturing costs,
- $4.2 million related to etrasimod and
- $2.8 million related to ralinepag.

General and administrative expenses. General and administrative expenses increased by $1.9 million to $36.0 million for the year ended December 31, 2015, from $34.1 million for the year ended December 31, 2014. This increase was primarily due to an increase of $1.5 million in salary and other personnel costs, primarily as a result of accrued severance costs following the retirement of our former Chief Executive Officer in October 2015, and an increase of $1.1 million in facility and equipment costs primarily resulting from increased depreciation costs following our 2014 purchase of the remaining portion of our building in Switzerland and increased costs for our enterprise resource planning, or ERP, system. These increases were partially offset by decreases of $0.4 million in legal, accounting and other professional fees and $0.6 million in product liability insurance expense primarily related to a refund we received for a prior year’s premium.

Restructuring charges. We recognized $4.0 million of restructuring charges for the year ended December 31, 2015, in connection with employee termination costs, including severance and other benefits, related to the workforce reductions to which we committed in the fourth quarter of 2015, compared to no restructuring charges for the year ended December 31, 2014.

Interest and other income (expense), net. Interest and other income (expense), net, was an expense of $4.8 million for the year ended December 31, 2015, compared to income of $44.8 million for the year ended December 31, 2014. This change of $49.6 million was primarily due to a gain on sale of available-for-sale securities of $49.6 million realized in the year ended December 31, 2014, related to our sale of shares we held in TaiGen Biopharmaceuticals Holding Limited, or TaiGen, and a $3.9 million decrease in non-cash gain on valuation of derivative liabilities, partially offset by $2.0 million in foreign currency transaction gains, net for the year ended December 31, 2015, compared to $2.2 million in foreign currency transaction losses, net for the year ended December 31, 2014.

LIQUIDITY AND CAPITAL RESOURCES

We have accumulated a large deficit since inception that has primarily resulted from the significant research and development expenditures we have made in seeking to identify and develop compounds that could become marketed drugs. Sales of lorcaserin to date have been less than we and others initially anticipated, and, because lorcaserin is the only approved and marketed drug in which we have a financial interest, our revenue for the near-term is substantially dependent upon the Eisai Agreement and sales of lorcaserin, unless we enter into a new collaboration regarding one of our current internal programs. We expect to continue to incur substantial losses for at least the short term.

To date, we have obtained cash and funded our operations to date primarily through the sale of common and preferred stock, the issuance of debt and related financial instruments, payments from collaborators and customers and sale leaseback transactions. From our inception through December 31, 2016, we have generated $2.0 billion in cash from these sources, of which $1.3 billion was through sales of equity, $513 million was through payments from collaborators and customers, $97 million was through the issuance of debt and related financial instruments and $77 million was from sale and leaseback transactions.

Short term liquidity.

At December 31, 2016, we had $90.7 million in cash and cash equivalents. In January 2017, we entered into an Equity Distribution Agreement, pursuant to which we may sell and issue shares of our common stock having an aggregate offering price of up to $50 million from time to time (the ATM Offering). Sales of the shares under the Equity Distribution Agreement may be made in transactions that are deemed to be “at-the-market” equity offerings as defined in Rule 415 under the Securities Act of 1933, as amended, including sales made by means of ordinary brokers’ transactions, including on the NASDAQ Stock Market. As of March 10, 2017, we sold 2,017,301 shares of our common stock at an average market price of $1.56 per share under the Equity Distribution Agreement, for aggregate gross proceeds of $3.2 million before deducting commissions and other issuance costs. As of March 10, 2017, aggregate gross proceeds of up to $46.8 million remained available to us under the Equity Distribution Agreement.

In addition to payments expected from Eisai for royalties, manufacturing support and purchases of product supply of BELVIQ, other potential sources of liquidity in the short term include (i) milestone and other payments from collaborators, (ii) entering into new collaboration, licensing or commercial agreements for one or more of our drug candidates or programs, (iii) the sale or lease of our facilities or other assets and (iv) sale of equity, issuance of debt or other transactions.

Long term liquidity.

It will require substantial cash to achieve our objectives of discovering, developing and commercializing drugs, and this process typically takes many years and potentially several hundreds of millions of dollars for an individual drug. We may not have adequate available cash, or assets that could be readily turned into cash, to meet these objectives in the long term. We will need to obtain significant funds under our existing collaborations, under new collaboration, licensing or other commercial agreements for one or more of our drug candidates and programs or patent portfolios, or from other potential sources of liquidity, which may include the sale of equity, issuance of debt or other transactions.

In addition to potential payments from our current collaborators, as well as funds from public and private financial markets, potential sources of liquidity in the long term include (i) upfront, milestone, royalty and other payments from any future collaborators or licensees and (ii) revenues from sales of any drugs we obtain regulatory approval to commercialize on our own. The length of time that our current cash and cash equivalents and any available borrowings will sustain our operations will be based on, among other things, the rate of adoption and commercial success of BELVIQ and any other drug we or our collaborators obtain regulatory approval to market, regulatory

decisions affecting our and our collaborator's drug candidates, prioritization decisions regarding funding for our programs, progress in our clinical and earlier-stage programs, the time and costs related to current and future clinical trials and nonclinical studies, our research, development, manufacturing and commercialization costs (including personnel costs), our progress in any programs under collaborations, costs associated with intellectual property, our capital expenditures, and costs associated with securing any in-licensing opportunities. Any significant shortfall in funding may result in us reducing our development and/or research activities, which, in turn, would affect our development pipeline and ability to obtain cash in the future.

We evaluate from time to time potential acquisitions, in-licensing and other opportunities. Any such transaction may impact our liquidity as well as affect our expenses if, for example, our operating expenses increase as a result of such acquisition or license or we use our cash to finance the acquisition or license.

Sources and uses of our cash.

Net cash used in operating activities decreased by $36.0 million to $62.1 million in the year ended December 31, 2016, compared to $98.1 million in the year ended December 31, 2015. This decrease was primarily due to (i) the $10.0 million we received

from Eisai in December 2016 pursuant to entering the Eisai Agreement, (ii) a decrease of $9.6 million in payments made for external clinical and preclinical study fees, (iii) reduced cash expenditures of approximately $9.4 million for personnel costs primarily resulting from the workforce reductions we effected at the end of 2015, in June 2016, and in July 2016, (iv) the $7.5 million payment we received from Boehringer Ingelheim, less $1.2 million of withholding taxes (which was refunded to us in October 2016), in February 2016 upon entering into the Boehringer Ingelheim Agreement, while we did not receive any similar upfront payments in the year ended December 31, 2015, and (v) reduced cash expenditures for research supply costs and facility and equipment costs primarily resulting from the workforce reductions. These decreases in net cash used in operations were partially offset by (i) the $3.0 million milestone payment we received from Ildong, less withholding taxes, in March 2015 for the marketing approval of BELVIQ in South Korea, while we did not receive any similar milestone payment in the year December 31, 2016, and (ii) net payments of $7.6 million we received for shipments of BELVIQ to Eisai and Ildong in the year ended December 31, 2016, compared to $10.4 million in the year ended December 31, 2015.

Net cash used in operating activities was $98.1 million in the year ended December 31, 2015, compared to net cash provided by operating activities of $101.4 million in the year ended December 31, 2014. This decrease was primarily due to (i) net payments of $10.4 million received for shipments of BELVIQ to Eisai and Ildong in the year ended December 31, 2015, compared to $4.8 million in the year ended December 31, 2014, (ii) the $4.0 million upfront payment from Roivant Sciences Ltd., or Roivant, (which subsequently assigned its rights and obligations to Axovant) that we received in May 2015 and (iii) the $3.0 million milestone payment from Ildong that we received, less withholding taxes, in March 2015 for the marketing approval of BELVIQ in South Korea. These decreases in net cash used in operations were partially offset by an increase of $6.1 million in payments made to Eisai related to our share of the cardiovascular outcomes trial, or CVOT, and other development expenses incurred.

Net cash used in investing activities decreased by $7.4 million to $0.8 million in the year ended December 31, 2016, compared to $8.2 million in the year ended December 31, 2015. This decrease was primarily due to $1.0 million in purchases of property and equipment in the year ended December 31, 2016, compared to $11.0 million in the year ended December 31, 2015, partially offset by (i) a $1.3 million decrease in net proceeds from the sale of equipment and (ii) a $0.8 million increase in deposits and restricted cash in the year ended December 31, 2016, compared to a $0.6 million decrease in deposits and restricted cash in the year ended December 31, 2015. Net cash used in investing activities was $8.2 million in the year ended December 31, 2015, compared to net cash provided by investing activities of $40.9 million in the year ended December 31, 2014. This change of $49.1 million was primarily due to (i) proceeds from the sale of available-for-sale securities of $49.6 million received in the year ended December 31, 2014, and (ii) $11.0 million in purchases of property and equipment in the year ended December 31, 2015, compared to $8.9 million in the year ended December 31, 2014, partially offset by net proceeds from our sale of an unoccupied building in San Diego of $2.2 million received in the year ended December 31, 2015.

Net cash of $2.3 million was used in financing activities in the year ended December 31, 2016, as a result of $3.0 million of principal payments on our lease financing obligations, partially offset by net proceeds of $0.4 million from stock option exercises and purchases under our employee stock purchase plan and a $0.3 million security deposit received from a sublessee. Net cash of $101.1 million was provided by financing activities in the year ended December 31, 2015, as a result of net proceeds of $100.7 million from our January 2015 offering of 21,000,000 shares of common stock and net proceeds of $3.0 million from stock option exercises and purchases under our employee stock purchase plan, which were partially offset by $2.5 million for principal payments on our lease financing obligations. Net cash of $3.2 million was provided by financing activities in the year ended December 31, 2014, as a result of net proceeds of $5.2 million from stock option exercises and purchases under our employee stock purchase plan, which were partially offset by $2.1 million for principal payments on our lease financing obligations.

Contractual Obligations

The following table summarizes our contractual obligations at December 31, 2016, in thousands:

	Payments due by period				
Contractual Obligations	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Financing obligations	$92,824	$8,712	$17,784	$16,715	$49,613
Purchase obligations	237	204	33	—	—
Operating leases	11,953	1,259	2,729	2,242	5,723
Total	$105,014	$10,175	$20,546	$18,957	$55,336

Our “financing obligations” relate to sale and leaseback transactions for certain of our properties. We have applied the financing method to these sale and leaseback transactions, which requires that the book value of the properties and related accumulated depreciation remain on our balance sheet with no sale recognized. The sales price of the properties is recorded as a financing obligation and a portion of each lease payment is recorded as interest expense. At December 31, 2016, we expect interest expense over the remaining term of these leases to total $37.5 million. Other of our properties are under operating leases and are included under

“operating leases” above. Our purchase obligations presented above reflect our minimum commitments to purchase goods or services under non-cancelable contracts as of December 31, 2016.

Off-balance sheet arrangements.

We do not have and did not have at December 31, 2016, any off-balance sheet arrangements that have or are reasonably likely to have a current or future material effect on our financial condition, results of operations, liquidity, capital expenditures or capital resources.

COLLABORATIONS

Lorcaserin - Eisai

In July 2010, we granted Eisai exclusive commercialization rights for lorcaserin solely in the United States and its territories and possessions. In May 2012, we and Eisai entered into the first amended and restated agreement, which expanded Eisai’s exclusive commercialization rights to include most of North and South America. In November 2013, we and Eisai entered into the second amended and restated agreement, or Second Amended Agreement, which expanded Eisai’s exclusive commercialization rights for lorcaserin to all of the countries in the world, except for South Korea, Taiwan, Australia, New Zealand and Israel.

On December 28, 2016, we and Eisai amended and restated the terms of the Second Amended Agreement by entering into the Eisai Agreement, which was determined to be a material modification of the Second Amended Agreement. Under the Eisai Agreement, we identified the following significant deliverables to Eisai which each qualify as a separate unit of accounting:

- An exclusive royalty-bearing license or transfer of intellectual property, or License, to commercialize lorcaserin world-wide relating to certain patents, regulatory approvals, samples, records, know-how related to lorcaserin, trademarks and domain names related to the lorcaserin brand names. We also assigned to Eisai our rights under the commercial lorcaserin distribution agreements with Ildong for South Korea, CYB for Taiwan and Teva for Israel. This is collectively referred to as the License Deliverable.
- Bulk inventory and precursor material for manufacturing lorcaserin, or Inventory Deliverable.
- A manufacturing and supply commitment for two years commencing December 28, 2016, or Manufacturing and Supply Commitment Deliverable.

The following table summarizes the revenues we recognized under our collaboration with Eisai for the periods presented, in thousands:

	Years ended December 31,		
	2016	2015	2014
Net product sales	$19,196	$14,236	$15,983
Amortization of upfront payments	66,014	7,541	7,630
Milestone payments	12,000	—	500
Reimbursement of development expenses	1,295	1,538	10,037
Reimbursement of patent and trademark expenses	392	426	444
Subtotal other Eisai collaboration revenue	79,701	9,505	18,611
Total	$98,897	$23,741	$34,594

Royalty payments

Pursuant to the Eisai Agreement, we are eligible to receive royalty payments from Eisai based on the global net sales of lorcaserin. The royalty rates are as follows:

- 9.5% on annual net sales less than or equal to $175.0 million
- 13.5% on annual net sales greater than $175.0 million but less than or equal to $500.0 million
- 18.5% of annual net sales greater than $500.0 million

We did not earn or recognize any revenue from these royalty payments in the year ended December 31, 2016. We expect to record revenues from those royalty payments in the period in which the net sales upon which the royalties are calculated occur as reported to us by Eisai.

Upfront payments

Prior to the Eisai Agreement, we received from Eisai total upfront payments of $115.0 million under prior agreements. Revenues from these upfront payments were previously deferred, as we determined that the exclusive rights did not have standalone value without our ongoing development and regulatory activities. Accordingly, these payments were recognized ratably as revenue over the periods in which we expected the services to be rendered. The Eisai Agreement eliminated our obligation to continue performing the development and regulatory activities required in the Second Amended Agreement. Therefore, on December 28, 2016, $58.5 million of deferred revenues from these upfront payments was allocated to the value of the License provided to Eisai and recognized as revenue in 2016. The remaining portion, $20.9 million, was deferred as of December 31, 2016.

Milestone payments

In July 2016, the US Food and Drug Administration, or FDA, approved the New Drug Application for BELVIQ XR. We earned from Eisai a $10.0 million substantive milestone payment from this achievement. In October 2016, Eisai announced the commercial launch of BELVIQ XR in the United States.

In July 2016, the Federal Commission for the Protection Against Sanitary Risk approved the Marketing Authorization Application in Mexico for our twice-daily formulation of lorcaserin for chronic weight management. The product will be sold under the brand name VENESPRI. We earned from Eisai a $1.0 million substantive milestone payment from this achievement.

In December 2016, the Brazilian Health Surveillance Agency provided regulatory approval in Brazil for BELVIQ. We earned from Eisai a $1.0 million substantive milestone payment from this achievement.

In addition to the $12.0 million in milestones mentioned above and the other $86.5 million in milestones previously achieved since we entered the original agreement in 2010, we are eligible to receive a substantive commercial milestone of $25.0 million upon the achievement of global net sales of lorcaserin for a calendar year first exceeding $250.0 million.

Product purchase price and inventory purchase

We manufacture lorcaserin at our facility in Zofingen, Switzerland. Under the Eisai Agreement, we have agreed to manufacture and supply, and Eisai has agreed to purchase from us, all of Eisai’s requirements (or specified minimum quantities if such quantities are greater than Eisai’s requirements), subject to certain exceptions, for lorcaserin for development and commercial use for an initial two-year period. The initial period may be extended by Eisai for an additional six months upon payment of an extension fee of CHF 2.0 million. Eisai will pay us agreed upon prices to deliver finished drug product during this time. Additionally, Eisai has agreed to pay up to CHF 13.0 million in manufacturing support payments during the initial two-year period supply period, and pay up to CHF 6.0 million in manufacturing support payments during the six-month extension period, if the extension option is exercised by Eisai.

On December 28, 2016, Eisai paid us $10.0 million to acquire our entire inventory of bulk lorcaserin and the precursor materials for manufacturing lorcaserin. This payment was included in the arrangement consideration allocated to the units of accounting under the Eisai Agreement. We expect this inventory will remain at our Zofingen, Switzerland facility for us to use to manufacture finished drug product in order to meet Eisai’s requirements during the initial two-year period and, if applicable, the six-month extension period. The inventory that is not expected to be used to manufacture finished drug product will be physically transferred to Eisai upon the earlier of Eisai’s request to transfer or the end of the manufacturing and supply commitment period.

Under the Second Amended Agreement, we sold lorcaserin to Eisai for Eisai's commercialization in the United States for a purchase price of 31.5% of Eisai's aggregate annual net product sales (which are the gross invoiced sales less certain deductions described in the Second Amended Agreement), or the Product Purchase Price. The amount that Eisai paid us for lorcaserin product supply was based on Eisai's estimated price at the time the order was shipped, which was Eisai's estimate of the Eisai Product Purchase Price, and was subject to change on April 1 and October 1 of each year. The Eisai Product Purchase Price for the product Eisai sold under the Second Amended Agreement was lower than the estimated price that Eisai paid us for such product, primarily due to an increase in deductions from savings cards and returns, partially offset by a decrease in vouchers. At the end of Eisai's fiscal year (March 31), the estimated price paid to us for product that Eisai sold to its distributors was compared to the Eisai Product Purchase Price of such product, and the difference was refunded back to Eisai for the overpayments. The $9.1 million classified as Payable to Eisai on our consolidated balance sheet at December 31, 2016, relates to product sold by Eisai to its distributors from April 1, 2015 through March 31, 2016. Under the Eisai Agreement, we will not refund to Eisai any net overpayment which would have been otherwise due to Eisai under the Second Amended Agreement for product we sold to Eisai under the Second Amended Agreement which Eisai did not sell to its distributors on or before March 31, 2016. For product which Eisai sold to its distributors from April 1, 2016, through December 28, 2016, we recognized the net overpayment which would have been otherwise due to Eisai under the Second Amended Agreement of $2.0 million as revenues and included this amount in net product sales for the year ended December 31, 2016.

We previously deferred recognition of revenue and the related cost at the time we sold lorcaserin to Eisai because we did not have the ability to estimate the amount of product that could have been returned to us and thus recognized revenues and the related costs from net product sales when Eisai shipped BELVIQ to its distributors. Pursuant to a change in the terms of the Eisai Agreement, we determined that we now have the ability to reasonably estimate the amount of returns and thus will now recognize revenue and the related cost from product sales when we ship BELVIQ to Eisai. On December 28, 2016, we recognized revenues of $6.7 million and costs of $1.9 million on net product sales which had been previously deferred.

Development payments

As part of the US approval of BELVIQ, the FDA, is requiring the evaluation of the effect of long-term treatment with BELVIQ on the incidence of major adverse cardiovascular events, or MACE, in overweight and obese patients with cardiovascular disease or multiple cardiovascular risk factors (which is the FDA-required portion of the cardiovascular outcomes trial), as well as the conduct of postmarketing studies to assess the safety and efficacy of BELVIQ for weight management in obese pediatric and adolescent patients. Under the Second Amended Agreement, Eisai and we were responsible for 90% and 10%, respectively, of the cost for the FDA-required portion of the CVOT, 50% and 50%, respectively, of the non-FDA portion of the studies and we were also obligated to share the cost of FDA-required studies in obese pediatric patients and for additional clinical studies in other territories.

Under the Eisai Agreement, Eisai is solely responsible for all costs and expenses in connection with further development of lorcaserin from and after July 1, 2016, and we were relieved of any obligations under the Second Amended Agreement to pay our share of future development costs of lorcaserin. Accordingly, on December 28, 2016, we recorded a reduction of research and development expenses which would have been otherwise due to Eisai under the Second Amended Agreement of $3.7 million for the period from July 1, 2016, through December 28, 2016.

Certain other terms

Eisai and we will each bear 50% of all future expenses and losses arising from any potential product liability claims during a specified period after the date of the Eisai Agreement. Thereafter, we and Eisai will each bear 50% of all expenses and losses arising from any alleged defective manufacturing of lorcaserin by Arena GmbH under the Eisai Agreement, and Eisai will be solely responsible for any expenses and losses associated with other product liability claims.

We may terminate the Transaction Agreement with respect to the United States, the European Union, China and Japan, (collectively, the Major Markets) if Eisai permanently ceases development and commercialization of lorcaserin products in such Major Market, or in its entirety if Eisai permanently ceases development and commercialization of lorcaserin products. We may also terminate the Transaction Agreement if Eisai challenges any patent currently controlled by us related to lorcaserin, if Eisai is debarred under the United States Federal Food, Drug, and Cosmetic Act, or if Eisai is in material breach of the standstill provisions.

Eisai may terminate the Transaction Agreement if, as a result of its change of control, it would be in breach of certain competition restrictions.

In the event the Transaction Agreement is terminated by us due to Eisai’s failure to develop and commercialize lorcaserin products, Eisai’s challenging of any of the licensed patents or Eisai’s debarment or material breach of the standstill provisions, or by Eisai after a change of control that would result in Eisai being in breach of certain competition restrictions, Eisai will grant us an exclusive, royalty-free license to certain patent rights and know-how necessary or useful for the development and commercialization of lorcaserin products, re-assign the assets purchased by Eisai under the Eisai Agreement, and provide certain other transition assistance.

Nelotanserin - Axovant Sciences Ltd.

In May 2015, we entered into the Axovant Agreement. In October 2015, Roivant assigned the exclusive rights to develop and commercialize nelotanserin to its subsidiary, Axovant. Under this agreement, Axovant has exclusive worldwide rights to develop and commercialize nelotanserin, subject to regulatory approval. We also provide certain services and will manufacture and sell nelotanserin to Axovant.

We received an upfront payment of $4.0 million, which was recorded as deferred revenues and is being recognized as revenue ratably over approximately five years, which is the period in which we expect to provide services under the arrangement. We will receive payments from sales of nelotanserin under the Axovant Agreement and are eligible to receive purchase price adjustment payments based on Axovant’s annual net product sales. We are eligible to receive up to an aggregate of $41.5 million in success milestones in case of full development and regulatory success of nelotanserin. Of these payments, two development milestones totaling $4.0 million are substantive and four regulatory milestones totaling $37.5 million are substantive.