INTERCEPT PHARMACEUTICALS INC
Form 10-K
February 29, 2016

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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015

OR

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

For the transition period from to

Commission file number: 001-35668

Intercept Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)	22-3868459 (I.R.S. Employer Identification No.)
450 West 15th Street, Suite 505 New York, NY (Address of Principal Executive Offices)	10011 (Zip Code)

(646) 747-1000

(Registrant s Telephone Number, Including Area Code)

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	**NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: **None**

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

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

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 x No o

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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).Yes x No o

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

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

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

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

The aggregate market value of the registrant s voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold on June 30, 2015 was approximately $3,860,970,135. As of January 31, 2016, there were 24,405,977 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2016 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, poten should, continue, and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;
the timing of and our ability to obtain and maintain regulatory approval of obeticholic acid, or OCA, and any other product candidates we may develop, particularly the possibility that regulatory authorities may require clinical outcomes data (and not just results based on achievement of a surrogate endpoint) as a condition to any marketing approval for OCA, and any related restrictions, limitations and/or warnings in the label of any approved product candidates;

our plans to research, develop and commercialize our product candidates;
our ability to obtain and maintain intellectual property protection for our product candidates;
our ability to successfully commercialize our product candidates;
the size and growth of the markets for our product candidates and our ability to serve those markets;
the rate and degree of market acceptance of any future products, which may be affected by the reimbursement that our products receive from payors;

the success of competing drugs that are or become available;
regulatory developments in the United States and other countries;
the performance of our third-party suppliers and manufacturers;
our collaborators election to pursue research, development and commercialization activities;
our ability to attract collaborators with development, regulatory and commercialization expertise;
our need for and ability to obtain additional financing;
our estimates regarding expenses, future revenues and capital requirements and the accuracy thereof;
our use of cash and short term investments; and
our ability to attract and retain key scientific or management personnel.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Item 1.A. Risk Factors, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

TABLE OF CONTENTS

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

Non-GAAP Financial Measures

This Annual Report on Form 10-K presents projected adjusted operating expense, which is a financial measure not calculated in accordance with U.S. generally accepted accounting principles, or GAAP, and should be considered in addition to, but not as a substitute for, operating expense that we prepare and announce in accordance with GAAP. We exclude certain items from adjusted operating expense, such as stock-based compensation and other non-cash items, that management does not believe affect our basic operations and that do not meet the GAAP definition of unusual or non-recurring items. We anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded in adjusted operating expenses as compared to operating expenses under GAAP. A reconciliation of projected non-GAAP adjusted operating expense to operating expense calculated in accordance with GAAP is not available on a forward-looking basis without unreasonable effort due to an inability to make accurate projections and estimates related to certain information needed to calculate, for example, future stock-based compensation expense. Management also uses adjusted operating expense to establish budgets and operational goals and to manage our company s business. Other companies may define this measure in different ways. We believe this presentation provides investors and management with supplemental information relating to operating performance and trends that facilitate comparisons between periods and with respect to projected information.

TABLE OF CONTENTS

Part I

All brand names or trademarks appearing in this Annual Report on Form 10-K are the property of their respective holders. Unless the context requires otherwise, references in this Annual Report on Form 10-K to Intercept, the Company, we, us, and our refer to Intercept Pharmaceuticals, Inc. and its consolidated subsidiaries.

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat non-viral, progressive liver diseases. Our product candidates have the potential to treat orphan and more prevalent liver diseases for which there currently are limited therapeutic solutions.

Our lead product candidate, obeticholic acid, or OCA, is a bile acid analog, a chemical substance that has a structure based on a naturally occurring human bile acid, that selectively binds to and activates the farnesoid X receptor, or FXR, which we believe has broad liver-protective properties. OCA has been tested in five placebo-controlled clinical trials, including a Phase 3 clinical trial in patients with primary biliary cirrhosis, recently renamed primary biliary cholangitis, or PBC, and two Phase 2 clinical trials in patients with nonalcoholic fatty liver disease, or NAFLD, and nonalcoholic steatohepatitis, or NASH. OCA met the primary efficacy endpoint in each of these trials with statistical significance. In addition, in October 2015, we announced results from a Phase 2 dose ranging trial of OCA in 200 patients with NASH in Japan conducted by our collaborator, Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo Dainippon.

In January 2015, OCA received breakthrough therapy designation from the U.S. Food and Drug Administration, or FDA, for the treatment of NASH patients with liver fibrosis. OCA has also been granted fast track designation by the FDA for the treatment of patients with PBC who have an inadequate response to or are intolerant of ursodiol. OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and primary sclerosing cholangitis, or PSC.

Our most advanced development program for OCA is for PBC as a second line treatment for patients who have an inadequate response to or who are unable to tolerate standard of care therapy and therefore need additional treatment. PBC is a chronic autoimmune liver disease that, if inadequately treated, may eventually lead to cirrhosis, liver failure and death. In March 2014, we completed a Phase 3 clinical trial, known as the POISE trial, in which OCA achieved the primary endpoint for the treatment of PBC. We intend to use these results, along with two previously completed randomized Phase 2 clinical trials of OCA in PBC, as the basis for seeking the first regulatory approvals to market OCA in the United States, Europe, Australia and Canada.

In June 2015, we completed our filings for marketing approval of OCA in PBC in the United States under the FDA s accelerated approval pathway. In August 2015, the FDA accepted for review our New Drug Application, or NDA, and granted Priority Review for OCA for the treatment of PBC. The FDA set a target date of May 29, 2016 to take action under the Prescription Drug User Fee Act, or PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. If we receive marketing approval from the FDA on the PDUFA date, we plan to initiate the commercial launch of OCA in PBC in the United States in June 2016.

In June 2015, we also received notice of the acceptance of the Marketing Authorization Application, or MAA, for

review by the European Medicines Agency, or EMA, for use of OCA in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned commercial launches thereafter in certain European countries. We also plan to apply for marketing approval of OCA in PBC in other markets across the world such as Australia and Canada.

OCA achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health. The FLINT trial was completed in late July 2014. We initiated our Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as the REGENERATE trial, in September 2015. In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients.

TABLE OF CONTENTS

In addition to PBC and NASH, we plan to continue our research on OCA in patient populations suffering from other liver diseases, as we believe that FXR has broad therapeutic potential. In December 2014, we initiated an international Phase 2 clinical trial, known as the AESOP trial, in patients with PSC to evaluate the effects of 24 weeks of treatment with varying doses of OCA compared to placebo. In October 2015, we initiated a Phase 2 clinical trial, known as the CARE trial, of OCA in pediatric patients with biliary atresia. This trial will evaluate the effects of 11 weeks of OCA treatment where patients with biliary atresia will be randomized to varying doses of OCA or a control group receiving only their current treatment. As part of our development program, in November 2015, we initiated a Phase 1 clinical trial of our second product candidate to enter clinical development, called INT-767, a dual FXR and TGR5 agonist, in healthy volunteers. We are currently evaluating our future development strategy for OCA in other indications, for INT-767 and for our pre-clinical candidates. The following chart shows the current stage of development of OCA in different patient populations and the preclinical programs for our other product candidates.

Pipeline Focused on Liver Diseases with Limited/No Approved Therapies

Our current patents for OCA are scheduled to expire at various times through 2033. Our current plan is to commercialize OCA ourselves in the United States and Europe for the treatment of PBC, NASH and other indications primarily by targeting physicians who specialize in the treatment of liver and intestinal diseases, including both hepatologists and gastroenterologists. We own worldwide rights to OCA outside of Japan, China and Korea, where we have exclusively licensed OCA to Sumitomo Dainippon along with an option to exclusively license OCA in certain other Asian countries.

By virtue of our patent portfolio and the proprietary know-how of our employees and our collaborators at the University of Perugia, we believe that we hold a leading position in the fields of bile acid chemistry and therapeutics. Starting with OCA and its underlying patents, which were assigned to us under our agreements with Professor Roberto Pellicciari, Ph.D., one of our co-founders, other researchers and the University of Perugia, our collaboration has resulted in a pipeline of bile acid analogs in addition to OCA, such as INT-767 and INT-777. Through our collaboration with Professor Pellicciari and TES Pharma Srl, we are continuing our research to rationally design compounds that bind selectively and potently to FXR and other bile acid receptors.

TABLE OF CONTENTS

Our Strategy

Our strategy is to develop and commercialize novel therapeutics for patients with non-viral, progressive liver diseases, beginning with OCA for the treatment of PBC, NASH and other follow-on indications that we believe are underserved by existing marketed therapies. The key elements of our strategy are to:

obtain marketing approval of OCA for the treatment of PBC in the United States, Europe and other countries;
commercialize OCA in the United States, Europe and other countries, initially for the treatment of PBC;
continue to develop OCA for the treatment of NASH and seek regulatory approval of OCA in this indication;
continue to develop OCA in other orphan and more prevalent liver diseases; and
advance the development of earlier-stage product candidates in our pipeline.

In order to achieve our strategic objectives, we have, and will remain, focused on hiring and retaining a highly skilled management team and employee base with extensive experience and specific skill sets relating to the selection, development and commercialization of therapies for liver diseases with high unmet medical need. We anticipate that we will continue to increase our product development, scientific, commercial and administrative personnel significantly in the United States and abroad as part of our longer-term growth strategy.

Overview of Liver Function, Bile Acids and Chronic Liver Diseases

The liver performs many functions that are crucial for survival, including the regulation of bile acid metabolism. Bile acids are natural detergent-like emulsifying agents that are released from the gallbladder into the intestine when food is ingested, and are essential for the absorption of dietary cholesterol and other nutrients. Cholesterol bound by bile acids is taken up by the liver, where the cholesterol is then converted into one of two primary bile acids. The bile acids are then actively secreted into bile ducts, which eventually empty into the gallbladder. This digestive cycle of bile flow from gallbladder to intestine to liver and back is called the enterohepatic recirculation of bile.

In addition to facilitating nutrient absorption, bile acids have a much broader role than previously realized in regulating multiple biological functions. They are also complex signaling molecules that integrate metabolic and immune pathways involved in the healthy functioning of various tissues and organs. For example, the actions of bile acids in the liver, intestine and kidney regulate repair mechanisms that modulate inflammation and fibrosis, or scarring, which can lead to progressive organ damage.

The biological effects of bile acids are mediated through dedicated receptors. The best understood is the farnesoid X receptor, a nuclear receptor that regulates bile acid synthesis and clearance from the liver, thereby preventing excessive bile acid build-up in the liver, which may be toxic. As a result, FXR is a target for the treatment of liver diseases such as PBC and PSC that involve impaired bile flow, a condition called cholestasis, in which the liver is exposed to higher than normal levels of bile acids, causing significant damage over time due to the detergent effects of bile acids. In addition, bile acid activation of FXR induces anti-fibrotic, anti-inflammatory, anti-steatotic and other mechanisms that are necessary for the normal regeneration of the liver and may play a role in the treatment of more prevalent liver diseases such as NASH and alcoholic hepatitis. Based on the discovery of similar FXR-mediated protective mechanisms in other organs exposed to bile acids, we believe that FXR may also be a potential target for the treatment of a number of intestinal, kidney and other diseases.

Our Lead Product Candidate: Obeticholic Acid (OCA)

Primary Biliary Cirrhosis (PBC; Renamed Primary Biliary Cholangitis)

Our current clinical focus is on the development of OCA, a novel, orally administered FXR agonist that we believe has broad liver-protective properties and may effectively counter a variety of chronic insults to the liver that cause fibrosis, which can eventually lead to cirrhosis, liver transplant and death. Our first targeted disease is PBC, an orphan indication with a significant unmet medical need.

TABLE OF CONTENTS

PBC is a rare liver disease that primarily results from autoimmune destruction of the bile ducts that transport bile acids out of the liver, resulting in cholestasis. As the disease progresses, persistent toxic build-up of bile acids causes progressive liver damage marked by chronic inflammation and fibrosis. In response to the bile acid mediated toxicity seen in PBC, liver cells release alkaline phosphatase, or ALP, a liver enzyme that is a key biomarker of the disease pathology. Elevated blood levels of ALP are used as the primary means of diagnosis of PBC and are closely monitored in patients as the most important indicator of treatment response and prognosis.

While PBC is rare, it is the most common cholestatic liver disease. An estimated 90% of patients are women, with approximately one in 1,000 women over the age of 40 afflicted by the disease. The mean age of diagnosis is about 40 years and the typical initial presentation occurs between the ages of 30 and 65 years. In the United States, the disease is currently the second leading indication for liver transplant among women. A majority of PBC patients are asymptomatic at the time of initial diagnosis, but most develop symptoms over time. Fatigue and pruritus, or itching, are the most common symptoms in PBC patients. Less common symptoms include dry eyes and mouth, as well as jaundice, which can be seen in more advanced disease. Based on the guidelines of the American Association for the Study of Liver Disease, or AASLD, and the European Association for the Study of the Liver, or EASL, the clinical diagnosis of PBC is established based on the presence of (i) a positive anti-mitochondrial antibody, or AMA, a marker of this autoimmune disease seen in up to 95% of PBC patients, and (ii) elevated serum levels of ALP. In the earlier stages of PBC, ALP is often the only abnormally elevated liver enzyme, rising to between two to ten times higher than normal values. Bilirubin is a marker of liver function and is also monitored in PBC to provide an indication of how well the liver is functioning. Liver biopsy can be used to confirm the diagnosis of PBC, but is not required and is becoming less-frequently performed.

Disease progression in PBC varies significantly, with median survival in untreated patients of 7.5 years if symptomatic at diagnosis and up to 16 years if asymptomatic at diagnosis. PBC patients whose disease is progressing have persistently elevated levels of ALP and other liver enzymes, with abnormal bilirubin levels heralding more advanced disease. Data from published long-term studies demonstrate that a significant portion of such patients with advancing disease progress to liver failure, transplant or death within five to ten years, despite receiving ursodiol, the standard of care therapy.

Currently Available Treatment Options for PBC

The only approved drug for the treatment of PBC is ursodeoxycholic acid, available generically as ursodiol, which is the standard initial course of therapy for all PBC patients. Ursodiol is a naturally occurring bile acid found in small quantities in humans and it is the least detergent of the various types of bile acids that make up the bile pool. In PBC patients, the typical daily dose of ursodiol of approximately one gram represents more than one-fifth of the entire bile pool and, after ongoing therapy, it will comprise at least half of the entire bile pool. It is believed that ursodiol treatment results in the bile pool being less toxic to the liver due to ursodiol s dilution of other more detergent bile acids.

In patients for whom ursodiol is effective, the treatment slows the progression of PBC, reducing the likelihood of liver failure and the need for transplant. As shown in numerous clinical trials of ursodiol treatment, a positive therapeutic response is primarily determined by sustained reduction of ALP levels, along with maintenance of normal bilirubin levels, indicating adequately compensated liver function. This biochemical improvement has been shown to correlate well with improved clinical outcomes such as transplant-free survival.

The outlook and treatment options for end-stage PBC patients who fail to respond to ursodiol are limited. Although other drugs such as colchicine, budesonide, methotrexate and others have been tested as treatments in PBC, none has

been shown to be both effective and safe in altering the course of the disease. While a liver transplant may be curative, many patients fail to receive a donor organ in time, and for those who do receive an organ, there are very significant clinical risks such as infection and organ rejection, as well as significant costs. In addition, the disease recurrence rate is as high as 18% at five years and up to 30% at ten years after liver transplant.

TABLE OF CONTENTS

Our PBC Opportunity

While ursodiol is the established standard of care for PBC, a majority of patients while on therapy remain at ALP levels above the upper limit of normal, or ULN. According to our analysis of industry data in PBC, approximately 70% of patients treated with ursodiol experience elevated ALP levels, with 35% of patients experiencing ALP levels greater than 1.67 times ULN. In addition, a small minority of PBC patients (estimated at approximately 3%) are intolerant to ursodiol therapy. Patients with the greatest elevations in ALP despite therapy and those intolerant to ursodiol represent a significant unmet medical need for second line therapy. Based on our Phase 3 POISE results, which evaluated OCA in these patient groups, we believe represent patients with these characteristics would be eligible for OCA as a novel therapy.

According to our analysis of industry data, there are approximately 290,000 people with PBC in our target markets consisting of the United States, certain European countries, Canada and Australia, of whom we believe approximately 110,000 have been diagnosed and are under the care of a physician for PBC. Although difficult to precisely estimate, based on our analysis of this data, we believe there are approximately 34,000 diagnosed PBC patients who still have an ALP level greater than 1.67 times ULN after treatment on ursodiol who may currently be eligible for treatment with OCA. Of those 34,000 PBC patients, approximately 15,000 are estimated to be in the United States and 19,000 in our target countries outside of the United States. We believe there are an additional 32,000 patients who have an elevated ALP between ULN and 1.67 times ULN in these target countries. Our estimates of the potential market opportunity for OCA for the treatment of PBC include a number of key assumptions related to prevalence rates, patients access to healthcare, diagnosis rates and patients response to or tolerance of OCA, which are based on available literature and epidemiology research in PBC, our industry knowledge gained through market research and other methods, industry publications, third-party research reports and other surveys.

Our Solution: OCA for PBC

Overview

Our lead product candidate, OCA, is a bile acid analog and an FXR agonist derived from the primary human bile acid chenodeoxycholic acid, or CDCA. CDCA, a natural FXR agonist, has historically been used safely as a chronic therapy for cholesterol gallstone disease. OCA has received orphan drug designation in the United States and Europe for the treatment of PBC and PSC. OCA, if approved, would represent the first potent FXR agonist to market for the treatment of PBC, and represents a distinct mechanism of action relative to ursodiol, which has no known FXR effects.

We have completed three double-blind, placebo-controlled trials of OCA in PBC patients, all of which met their primary and secondary endpoints. We believe that the results of our POISE trial of OCA in PBC and our long-term safety extension trials in PBC patients, which include a small group of patients who have been on OCA therapy for more than four years, demonstrate that OCA produces a durable therapeutic response.

We have also completed two randomized, placebo-controlled Phase 2 trials of OCA in PBC patients, one with OCA in combination with ursodiol and one with OCA as monotherapy, and our POISE trial. We intend to use the POISE trial results, along with two previously completed randomized Phase 2 clinical trials of OCA in PBC, as the basis for seeking the first regulatory approvals to market OCA in the United States and Europe.

We own worldwide rights to OCA outside of Japan, China and Korea, where we have exclusively licensed OCA to Sumitomo Dainippon along with an option to exclusively license OCA in certain other Asian countries.

OCA Benefits in PBC

We believe that OCA has the potential to provide the following benefits in the treatment of PBC:

Efficacy. In addition to achieving the primary endpoint in our Phase 2 and Phase 3 trials, 80% of OCA-treated patients across each of our Phase 2 and Phase 3 trials experienced a reduction in ALP levels of at least 10%, which we consider to be a clinically meaningful improvement, as compared to 13% of placebo-treated patients.

TABLE OF CONTENTS

Pharmacological Activity. Unlike ursodiol, which has no FXR-agonist activity, OCA is approximately 100-times more potent than CDCA in activating the FXR receptor. In numerous animal models, sustained FXR activation with OCA treatment has resulted in the prevention, and even reversal, of liver fibrosis. In our clinical trials, patients taking OCA also have experienced significant reductions in common indicators of autoimmune activity such as interleukin 12, or IL-12, tumor necrosis factor alpha, or TNF-a, immunoglobulin M, or IgM, and C-reactive protein, or CRP. We believe that these observations demonstrate potential disease-modifying therapeutic activity directly addressing the underlying autoimmune pathology.

Ease of Use. We anticipate seeking approval of OCA for the treatment of PBC with the administration of a single tablet each day. With proposed tablets containing 5 mg or 10 mg of OCA, any of these doses is a small fraction of the amount of ursodiol that a PBC patient is typically prescribed.

Phase 3 PBC Program for OCA

Completed Phase 3 Trial: OCA as Combination Therapy in PBC Patients (POISE)

In March 2014, we announced that the primary endpoint was achieved in our international POISE trial studying the safety and efficacy of once-daily treatment with OCA in PBC patients with an inadequate therapeutic response to, or who are unable to tolerate, ursodiol. In the trial, 217 patients were randomized to one of three groups: placebo, 10 mg OCA or 5 mg OCA for six months titrated to 10 mg OCA based on clinical response. Except for a small number of patients who were intolerant of ursodiol, the patients in the placebo and OCA dosing groups received standard of care ursodiol treatment throughout the trial.

The POISE data showed that OCA, at both a 10 mg dose and a 5 mg dose titrated to 10 mg, met the trial s primary endpoint of achieving a reduction in serum ALP to below a threshold of 1.67 times ULN, with a minimum of 15% reduction in ALP level from baseline, and a normal bilirubin level after 12 months of therapy. Patients with ALP and bilirubin levels below the thresholds set forth in the POISE trial primary endpoint have been shown in long-term observational meta-analyses to have a significantly lower risk of progressing to liver transplant and death. The percentage of patients meeting the POISE trial primary endpoint was 10% in the placebo group, 47% in the 10 mg OCA group and 46% in the OCA titration group (both dose groups $p < 0.0001$ as compared to placebo) in an intention-to-treat analysis. The placebo group experienced a mean decrease in ALP from baseline of 5%, compared to a significant mean decrease of 39% in the 10 mg OCA dose group and 33% in the OCA titration group (both dose groups $p < 0.0001$ as compared to placebo). OCA treated patients achieved highly statistically significant reductions in ALP beginning as early as two weeks after initiation of treatment, with a peak effect achieved by six months.

POISE Trial: Primary Endpoint

TABLE OF CONTENTS

In addition, both OCA dose groups met pre-specified secondary endpoints of improving other clinically relevant liver enzymes. Reductions in gamma glutamyl transferase, or GGT, of 64% in the 10 mg OCA dose group and 50% in the OCA titration group, alanine transaminase, or ALT, of 42% in the 10 mg OCA dose group and 36% in the OCA titration group, and aspartate transaminase, or AST, of 24% in the 10 mg OCA dose group and 22% in the OCA titration group, were observed, respectively (both OCA dose groups $p < 0.0005$ as compared to placebo). PBC patients typically have dyslipidemia with unique features, characterized by significantly elevated levels of high-density lipoprotein cholesterol, or HDL-C, and modestly or significantly elevated levels of low-density lipoprotein cholesterol, or LDL-C. OCA treatment led to a rapid and sustained dose-dependent decrease in HDL-C levels, similar to those seen in the prior PBC clinical trials, with most patients experiencing HDL-C within normal levels. No meaningful sustained changes in LDL-C were observed in this setting.

Pruritus, generally mild to moderate, was the most frequently reported adverse event associated with OCA treatment and was observed in 38% of patients on placebo, 70% of patients in the 10 mg OCA group and 56% of patients in the OCA titration group. Eight patients discontinued due to pruritus, of whom none were in the placebo group, seven (10%) patients were in the 10 mg OCA group and one (1%) patient was in the OCA titration group. Pruritus has also been observed in other clinical trials of OCA. As shown in the graph below, patient-reported pruritus severity, as measured by the visual analog score, or VAS, was not different between OCA and placebo groups at the end of the study. A majority of the pruritus events were found to be transient in nature, starting within the first month of dosing and decreasing in severity over time with continued treatment.

POISE Trial: Pruritus Scores

Apart from pruritus, the incidence of adverse events was generally similar across both OCA and placebo groups (placebo: 90%, OCA 10 mg: 86%, OCA titration: 89%). Overall, serious adverse events, or SAEs, occurred in 22 (10%) of the patients and, although there were more SAEs in the OCA treatment groups, none were considered drug-related and there were no apparent patterns in the SAEs.

TABLE OF CONTENTS

Ongoing Open-Label Long-Term Safety Extension of the POISE Trial

Following the completion of the double-blind portion of the POISE trial described above, patients were given the option to enroll in an open-label long-term safety and efficacy extension trial, or the POISE LTSE. The POISE LTSE is currently ongoing. Patients continue to receive open-label OCA in this phase, and have been increased from a starting dose of 5 mg to as high as 25 mg, as clinically indicated. Of the 198 patients who completed the double-blind phase of the POISE trial, more than 95% continued in the LTSE phase of the trial.

Regulatory Pathway

OCA was granted Fast Track designation by FDA in May 2014 for the treatment of patients with PBC who have an inadequate response to or are intolerant of ursodiol. The Fast Track process allows a company to submit individual sections of its NDA for review by the FDA on a rolling basis as they are completed. In June 2015, we completed our filings for marketing approval of OCA in PBC in the United States under the FDA s accelerated approval pathway. In August 2015, the FDA accepted for review our NDA and granted Priority Review for OCA for the treatment of PBC. The FDA set a target date of May 29, 2016 to take action under PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. If we receive marketing approval from the FDA on the PDUFA date, we plan to initiate the commercial launch of OCA in PBC in the United States in June 2016.

In June 2015, we also received notice of the acceptance of the MAA for review by the EMA for use of OCA in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned commercial launches thereafter in certain European countries. We also plan to apply for marketing approval of OCA in PBC in other markets across the world such as Australia and Canada.

A number of published clinical studies have demonstrated that lower levels of ALP, both independently or in conjunction with normal bilirubin levels, correlate with a significant reduction in adverse clinical outcomes such as liver transplant and death. We believe that one of the key factors in the FDA s and EMA s potential acceptance of our POISE trial primary endpoint as a basis for accelerated approval will be the result of meta-analyses of PBC clinical outcomes data of more than 6,000 PBC patients from 15 academic centers in eight countries that have been compiled by the Global PBC Study Group, which we sponsored, as well as a dataset of over 6,000 PBC patients across the United Kingdom compiled by the UK PBC Group. These represent the largest prospective PBC clinical datasets assembled to analyze the correlation of biochemical therapeutic response with clinical outcomes in PBC patients.

In the largest meta-analysis of individual PBC patient data conducted to date, published in the December 2014 issue of *Gastroenterology*, the Global PBC Study Group researchers confirmed that levels of ALP and bilirubin correlated with clinical outcomes of patients with PBC. Of the 4,845 patients included in the analysis, 1,118 reached a clinical outcome defined as liver transplantation or death. The researchers reported an association between ALP values and liver transplant-free survival, with higher ALP values associated with worse prognosis. At one year after study enrollment, an ALP level of two times ULN best predicted patient outcome but not significantly better than other lower ALP thresholds such as 1.67 times ULN. Among patients with ALP levels less than or equal to two times ULN, 84% survived for at least a ten year follow-up period compared with 62% of those with levels exceeding two times ULN ($p < 0.0001$). Elevated bilirubin levels were strongly correlated with worse prognosis and only 41% of such patients had not had a liver transplant or died over the subsequent 10 years compared with 86% of patients with normal bilirubin levels ($p < 0.0001$). We believe that these results, along with the published results of the UK PBC Group, show that the achievement of an ALP level of less than 1.67 times ULN, together with a normal bilirubin level, correlates with a highly statistically significant reduction of risk and adverse clinical outcomes such as liver transplant and death in PBC patients.

TABLE OF CONTENTS

Ongoing Confirmatory Clinical Outcomes Trial: The COBALT Trial

As part of our strategy for filing the NDA for OCA under the accelerated approval pathway, in December 2014 we initiated our COBALT confirmatory clinical outcomes trial in PBC, as required under FDA guidelines for accelerated approval, with detailed input on the trial design from both FDA and EMA. The goal of the trial is to confirm that reduction of ALP with OCA treatment is associated with a longer term benefit on liver-related clinical outcomes. This trial is currently enrolling patients and is expected to be completed on a post-marketing basis.

COBALT is designed to assess the effect of a once-daily dose of 5 mg or 10 mg of OCA in approximately 350 PBC patients with an inadequate therapeutic response to ursodiol or who are unable to tolerate ursodiol. In this trial, eligible patients with PBC continue their ursodiol treatment, except for those patients unable to tolerate ursodiol, and are being randomized into one of two arms of approximately 175 patients each. Patients receive, in addition to ursodiol, either placebo or 5 mg of OCA increasing over the course of the trial to 10 mg of OCA based on tolerability. The primary endpoint of the trial is based on clinical outcomes as measured by time to first occurrence of any of the following adjudicated events: death (all-cause), liver transplant, Model of End stage Liver Disease, or MELD, score greater than 15, hospitalization due to variceal bleeding, encephalopathy or spontaneous bacterial peritonitis, uncontrolled ascites or hepatocellular carcinoma.

Nonalcoholic Steatohepatitis (NASH)

NASH is a common and serious chronic liver disease caused by excessive fat accumulation in the liver, or steatosis, that induces inflammation and may lead to progressive fibrosis and cirrhosis, followed by eventual liver failure and death. In NASH patients, for reasons that are as yet not completely understood, steatosis and other factors such as insulin resistance induce chronic inflammation in the liver and may lead to progressive fibrosis and cirrhosis, followed by eventual liver failure and death.

NASH is a more serious form of NAFLD. Although difficult to precisely estimate, we believe that roughly one quarter of the total U.S. population and roughly 20% of the total population in France, Germany, Italy, Spain and the United Kingdom, or the EU5 countries, has NAFLD. Of the NASH population in both the United States and the EU5 countries, more than 15% of patients are believed to have fibrosis of stage 2 or greater. We believe that similar prevalence will be found in other European countries, Japan and other developed countries. Additionally, NASH has become a highly prevalent liver disease in developing countries such as India and China. Although the prevalence of NASH is lower in children, it has also become a serious disease burden in the pediatric population. There are currently no drugs approved for the treatment of NASH.

Other common co-existing conditions such as obesity and type 2 diabetes, which are present in the majority of all NASH patients, are important risk factors. NASH has been linked in both developed and developing countries to the adoption of a Western diet, with increased consumption of processed foods containing polyunsaturated fatty acids and fructose. More than 20% of NASH patients progress to cirrhosis within a decade of diagnosis. Owing to the rapidly increasing prevalence of the disease, NASH has become the second most common reason for liver transplant in the United States and is projected to become the leading indication for transplant in the next few years, overtaking both chronic hepatitis C infection and alcoholic liver disease. NASH patients have a ten-fold greater risk of liver-related mortality as compared to the general population and a six-fold greater risk of liver-related mortality as compared to patients with less severe NAFLD. The presence of type 2 diabetes in the broader NAFLD population is associated with a much greater mortality risk, with a 23-fold higher rate of liver-related mortality as compared to non-diabetic NAFLD patients. Additionally, NASH is now considered to be the leading, and a rapidly increasing, cause of hepatocellular carcinoma, or primary liver cancer, of which up to 40% of cases in NASH patients develop prior to

developing cirrhosis.

TABLE OF CONTENTS

Currently, a definitive diagnosis of NASH is based on a histologic assessment of a liver biopsy for several key features associated with NASH, including, but not limited to, steatosis, lobular inflammation and hepatocyte ballooning. However, non-invasive methods of diagnosis are being explored, including transient elastography (an ultrasound technology approved in Europe and more recently in the United States for the measurement of liver fibrosis), magnetic resonance imaging and serum biomarkers. NASH diagnosis rates in the United States and the EU5 countries are very low, driven by a lack of approved treatment options and a lack of non-invasive diagnosis options. We believe the availability of novel therapeutics and non-invasive technologies will be critical to increase diagnosis rates.

Currently Available Treatment Options for NASH

There are currently no drugs approved for the treatment of NAFLD or NASH. However, various therapeutics are used off-label for the treatment of NASH, such as vitamin E (an antioxidant), insulin sensitizers (e.g., metformin), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol. Lifestyle changes, including modification of diet and exercise to reduce body weight, as well as treatment of concomitant diabetes and dyslipidemia, are commonly accepted as the standard of care, but have not conclusively been shown to prevent disease progression.

NASH Unmet Medical Need

Although some of the off-label treatments described above have been studied as possible treatments for NASH, none has been approved by the FDA or EMA as a treatment for this disease. Currently, the outlook and treatment options for end-stage NASH patients are limited. Although liver transplant can be curative, many patients fail to receive a donor organ in time, and for those who do, there are very significant clinical risks, such as infection and organ rejection, as well as significant costs. In addition, the post-transplant recurrence rate of NASH has been shown to be as high as 25% at 18 months. Given the lack of available treatment options, we believe that there is a significant unmet need for a novel therapy for NASH, particularly in those patients with advanced fibrosis and cirrhosis and those with a high risk of disease progression due to other co-morbidities such as type 2 diabetes.

Our Solution: OCA for NASH

OCA s Potential Benefits in NASH

FXR activation has been shown to play a key role in the regulation of the metabolic pathways relevant to NASH, highlighting FXR as a potential drug target for treatment of the disease. Given the significant unmet medical need of patients with NASH, we believe that the potent ability of OCA to activate FXR could result in a major clinical benefit through potential amelioration or reversal of liver fibrosis, inflammation, steatosis, and insulin resistance. We believe that OCA has the potential to provide the following benefits in the treatment of NASH:

Pharmacological Activity. In addition to achieving the primary endpoint in the Phase 2b FLINT trial in NASH patients, a significantly greater number of OCA-treated patients achieved an improvement of at least one fibrosis stage (35% vs 19%, p = 0.004), with OCA showing greater response rates as compared to placebo across all stages of fibrosis. In animal models, sustained FXR activation with OCA treatment has resulted in the reversal of liver fibrosis, the reversal of portal hypertension, the prevention of atherosclerosis, and improvements in triglycerides, inflammation, steatosis and insulin sensitivity. Mice that lack functional FXR (so-called knockout mice) spontaneously develop NASH accompanied by hypertriglyceridemia and insulin resistance, and go on to develop hepatocellular carcinoma, or primary liver cancer. We believe that the combined mechanisms of FXR activation, coupled with the occurrence of NASH in animals lacking FXR, support the potential disease-modifying therapeutic

potential of OCA in directly addressing the underlying disease pathology in NASH.

Ease of Use. We anticipate seeking approval of OCA for the treatment of NASH at a single daily dose.

TABLE OF CONTENTS

Phase 2 NASH Program for OCA

Phase 2 Trial: OCA as Therapy in Type 2 Diabetic Patients with NAFLD

We previously completed a double-blind, placebo-controlled Phase 2 clinical trial of OCA in 64 type 2 diabetic patients with NAFLD. We believe that a majority of the patients in this trial were likely to have had NASH and, not simple steatosis, given the disease s association with obesity and diabetes and based upon an evaluation of serum fibrosis biomarkers from trial participants. In this trial, OCA therapy significantly improved insulin sensitivity both in the liver and peripheral tissues, thereby meeting the primary endpoint in the trial with a mean improvement in liver insulin sensitization from baseline of approximately 24.5% in the combined OCA dose groups, as compared to a worsening of approximately 5.5% in the placebo group ($p = 0.011$). Insulin resistance, particularly in the liver, is considered to be an important contributor to NASH disease pathology. In this trial, significant improvements in weight loss were also noted in patients receiving OCA therapy, along with improvements in liver enzymes such as GGT and AST.

OCA was generally well-tolerated by the trial patients, with side effects in the treatment groups not meaningfully different than those reported on placebo (apart from mild constipation in the 50 mg group). Consistent with anticipated FXR-related lipid metabolic effects starting with the clearance of excess lipid load from the liver, there were changes in mean serum lipid profiles observed in the OCA treatment groups compared with the placebo group that included decreased concentrations of triglycerides, increased concentrations of LDL-C and slightly decreased concentrations of HDL-C from baseline. In our publication of the results, we observed that once-daily treatment for six weeks at the 25 mg OCA dose, which we subsequently selected to advance in our NASH development program, led to an approximately 12% decrease in mean triglycerides to 170 mg/dL from a baseline mean level of 193 mg/dL, an approximately 22% increase in mean LDL cholesterol to 120 mg/dL from a baseline mean level of 98 mg/dL, and an approximately 5% decrease in mean HDL cholesterol to 35 mg/dL from a baseline mean level of 37 mg/dL.

Phase 2b FLINT Trial for NASH

OCA achieved the primary endpoint in the Phase 2b trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the NIDDK, a part of the National Institutes of Health. A significantly greater number of OCA-treated patients also achieved an improvement of at least one fibrosis stage (35% vs 19%, $p = 0.004$), with OCA showing greater response rates as compared to placebo across all stages of fibrosis. After FLINT was completed in late July 2014, we disclosed top-line results in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 and the results were subsequently published online in the *Lancet* in November 2014. The summary of the FLINT trial results described below are based on information and data provided to us by the NIDDK. This trial was a double-blind, placebo-controlled trial of a once-daily dose of 25 mg of OCA or placebo given for 72 weeks in 283 patients with biopsy-proven NASH.

a. Primary Endpoint

The percentage of patients meeting the FLINT primary histological endpoint, defined as a decrease in the NAFLD Activity Score, or NAS, of at least two points with no increase in the fibrosis score following 72 weeks of treatment, was 45% in the OCA treatment group and 21% in the placebo group ($p = 0.0002$, $n = 219$). The mean pre-treatment baseline NAS for patients in the OCA treatment group was 5.3 of a total possible score of eight (comprised of hepatocellular ballooning 0 2, lobular inflammation 0 3 and steatosis 0 3). Subgroup analyses showed significant response rates in the OCA treatment group in patients with risk factors for disease progression, including baseline fibrosis stage, co-morbid type 2 diabetes mellitus, ALT, insulin resistance and severe obesity (each factor $p < 0.05$ for

OCA compared to placebo based on 95% confidence interval of published odds ratios). The graph below shows the results of the primary endpoint in the FLINT trial and the improvements in NAS for various subgroups published in the *Lancet*.

a. Primary Endpoint

TABLE OF CONTENTS

Primary Endpoint: Improvement in NAS by Two Points with no Worsening of Fibrosis

** p < 0.05, *** p < 0.001. P-values calculated with the Cochran-Mantel-Haenszel test, stratified by clinic and diabetes status.*

b. Secondary Efficacy Endpoint: Fibrosis Improvement

A significantly greater number of OCA-treated patients also achieved an improvement of at least one fibrosis stage (35% versus 19%, p = 0.004). Based on our retrospective analyses of the FLINT data, more OCA-treated patients exhibited fibrosis improvement of at least two fibrosis stages (15% versus 6%, not significant) and exhibited fibrosis improvements regardless of baseline fibrosis stage and a significantly greater number of OCA-treated patients also achieved complete resolution of fibrosis (17% versus 5%, p = 0.0018). Also, our retrospective analysis of the FLINT data showed that fewer OCA-treated patients progressed to bridging fibrosis (15% versus 18%, not significant) or to cirrhosis (2% versus 5%, not significant). The NASH clinical research network fibrosis staging system was used to categorize the pattern of fibrosis and architectural remodeling of the liver: no fibrosis (F0), perisinusoidal or periportal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis (F3) and cirrhosis (F4). Fibrosis sub-stages 1a, 1b and 1c were considered F1 for the analysis.

c. Secondary Efficacy Endpoint: NASH Resolution

The secondary endpoint of NASH resolution, based on a global histological assessment, also showed improvement, although not statistically significant (22% versus 13%, p = 0.0832, not significant). A central reading of all baseline and end-of-trial biopsies was performed at the end of the trial, based on which only 80% of patients were confirmed to have definite NASH, while the remaining 20% were diagnosed as borderline NASH (10%) or not-NASH (10%). A retrospective subgroup analysis on the completer population comprised only of definite NASH patients at baseline showed that a significantly greater number of OCA-treated patients achieved NASH resolution compared with placebo-treated patients (19% versus 8%; p = 0.0278).

The graph below shows these results from the FLINT trial for fibrosis improvement, fibrosis resolution, fibrosis progression and NASH resolution.

TABLE OF CONTENTS

FLINT Trial: Improvement in Histological Endpoints

**p < 0.05, **p < 0.01. P-values calculated with the Cochran-Mantel-Haenszel test, stratified by clinic and diabetes status. NS indicates that the results are not significant.*

Retrospective analyses after the unblinding of results can potentially introduce bias and regulatory authorities typically give greatest weight to results from pre-specified analyses as compared to retrospective analyses.

d. Additional Secondary Endpoints

More OCA-treated patients experienced significant improvements in the major histological features of NASH, including steatosis (61% versus 38%, p = 0.001), lobular inflammation (53% versus 35%, p = 0.006) and hepatocellular ballooning (46% versus 31%, p = 0.03), as compared to the placebo treatment group. Trends were similar between the two treatment groups for portal inflammation, which is not a component of the NAS and is typically mild in adult NASH patients.

The histological improvements observed in OCA-treated patients versus placebo were accompanied by significant reductions in relevant biochemical parameters, including the serum liver enzymes ALT (p < 0.0001), AST (p = 0.0001) and GGT (p < 0.0001), each of which were above generally accepted normal limits at baseline, and total bilirubin (p = 0.002). A modest but statistically significant increase in ALP (p < 0.0001) in the OCA treatment group was also observed, but levels remained within typical normal limits.

OCA treatment was associated with serum lipid changes, including average increases in total cholesterol and LDL-C and an average decrease in HDL-C, that developed within 12 weeks of treatment initiation, then began reversing through the end of treatment and returned to baseline during the 24-week post-treatment follow-up phase. Based on these observations, lipid management was emphasized partway into the trial, using generally accepted guidelines. At 72 weeks as compared to baseline, the following effects were observed in the OCA treatment group: an increase in mean total cholesterol (0.16 mmol/L or 6 mg/dL increase OCA versus 0.19 mmol/L or 7mg/dL decrease placebo, p < 0.0009), an increase in mean LDL-C (0.22 mmol/L or 9 mg/dL increase OCA versus 0.22 mmol/L or 8 mg/dL decrease placebo, p < 0.0001), a decrease in mean HDL-C (0.02 mmol/L or 1 mg/dL decrease OCA versus 0.03 mmol/L or 1 mg/dL increase placebo, p = 0.01)

TABLE OF CONTENTS

and a decrease in triglycerides (0.22 mmol/L or 20 mg/dL decrease OCA versus 0.08 mmol/L or 7 mg/dL decrease placebo, p = 0.88, not significant).

A post-hoc analysis showed OCA-treated patients who initiated statins during the FLINT trial (n=26) experienced a rapid reversal of their observed mean LDL-C increase to below baseline levels, with a mean decrease after 72 weeks of treatment of -18.9 mg/dL. In contrast, other OCA-treated patients with no reported initiation or change in statin therapy experienced an increase in LDL-C that peaked at week 12 and was sustained over the 72 week treatment period. Patients treated with statins at baseline who maintained statin treatment over the duration of the study (n=50) experienced a mean LDL-C increase of 8.7 mg/dL at 72 weeks. Patients not treated with statins during the study (n=65) experienced a mean LDL-C increase of 16.0 mg/dL. Treatment related LDL-C increases in all groups reversed with treatment discontinuation. This analysis suggests that the OCA-associated LDL-C increase reaches a maximum peak and plateaus soon after initiation of therapy and that concomitant statin use in NASH patients receiving OCA may mitigate treatment-related LDL-C increases.

In the FLINT trial, statistically significant weight loss of an average of 2.3 kilograms was observed in OCA patients compared to no weight loss in the placebo group (p = 0.008), and this weight loss reverted towards baseline during the 24-week follow-up phase. A pre-specified sensitivity analysis conducted by the investigators showed that weight loss was not a driver of the primary endpoint. An increase in a marker of hepatic insulin resistance known as HOMA-IR (calculated using the product of fasting plasma insulin and glucose) was observed at 72 weeks in the OCA treatment group (p = 0.01). However, there was an imbalance in baseline plasma insulin levels (201 pmol/L OCA versus 138 pmol/L placebo), and an even larger relative and absolute increase in HOMA-IR was observed in the placebo group at the conclusion of the 24-week follow-up phase. This is potentially attributable to the inherent variability in HOMA-IR measurements, particularly in patients with type 2 diabetes, that have been shown to make single time-point to time-point changes of this magnitude clinically uninterpretable. There were virtually no changes in mean hemoglobin A1c, a measure of average blood sugar control over a period of approximately three months, in either OCA or placebo groups at 72 weeks. In a previous study of OCA in diabetic NAFLD patients, described in more detail above, employing the hyperinsulinemic-euglycemic insulin clamp, the gold standard for detecting changes in insulin resistance, OCA improved the glucose disposal rate consistent with reduced insulin resistance.

e. Safety and Tolerability

OCA was generally well tolerated in the FLINT trial. Adverse events were generally mild to moderate in severity and the incidence in the OCA and placebo treatment groups was similar for all symptoms except pruritus. Pruritus in the OCA treatment group occurred more frequently (23% versus 6%, p < 0.0001), at a higher grade (predominantly moderate pruritus) but resulted in only one patient discontinuation. The incidence of severe or life threatening events was not different between the two treatment groups and most of the events in both groups were deemed to be unrelated to treatment, including all severe or life threatening cardiovascular events. As previously disclosed, two deaths occurred in the OCA treatment group, but neither was considered related to OCA treatment.

Phase 2 Sumitomo Dainippon Trial for NASH

In October 2015, we announced the results of a 72-week Phase 2 dose ranging trial of OCA in 200 adult patients with NASH in Japan. The trial was conducted by our collaborator, Sumitomo Dainippon. In this trial, 202 Japanese biopsy-proven NASH patients (NAS of 5-8) were randomized into one of four arms to receive either a 10 mg, 20 mg or 40 mg dose of OCA, or placebo, and 200 of these patients 50 per group initiated treatment for a 72-week double-blind treatment phase, followed by a 24-week off treatment phase. The primary endpoint was histologic improvement defined as at least a two point improvement in NAS with no worsening of fibrosis.

The primary efficacy analysis was conducted on an intention to treat, or ITT, basis, testing the dose dependent effects of once daily OCA (10 mg, 20 mg and 40 mg) versus placebo on the primary endpoint. The ITT analysis included all randomized patients who received treatment (50 per group), and patients who discontinued or did not have a repeat biopsy were treated as non-responders. A pre-specified completer analysis was conducted on the patients who had biopsies at both baseline and 72 weeks (45, 44, 44 and 37 patients in the placebo, 10 mg, 20 mg and 40 mg OCA groups, respectively).

TABLE OF CONTENTS

This trial did not meet its primary endpoint with statistical significance. The ITT results in the table below show a dose dependent increase in the percentage of OCA treated patients compared to placebo who achieved the primary endpoint (p=0.053, not significant). The 40 mg OCA dose group achieved statistical significance on the primary endpoint compared to placebo (p=0.0496). Dose-dependent trends not reaching statistical significance were also observed for several other pre-specified histologic endpoints, including the percentage of patients with steatosis and inflammation improvement, ballooning resolution and NASH resolution. No difference was seen in fibrosis improvement in the OCA groups compared to placebo.

ITT Results	Placebo N=50	10 mg N=50	20 mg N=50	40 mg N=50	
NAS improvement ≥ 2 points with no worsening of fibrosis	10 (20%)	11 (22%) p=0.8070**	14 (28%) p=0.3378**	19 (38%) p=0.0496**	p=0.053*

* Primary efficacy analysis is a stratified Cochran-Armitage test with multiple contrast coefficients. Statistical significance is based on a p-value < 0.05.

** The secondary efficacy analysis is a CMH (Cochran-Mantel-Haenszel) test stratified by baseline fibrosis stage for pairwise comparison of each OCA group compared to the placebo group. The multiplicity was not adjusted.

In the completer analysis, similar dose dependent effects were observed, with 51% of patients in the 40 mg dose group compared to 22% in the placebo group meeting the primary endpoint (p=0.0061).

With the exception of dose dependent pruritus, OCA appeared to be generally safe and well tolerated. The number of pruritus associated discontinuations were 0, 0, 2 and 5 patients in the placebo, 10 mg, 20 mg and 40 mg OCA groups, respectively. Changes in lipid parameters, including LDL-C, HDL-C and triglycerides, appeared to be consistent with previously reported lipid changes in Western NASH patients. No other meaningful differences in the rate of adverse events between the OCA and placebo groups were noted.

We have been informed by Sumitomo Dainippon that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan.

REGENERATE: Phase 3 Trial in NASH with Advanced Liver Fibrosis

In September 2015, we initiated the previously announced international Phase 3 trial of OCA in patients with non-cirrhotic NASH with advanced liver fibrosis, known as the REGENERATE trial, which is currently enrolling patients. The REGENERATE trial was designed following discussions with the FDA and EMA. The study population is expected to primarily be comprised of Western NASH patients with histologic evidence of stage 2 or stage 3 liver fibrosis. In addition, the trial will include an exploratory cohort of NASH patients with histologic evidence of early stage 1 liver fibrosis and concomitant diabetes, obesity or elevated ALT, who are at increased risk of progression to cirrhosis. These patients with early stage 1 liver fibrosis will not be included in the primary endpoint analysis.

REGENERATE is designed as a double-blind, placebo-controlled Phase 3 clinical trial and is expected to enroll approximately 2,000 NASH patients at up to 300 qualified centers worldwide and assess the potential benefits of OCA treatment on liver-related and other clinical outcomes. Patients are being randomized into one of three groups receiving a once-daily dose of placebo, 10 mg OCA or 25 mg OCA. The trial will include a pre-planned interim histology analysis after 72 weeks of treatment in 1,400 patients, which if successful is intended to serve as the basis for seeking initial U.S. and international marketing approvals of OCA for the treatment of NASH patients with liver fibrosis. The REGENERATE trial will remain blinded after the interim analysis and continue to follow patients until

the occurrence of a pre-specified number of adverse liver-related clinical events, including progression to cirrhosis, to confirm clinical benefit on a post-marketing basis.

Two co-primary endpoints will be assessed in the interim analysis: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening of NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. The REGENERATE trial will also assess secondary outcome measures such as improvement of both fibrosis and NASH and the resolution of fibrosis.

TABLE OF CONTENTS

Additional NASH Clinical Programs

In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients. CONTROL is expected to enroll 80 NASH patients who are naïve to statin therapy or have undergone a statin washout, and will include a 16-week double-blind phase followed by an optional two year long term safety extension phase.

We intend to complete our planning for a Phase 2 program in NASH patients with cirrhosis in 2016. The objectives of this trial are to understand the safety and tolerability of OCA in NASH patients with cirrhosis and portal hypertension and to evaluate the effect of OCA in reducing portal pressure as assessed by hepatic venous pressure gradient, or HVPG.

NASH Regulatory Pathway

In January 2015, OCA received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis. The breakthrough therapy designation was created by the FDA to speed the availability of new therapies for serious or life-threatening conditions. Drugs qualifying for this designation must show credible evidence of a substantial improvement on a clinically significant endpoint over available therapies, or over placebo if there is no available therapy. The breakthrough therapy designation constitutes one of four expedited programs for serious conditions including accelerated approval, priority review and fast-track designation, all of which can also be granted to the same drug if relevant criteria are met. The breakthrough therapy designation confers several benefits, including intensive FDA guidance and discussion and eligibility for submission of a rolling NDA.

Primary Sclerosing Cholangitis (PSC)

PSC is a rare, serious life-threatening, chronic cholestatic liver disease characterized by progressive destruction of bile ducts with eventual onset of cirrhosis and its complications. PSC has about one-third the prevalence of PBC and more than 60% of cases occur in men.

PSC is usually diagnosed by preliminary assessment of liver biochemistry, with or without reported symptoms, and confirmed by cholangiography, typically magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography, or ERCP. ALP is elevated in most PSC patients, consistent with cholestasis, and ALT and GGT are also typically elevated, but not in all cases. Bilirubin is often normal in early-stage PSC but increases with progression of the disease. The mean age at diagnosis is 40 years. Approximately 75% of PSC patients have overlapping inflammatory bowel disease, principally ulcerative colitis.

Median survival for PSC patients has been previously estimated as 8 to 12 years from diagnosis in symptomatic patients, depending upon stage of the disease at the time of diagnosis. Complications involving the biliary tree are common and include cholangitis as well as ductal strictures and gallstones, both of which may require frequent endoscopic or surgical interventions. PSC is often complicated by the development of malignancies, with cholangiocarcinoma being the most common.

Despite evaluation of multiple treatments, liver transplant is currently the only treatment shown to improve clinical outcomes. Ursodiol is often used for the treatment of PSC due to improvements in liver biochemistry following initiation of therapy. Despite general biochemical improvement, ursodiol has not been shown to improve transplant-free survival and, at high doses, has been associated with increased risk for serious complications.

However, as there are no approved drugs for the treatment of PSC, some physicians treat patients with ursodiol, typically at a dose of 13 to 15 mg/kg/day. PSC is the fourth leading indication for liver transplant. However, the post-transplant recurrence rate of PSC has been shown to be as high as 20%.

Phase 2 AESOP Trial: OCA as Therapy in PSC

In December 2014, we initiated an international Phase 2 clinical trial, referred to as the AESOP trial, to evaluate the effects of 24 weeks of treatment with varying doses of OCA compared to placebo in patients with PSC. The primary endpoint is the reduction of serum ALP levels, as compared to placebo. In addition, OCA s effect on other secondary liver function endpoints, as well as symptoms of ulcerative colitis (a disease occurring in a majority of patients with PSC), will be assessed. This trial is anticipated to enroll

TABLE OF CONTENTS

approximately 75 patients in the United States and Europe. Following the completion of the 24-week double-blind portion of the trial, patients will be given the option to enroll in an open-label long-term safety and efficacy extension trial.

Biliary Atresia

Biliary atresia is a life-threatening condition in infants in which the bile ducts inside or outside the liver do not have normal openings. With biliary atresia, bile becomes trapped, builds up, and damages the liver. The damage leads to scarring, loss of liver tissue, and cirrhosis. The two types of biliary atresia are fetal and perinatal. Fetal biliary atresia appears while the baby is in the womb. Perinatal biliary atresia is much more common and does not become evident until two to four weeks after birth. Some infants, particularly those with the fetal form, also have birth defects in the heart, spleen, or intestines. Biliary atresia is rare and only affects about one out of every 18,000 infants. The disease is more common in females, premature babies, and children of Asian or African American heritage. Biliary atresia is not an inherited disease and is most likely caused by an event in the womb or around the time of birth. No single test can definitively diagnose biliary atresia, resulting in the need for a series of tests. All infants who still have jaundice two to three weeks after birth, or who have gray or white stools after two weeks of birth, should be checked for liver damage.

Once diagnosed, biliary atresia is treated with a liver transplant or, more frequently, a surgery called the Kasai procedure, in which the bile ducts are connected directly to the small intestine. After the Kasai procedure, some infants continue to have liver problems and, even with the return of bile flow, some infants develop cirrhosis. Possible complications after the Kasai procedure include ascites, bacterial cholangitis, portal hypertension, and pruritus. Even after a successful Kasai surgery, most infants with biliary atresia slowly develop cirrhosis over the years and require a liver transplant by adulthood.

Phase 2 CARE Trial: OCA as Therapy in Biliary Atresia

In October 2015, we initiated a Phase 2 clinical trial of OCA, referred to as the CARE trial, in pediatric patients with biliary atresia. The CARE trial will evaluate the effects of 11 weeks of OCA treatment where patients with biliary atresia will be randomized to varying doses of OCA or a control group receiving only their current treatment. The primary endpoint is to evaluate the pharmacokinetics and the safety and tolerability of OCA treatment. In addition, OCA s effect on hepatobiliary indices and biomarkers will be assessed. This trial is anticipated to enroll approximately 60 patients in the United States and Europe. All patients will be given the option to enroll in an open-label long-term safety and efficacy extension trial. In addition to studying the effects of OCA treatment in biliary atresia, this trial is a part of the approved Paediatric Investigation Plan, or PIP, in support of the MAA for OCA in PBC in the European Union.

Potential Future Product Candidates

In addition to OCA, we are developing other novel bile acid analog compounds targeting FXR and a second dedicated bile acid receptor called TGR5, which is a target of interest for the treatment of type 2 diabetes and other gastrointestinal indications. We intend to continue advancing these and other product candidates as we build our pipeline.

INT-767

INT-767 is an orally administered dual FXR and TGR5 agonist that, like OCA, is derived from the primary human bile acid CDCA. This product candidate has been shown to be approximately three times more potent than OCA as an FXR agonist. In animal models of chronic liver, intestinal and kidney diseases, INT-767 has consistently demonstrated greater anti-fibrotic and anti-inflammatory effects than OCA.

We have received assignments of rights to the INT-767 patent portfolio from all inventors, with the exception of one inventor. That inventor is contractually obligated to provide an assignment to us. Thus, we believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the patent assignments we have received.

In November 2015, we announced the initiation of a Phase 1 clinical trial of INT-767 in healthy volunteers. The goal of the Phase 1 trial is to assess safety and pharmacokinetics in a single ascending dose escalation phase followed by a multiple ascending dose phase in healthy volunteers.

TABLE OF CONTENTS

INT-777

INT-777 is an orally administered TGR5 agonist that is derived from the primary human bile acid cholic acid. We have completed the preclinical studies necessary for the filing of an IND. By virtue of the patent assignments we have received and other contractual obligations owed to us, we believe we are the exclusive owner of the INT-777 patent portfolio.

Our in vitro studies of INT-777 showed that the product candidate has the potential to selectively target TGR5, a receptor that has been shown to directly regulate the release of glucagon like peptide-1, or GLP-1, in the intestine with resulting insulin sensitizing effects. There are several important and effective marketed drugs that enhance the effects of GLP-1 through different mechanisms, but none are able to induce the endogenous production of this hormone, and we believe there is interest in the potential for a TGR5 agonist to provide additive benefits. TGR5 has also been shown in animal models to regulate other metabolic pathways in brown fat and skeletal muscle that drive energy expenditure. The receptor may also play a role in the control of inflammation, which is increased in insulin resistant diabetic conditions.

In animal models of diabetes, treatment with INT-777 induced GLP-1 secretion, with resulting insulin sensitivity and normalization of glycemic control, increased basal energy expenditure and prevention of weight gain, and a reduction in blood lipid levels together with liver steatosis and fibrosis. We believe that these preclinical results could support further development of INT-777 and our other TGR5 agonists in the treatment of type 2 diabetes, associated metabolic disorders and other gastrointestinal indications. We intend to continue development of INT-777 through potential collaborations with third parties, over the next several years.

Strategic Collaborations and Research Arrangements

Sumitomo Dainippon Pharma

On March 29, 2011, we entered into a license agreement with Sumitomo Dainippon Pharma Co., Ltd., under which we granted Sumitomo Dainippon an exclusive license to research, develop and commercialize OCA as a therapeutic for the treatment of PBC and NASH in Japan and China (excluding Taiwan). Under the terms of the agreement, Sumitomo Dainippon is required to use commercially reasonable efforts to develop and commercialize OCA in its licensed territories for the treatment of PBC and NASH, and we are obligated under the agreement to use commercially reasonable efforts to develop OCA outside of Sumitomo Dainippon s licensed territories. We are also responsible for supplying Sumitomo Dainippon with clinical and commercial supply of OCA requested by Sumitomo Dainippon pursuant to clinical and commercial supply agreements that include terms specified in the agreement. Sumitomo Dainippon has agreed during the term of the agreement to not commercialize any compound that is an FXR agonist for use in the treatment of PBC or NASH other than pursuant to the agreement.

We granted Sumitomo Dainippon an option under the agreement to obtain an exclusive license to commercialize OCA for indications other than PBC and NASH on the same terms as are set forth in the agreement. Sumitomo Dainippon may exercise this option with respect to any indication at any time during the two-year period commencing on the date we notify Sumitomo Dainippon of the commencement of a Phase 3 clinical trial involving OCA for such indication, subject to Sumitomo Dainippon s payment of an option fee for each additional indication. No option fee is required to be paid by Sumitomo Dainippon if it exercises its option for any additional indication only in China.

In addition to Japan and China, which are the original licensed territories, we also granted Sumitomo Dainippon an option under the agreement to add Korea, Taiwan, Malaysia, Vietnam, the Philippines, Thailand, Singapore and/or

Indonesia to its exclusive license on the same terms as are set forth in the agreement. Sumitomo Dainippon may exercise this option with respect to any such country at any time up until the date on which regulatory approval to commercialize OCA is granted in Japan, subject to Sumitomo Dainippon s payment of an option fee for each country. If we accept or make a bona fide offer of exclusive rights to a third party to develop and commercialize OCA in any of these countries, we must first notify Sumitomo Dainippon and Sumitomo Dainippon has the right to exercise its option with respect to any such country. In addition, prior to accepting or making a bona fide offer of any exclusive development and commercialization rights involving OCA in the United States and Canada to a third party, we must first engage in good faith

TABLE OF CONTENTS

negotiations with Sumitomo Dainippon with respect to the grant to Sumitomo Dainippon of exclusive rights to develop and commercialize OCA in such countries. In May 2014, Sumitomo Dainippon exercised its option to add Korea to its licensed territories.

Sumitomo Dainippon made up-front payments to us in the amount of $16.0 million, including $1.0 million upon the exercise of its option to add Korea to its licensed territories. In addition, Sumitomo Dainippon may be required to pay us up to an aggregate of approximately $30.0 million for the achievement of development milestones, $70.0 million for the achievement of regulatory approval milestones and $200.0 million for the achievement of sales milestones based on aggregate sales amounts. As of March 2, 2015, we have achieved $1.0 million of the development milestones. Sumitomo Dainippon is also obligated to pay us tiered royalties ranging from the tens to the twenties in percent based on net sales of OCA products in Japan and the other Asian countries covered by this agreement. The term of the agreement, and Sumitomo Dainippon s obligation to pay royalties to us for each OCA product, expires on a country-by-country basis on the later of the expiration of the exclusivity period in such country, whether through the expiration of applicable patents or the introduction of generic drugs that compete with the OCA product, or ten years after the first commercial sale of such OCA product for the first or second indication in that country. Royalty rates are subject to reduction under the agreement in specified circumstances, including, with respect to any country in the exclusive territory, if sales of generic products reach a certain threshold market share in that country over a specified period.

Sumitomo Dainippon may terminate the agreement in its entirety or on a country-by-country or indication-by-indication basis upon 90 days written notice. Either we or Sumitomo Dainippon may terminate the agreement in the event of the uncured material breach by or bankruptcy of the other party, subject to certain dispute resolution procedures. If Sumitomo Dainippon were to terminate the agreement for our material breach, it would have a perpetual license following the effective date of termination, subject to the payment by Sumitomo Dainippon of a royalty based on net sales of OCA products, the amount of which will depend on whether the effective date of termination occurs prior to or after the date of first commercial sale of an OCA product. If we were to terminate the agreement for Sumitomo Dainippon s material breach or if Sumitomo Dainippon were to voluntarily terminate the agreement, Sumitomo Dainippon s license under the agreement would terminate.

Commercialization

In anticipation of the potential marketing authorization of OCA in PBC in the United States and Europe in 2016, we are in the final stages of establishing a commercial organization and distribution capabilities. In the United States and Europe, due to the nature of chronic liver diseases and the limited options for treatment, patients suffering from diseases such as PBC often have a high degree of organization, which may make it easier to identify target populations if and when OCA is approved for PBC and subsequently for other indications. We believe that the market for the treatment of PBC, NASH and other indications is a specialty care market driven by key opinion leaders in the hepatology and gastroenterology fields. Most patients are treated by physicians who specialize in the treatment of liver disease, including hepatologists and certain gastroenterologists and endocrinologists.

Our current plan is to commercialize OCA ourselves in the United States, certain European countries, Canada and Australia if it is approved. We anticipate that our commercialization efforts will include our internal commercial organization, sales people and other specialists, and contracted outside resources. Outside of the United States, Europe, Canada and Australia, subject to obtaining necessary marketing approvals, we likely will seek to commercialize OCA through distribution or other collaboration arrangements. We believe that the build out of our U.S. commercial infrastructure is mostly complete with the recent hiring of the U.S. territory business managers and other field personnel in October 2015. We also significantly expanded our commercial and other infrastructure

internationally in 2015, and plan on making additional investments over 2016 should key regulatory milestones be achieved on a timely basis.

If OCA is approved for the treatment of patients with PBC, we believe that it will be possible to commercialize OCA for this indication with a relatively small specialty sales organization that would target a limited and focused group of specialist physicians. As a result of our ongoing clinical work, we have been engaged in dialogue with specialists who treat patients with PBC. We believe that these activities have

TABLE OF CONTENTS

provided us with a growing knowledge of the physicians we plan to target for the commercial launch of OCA for PBC in the United States and Europe, subject to the receipt of applicable marketing approvals. We intend to leverage the infrastructure and capabilities of our PBC-focused specialty sales organization during our pre-commercial preparation for the commercialization of OCA in NASH and other potential indications, if approved for these indications. Though we are continuing our market research and other pre-commercial planning for OCA in NASH, we currently anticipate that we would require a larger specialty sales organization that would target a broader group of hepatologists, gastroenterologists and other specialists focused on NASH if we receive marketing approval for this indication.

We exclusively licensed rights to OCA to Sumitomo Dainippon in Japan, China and Korea, along with an option to expand this exclusive license into certain other Asian countries. We will rely on Sumitomo Dainippon to commercialize OCA in its territory.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Although we believe that we hold a leading position in bile acid chemistry, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price, the level of generic competition and reimbursement.

Our most advanced product candidate, OCA, is an FXR agonist currently being developed to treat non-viral, progressive liver diseases. We are aware of other companies, including Novartis International AG, Gilead Sciences, Inc., Enanta Pharmaceuticals, Inc., Eli Lilly, Co., ENYO Pharma SAS, Exelixis, Inc. and Akarna Therapeutics Ltd. that have FXR agonists in Phase 2 or earlier stages of clinical or preclinical development that could be used to treat PBC, NASH and the other liver diseases we are targeting.

OCA is currently being developed as a second line treatment for PBC where ursodiol is the only therapy that is approved for treatment and is generically available at a significantly lower cost than branded products. While fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported, though many fibrates are specifically contraindicated for use in PBC due to potential concerns over acute and long-term safety in this patient population. Ongoing Phase 3 clinical trials for the treatment of PBC include an investigator-sponsored trial of bezafibrate, a fibrate that has not been approved for commercialization by the FDA and is only available outside of the United States, and a combination of ursodiol and budesonide, a steroid, sponsored by Dr. Falk Pharma GmbH. We are aware of several other companies that have product candidates in Phase 2 or earlier clinical or preclinical development for the treatment of PBC, including FXR agonists from Novartis International AG (LJN452) and Enanta Pharmaceuticals, Inc. (EDP-305), Bristol-Myers Squibb s marketed anti-CTL4 fusion protein (abatacept) and FF Pharmaceuticals anti-CD40 monoclonal antibody (FFP104). Additionally, several companies have product candidates aimed at the cholestatic-induced pruritus associated with PBC, including apical sodium dependent bile acid transport inhibitors being developed by GlaxoSmithKline (GSK2330672) and Albireo (A4250).

There are currently no therapeutic products approved for the treatment of NASH, NAFLD, portal hypertension, complications of cirrhosis or alcoholic hepatitis. There are several marketed therapeutics that are currently used off-label for the treatment of NASH, such as vitamin E (an antioxidant), insulin sensitizers (e.g., metformin),

antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol, but none has been clearly shown in clinical trials to show a significant reversal in liver fibrosis. Genfit SA has an ongoing Phase 3 clinical trial of GFT505, a dual PPAR alpha/delta agonist. Gilead Sciences, Inc. is conducting multiple Phase 2 clinical trials in NASH patients of various disease severity with both simtuzumab, an anti-body against the lysyl oxidase-like 2 enzyme, and GS-4997, an inhibitor of the apoptosis signal-regulating kinase 1. Gilead Sciences, Inc. is also studying an FXR agonist (GS-9674) for the treatment of NASH. We are aware of several other companies that have product candidates in Phase 2 clinical or earlier clinical or preclinical development for the treatment of NASH, including Novo Nordisk A/S, Conatus Pharmaceuticals

TABLE OF CONTENTS

Inc., Nitto Denko Corporation, Tobira Therapeutics, Inc., Cempra Pharmaceuticals, Islet Sciences, Inc., Galectin Therapeutics Inc., Zydus Pharmaceuticals Inc., NGM Biopharmaceuticals Inc., Galmed Medical Research Ltd., Bristol-Myers Squibb, MediciNova, Inc., FibroGen, Inc., Genkyotex SA, Viking Therapeutics, Inc., AstraZeneca plc, Enanta Pharmaceuticals, Inc., Durect Corporation, Immuron Ltd., Boehringer Ingelheim GmbH, MiNA Therapeutics, NuSirt Biopharma, Inc., Protalix Biotherapeutics, and Medivation, Inc. While there is no approved treatment for PSC, ursodiol is often prescribed off-label for PSC patients. We are aware of several companies that have product candidates in Phase 2 clinical or earlier stage clinical or preclinical development for the treatment of PSC, including Tobira Therapeutics, Inc., Biotie Therapies Corp. (acquired by Acorda Therapeutics, Inc.), Dr. Falk Pharma GmbH, Gilead Sciences, Inc. and Shire plc.

We believe that OCA offers key potential advantages over ursodiol and other products in development that could enable OCA, if approved for these indications, to capture meaningful market share. However, many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than us in obtaining approval from the FDA or from other regulators for drugs and achieving widespread market acceptance. Our competitors drugs may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of their development and commercialization. We anticipate that we will face intense and increasing competition as new drugs enter the market and other advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete. NASH is a complex disease and it is unlikely that any one therapeutic option will be optimal for every NASH patient. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products.

Intellectual Property

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. We have sought patent protection in the United States and internationally for OCA, INT-767 and INT-777, and our discovery programs, and other inventions to which we have rights, where available and when appropriate. Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. For this and more comprehensive risks related to our intellectual property, please see Item 1A. Risk Factors Risks Relating to Our Intellectual Property.

OCA (lead product candidate; FXR agonist)

The patent portfolio for OCA contains patents and patent applications directed to compositions of matter, manufacturing methods, and methods of use. As of December 31, 2015, we owned seven U.S. patents, seven pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in 31 European countries as well as Australia, Canada, China, Israel, Japan, and Macao. In January 2016, we received notification of grant of additional OCA composition of matter patents. We expect the composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2022 (worldwide) at the soonest and 2033 at the latest. It is possible that the 2022 expiration date of the composition of matter patent in the United States may be extended up to five

TABLE OF CONTENTS

additional years under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from 2022 to 2033.

INT-767 (dual FXR/TGR5 agonist)

The patent portfolio for INT-767 contains patents and patent applications directed to compositions of matter and methods of use. As of December 31, 2015, we owned three U.S. patents, two pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in Australia, China, 34 European countries as well as Hong Kong, India, Israel and Japan. We expect the issued composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2029. It is possible that the term of the composition of matter patent in the United States may be extended up to five additional years under the provisions of the Hatch-Waxman Act. We expect the foreign composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2027. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2027 to 2029. We have received assignments of rights to the INT-767 patent portfolio from all inventors, with the exception of one inventor. That inventor is contractually obligated to provide an assignment to us. Thus, we believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the patent assignments we have received.

INT-777 (TGR5 agonist)

The patent portfolio for INT-777 contains patents and patent applications directed to compositions of matter and methods of use. As of December 31, 2015, we owned three U.S. patents, two pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in Australia, China, 9 Eurasian countries, 30 European countries, Hong Kong, Israel, Japan, Macao, Mexico, Singapore, South Korea, and South Africa. We expect the composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2030. It is possible that the term of the composition of matter patent in the United States may be extended up to five additional years under the provisions of the Hatch-Waxman Act. We expect the foreign composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire beginning in 2028. Patent term extension may be available in certain foreign countries upon regulatory approval. We expect the other patents in the portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2028 to 2030.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredient, or API, and finished product for clinical trials and preclinical studies that we are conducting and plan to conduct prior to and after seeking regulatory approval. We are currently seeking to contract to qualify one or more back-up API manufacturers. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates. We currently obtain these supplies and services from our third-party contract

TABLE OF CONTENTS

manufacturers on a purchase order basis. We intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial production of those products. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA, EMA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and analogous authorities in other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the EMA through the MAA process before they may be legally marketed in Europe. Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA s good laboratory practice, or GLP, regulations;

submission to the FDA of an IND, which must take effect before human clinical trials may begin;

approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;

preparation and submission to the FDA of an NDA;

review of the product by an FDA advisory committee, where appropriate or if applicable;

satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product s identity, strength, quality and purity;

satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data;

payment of user fees and securing FDA approval of the NDA; and

compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval outcomes studies required by the FDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and

analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the

TABLE OF CONTENTS

parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must timely report to FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug. An IRB at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject s legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
Phase 2. Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the drug has been associated with unexpected serious harm to patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, or the clinical monitoring board or data safety monitoring board, or DSMB. This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based on the limited access to data from the ongoing trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new drug. If a Phase 2 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a special protocol

assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

TABLE OF CONTENTS

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for an SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug representing a significant improvement over available therapies in treatment, prevention or diagnosis of disease may receive priority review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA has publicly announced a planned advisory committee meeting date of April 7, 2016 relating to OCA in PBC. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Fast Track, Breakthrough Therapy, Priority Review and Accelerated Approval

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products,

sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product s NDA before the application is complete.

A product may also be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough

TABLE OF CONTENTS

therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner. In January 2015, OCA received breakthrough therapy designation from the FDA for the treatment of NASH patients with liver fibrosis.

The FDA may also designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA s goal for taking action on a marketing application from ten months to six months.

In addition, the FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. In the case of unprecedented accelerated approval endpoints, this determination occurs during the review of the NDA. Unless otherwise informed by the FDA, an applicant must submit to the FDA for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

OCA has been granted fast track designation by the FDA for the treatment of patients with PBC who have an inadequate response to or are intolerant of ursodiol. In August 2015, the FDA accepted for review our NDA and granted priority review for OCA in PBC. The FDA has set a target date of May 29, 2016 to take action under PDUFA, after giving effect to a 90 day extension. The FDA has publicly announced a planned advisory committee meeting date of April 7, 2016.

In accordance with the applicable requirements under the accelerated approval pathway, we initiated a clinical outcomes confirmatory trial for OCA in PBC, known as the COBALT trial, in December 2014, following discussions with the FDA. We do not expect completion of this trial to be a condition to the receipt of marketing approval and, as a result, plan to complete the trial following our receipt of marketing approval. Approval of a drug may be withdrawn if trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug (e.g., show a significantly smaller magnitude or duration of benefit than was anticipated based on the observed effect on the surrogate).

Post-approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product

may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

TABLE OF CONTENTS

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject us to administrative or judicial sanctions, any of which could have a material adverse effect on us.

These sanctions could include:

refusal to approve pending applications;
withdrawal of an approval;
imposition of a clinical hold;
warning letters;
product seizures;
total or partial suspension of production or distribution; or
injunctions, fines, disgorgement, or civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Patent Term Extension and Data Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits an extension patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, the extension of patent term cannot extend the remaining term of a patent beyond a total of 14 years from the product s approval date. The patent term extension period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and

the application for extension must be made prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add

TABLE OF CONTENTS

patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity 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. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved 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, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent for other conditions of use. 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.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, or BPCA, certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA, or a Written Request, relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA s filing requirements.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, biologics license application and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

As part of the FDASIA, Congress made a few revisions to BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

TABLE OF CONTENTS

Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to regulations of other countries governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications under a centralized, decentralized or mutual recognition marketing authorization procedure. The centralized procedure provides for the grant of a single marketing authorization for a medicinal product by the European Commission on the basis of an opinion by the EMA. A centralized marketing authorization is valid for all European Union member states and three of the four EFTA States (Iceland, Liechtenstein and Norway). The decentralized marketing authorization procedure involves the submission of an application for marketing authorization to the competent authority of all European Union member states in which the product is to be marketed. One national competent authority, selected by the applicant, assesses the application for marketing authorization. The competent authorities of the other European Union member states are subsequently required to grant marketing authorization for their territory on the basis of this assessment, except where grounds of potential serious risk to public health require this authorization to be refused. The mutual recognition procedure provides for mutual recognition of marketing authorizations delivered by the national competent authorities of European Union member states by the approval authorities of other European Union member states. The holder of a national marketing authorization may submit an application to the competent authority of a European Union member state requesting that this authority recognize the marketing authorization delivered by the competent authority of another European Union member state.

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

It is also possible that a marketing authorization from the EMA could be conditional on post-approval studies and not considered a full approval. A manufacturer s ability to obtain and maintain conditional marketing authorization in the European Union will be limited to specific circumstances and subject to several conditions and obligations, if obtained at all. Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under European Union law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions.

Similarly to the United States, both marketing authorization holders and manufacturers of medicinal products are

subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual European Union member states both before and after grant of the manufacturing and marketing authorizations. This includes European Union cGMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third party manufacturers are required to ensure that all of our processes, methods and equipment are compliant with cGMP.

TABLE OF CONTENTS

Failure by us or by any of our third party partners, including suppliers, manufacturers and distributors to comply with European Union laws and the related national laws of individual European Union member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of marketing authorization, may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our drug candidate is determined to be contained within the competitor s product for the same indication or disease. 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. 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.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the orphan-designated product.

OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and PSC. Any of our orphan-designated products and product candidates can lose orphan designation, and the related benefits, if it is demonstrated that the orphan designation criteria are no longer met.

Pricing and Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance plans and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these

TABLE OF CONTENTS

third-party payors do not consider our products to be effective (or cost-effective in some markets outside of the United States) compared to other therapies, they may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

Medicare is a U.S. federal healthcare program that provides coverage for certain healthcare items and services to individuals aged 65 years or older, as well as individuals of any age with certain disabilities and illnesses. Medicare Part D may affect reimbursement of our products upon approval. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered outpatient drugs, and each Part D plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D plan drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D plan will likely be lower than the prices we might otherwise obtain. Moreover, while Part D provides prescription drug benefits only to Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment made by Medicare may result in a similar reduction in payments from non-governmental payors.

Medicaid is a government healthcare program that provides coverage for certain healthcare items and services to low-income children, families, pregnant women and people with disabilities. It is jointly funded by the federal and state governments, and it is administered by individual states with parameters established by the federal government. Therefore, coverage and reimbursement for drugs may vary by state Medicaid program. A manufacturer must enter into a Medicaid Rebate Agreement to have its products be eligible for coverage by Medicaid. Under the Medicaid program, and per the Medicaid Rebate Agreement, manufacturers agree to report certain prices to the government and pay rebates to state Medicaid programs based on Medicaid utilization of the manufacturer s covered drugs. In January 2016, the Centers for Medicare & Medicaid Services, or CMS, released a final rule impacting the calculation and reporting of prices by manufacturers under the Medicaid program. We continue to evaluate how this final rule may affect the reimbursement of our product candidate and rebates paid to state Medicaid programs.

Federal law requires any company that participates in the Medicaid Drug Rebate Program to also participate in the Public Health Service s 340B drug pricing program in order for federal funds to be available for the manufacturer s drugs under Medicaid. The 340B pricing program requires participating manufacturers to charge statutorily-defined covered entities no more than the 340B ceiling price for the manufacturer s covered outpatient drugs. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the ACA, extended eligibility to participate in the 340B pricing program to certain additional types of hospitals (including critical access hospitals, sole community hospitals, rural referral centers and freestanding cancer hospitals). However, for purposes of these newly eligible covered entities, the ACA specifically excluded from the definition of covered outpatient drugs certain drugs designated as orphan drugs under section 526 of the FDCA, such as our product candidate.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private

payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a

TABLE OF CONTENTS

competitor s product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

U.S. Fraud and Abuse Laws

Any present or future arrangements with third-party payors, healthcare providers and professionals and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, and are not limited to, anti-kickback and false claims statutes.

The federal Anti-Kickback Statute (42 U.S.C. §1320a-7b(b)) prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. Remuneration is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including for example, gifts, discounts, coupons, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others.

The federal False Claims Act imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and *qui tam* relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be presented to the government. There is also a separate false claims provision imposing criminal penalties.

Other 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, imposes criminal liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services.

The federal Physician Payments Sunshine Act requirements under the ACA, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value made to covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

TABLE OF CONTENTS

A number of states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act that apply to items and services reimbursed under Medicaid and other state programs. Some state anti-kickback statutes apply not just to government payors, but to all payors, including commercial payors.

Employees

As of December 31, 2015, we had 405 employees, of which 216 employees were in our drug development operations, 117 employees were in our commercial group and 72 employees were in our corporate group. As of December 31, 2015, 309 employees were based in the United States, 89 employees were based in Europe and 7 employees were based in Canada. None of our employees are represented by a labor union and we consider our employee relations to be good.

Corporate Information

We were incorporated in the State of Delaware on September 4, 2002. Our principal executive offices are located at 450 West 15th Street, Suite 505, New York, NY 10011, and our telephone number is (646) 747-1000. We also have administrative offices in San Diego, California and London, United Kingdom.

Our corporate website address is *www.interceptpharma.com.* Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. The Securities and Exchange Commission maintains an internet site that contains our public filings with the Securities and Exchange Commission and other information regarding our company, at *www.sec.gov.* These reports and other information concerning our company may also be accessed at the Securities and Exchange Commission s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the Securities and Exchange Commission at 1-800-SEC-0330. The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

Legal Proceedings

From time to time we are party to legal proceedings in the course of our business in addition to those described below. We do not, however, expect such other legal proceedings to have a material adverse effect on our business, financial condition or results of operations.

On February 21, 2014 and February 28, 2014, purported shareholder class actions, styled *Scot H. Atwood v. Intercept Pharmaceuticals, Inc. et al.* and *George Burton v. Intercept Pharmaceuticals, Inc. et al.*, respectively, were filed in the United States District Court for the Southern District of New York, naming us and certain of our officers as defendants. These lawsuits were filed by stockholders who claim to be suing on behalf of anyone who purchased or otherwise acquired our securities between January 9, 2014 and January 10, 2014.

The lawsuits allege that we made material misrepresentations and/or omissions of material fact in our public disclosures during the period from January 9, 2014 to January 10, 2014, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate to our January 9, 2014 announcement that the FLINT trial had been stopped early based on a

pre-defined interim efficacy analysis. Specifically, the lawsuits claim that the January 9, 2014 announcement was misleading because it did not contain information regarding certain lipid abnormalities seen in the FLINT trial in OCA-treated patients compared to placebo.

On April 22, 2014, two individuals each moved to consolidate the cases and a lead plaintiff was subsequently appointed by the Court. On June 27, 2014, the lead plaintiff filed an amended complaint on behalf of the putative class as contemplated by the order of the Court. On August 14, 2014, the defendants filed a motion to dismiss the complaint. Oral arguments on the motion to dismiss were held on February 24, 2015. On March 4, 2015, the defendants motion to dismiss was denied by the Court. The defendants answered the amended complaint on April 13, 2015. On July 15, 2015, the plaintiff moved for class

TABLE OF CONTENTS

certification and appointment of class representatives and class counsel. On September 14, 2015, the defendants opposed the plaintiff s class certification motion. The plaintiff filed its reply to the defendants opposition on October 14, 2015, to which the defendants filed a sur-reply on November 10, 2015. Oral arguments on the class certification motion were held on January 20, 2016. No decision has been made by the Court on the class certification motion. The parties are currently undergoing discovery in relation to this matter. Dispositive motions are due on September 16, 2016.

The lead plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorneys fees.

We believe that we have valid defenses to the claims in the lawsuit, have denied liability and intend to defend ourselves vigorously. There can be no assurance, however, that we will be successful. At this time, no assessment can be made as to the likely outcome of this action or whether the outcome will be material to us. Therefore, we have not accrued for any loss contingencies related to this lawsuit.

TABLE OF CONTENTS

Item 1A. Risk Factors

Except for the historical information contained herein, this Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in this Annual Report on Form 10-K. Important factors that could cause or contribute to these differences include, but are not limited to, those discussed in the following section, as well as those discussed in Part II, Item 7 entitled Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere throughout this Annual Report on Form 10-K.

You should consider carefully the following risk factors, together with all of the other information included in this Annual Report on Form 10-K. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have never been profitable. Currently, we have no products approved for commercial sale, and to date we have not generated any revenue from product sales. As a result, our ability to reduce our losses and reach profitability is unproven, and we may never achieve or sustain profitability.

We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses in each year since our inception, including net losses of $226.4 million, $283.2 million and $67.8 million for the years ended December 31, 2015, 2014 and 2013, respectively. To date, we have financed our operations primarily through private placements of our convertible preferred stock, convertible notes and warrants to purchase common stock, public offerings of our common stock and payments received under our licensing and collaboration agreements with Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo Dainippon, and Les Laboratoires Servier and Institut de Recherches Servier, which are collectively referred to as Servier. At December 31, 2015, we had $628.1 million in cash, cash equivalents and investment securities.

We have devoted substantially all of our resources to our development efforts relating to our product candidates, including conducting clinical trials of our product candidates, providing general and administrative support for these operations, protecting our intellectual property and engaging in activities to prepare for the commercialization of our product candidates. Although we have a target date of May 29, 2016 for the U.S. Food and Drug Administration, or FDA, to take action under the Prescription Drug User Fee Act, or PDUFA, we do not yet have any products approved for sale and have not generated any revenues from product sales. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, obeticholic acid, or OCA, which is our lead product candidate, and our other product candidates, prepare for and begin the commercialization of any approved products, and add infrastructure and personnel in the United States and Europe to support our product development and commercialization efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years as we continue our confirmatory clinical outcomes trial of OCA, referred to as the COBALT trial, in primary biliary cirrhosis, recently

renamed primary biliary cholangitis, or PBC, continue our long-term safety extension phases of our clinical trials of OCA in PBC, continue our Phase 3 clinical program of OCA in nonalcoholic steatohepatitis, or NASH, including the Phase 3 REGENERATE trial in non-cirrhotic NASH patients with liver fibrosis, continue our AESOP Phase 2 clinical trial of OCA for primary sclerosing cholangitis, or PSC, and finalize other planned activities for regulatory approval of OCA in PBC. We also expect that continuing the development of OCA in additional diseases, such as biliary atresia, a rare pediatric disease characterized by deficient bile duct development for which we initiated a Phase 2 trial in OCA called CARE. We also initiated a Phase 2 clinical trial, referred to as the CONTROL trial, to assess the lipid metabolic effects of OCA and the effects of concomitant statin administration in NASH patients. Furthermore, in November 2015, we initiated a Phase 1 clinical trial for INT-767, an earlier stage product candidate. Our expenses could increase if

We have never been profitable. Currently, we have no products approved forcommercial sale, and to date we have

TABLE OF CONTENTS

we are required by the FDA or the European Medicines Agency, or EMA, to perform studies or trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates. We also anticipate that we will continue to increase our product development, scientific, commercial and administrative personnel significantly and expand our facilities and infrastructure in the United States and abroad as part of our longer-term growth strategy.

Our ability to generate profits from operations and become profitable will depend on our ability to obtain marketing approval for, and commercialize, our product candidates. We do not expect to generate significant revenues unless and until we obtain marketing approval for, and commercialize, OCA for the treatment of PBC and other indications. This will require us to be successful in a range of challenging activities, including:

obtaining approval to market OCA for the treatment of PBC, NASH and other indications and patient populations;
expanding our manufacturing of commercial supply for OCA;
establishing sales, marketing and distribution capabilities to effectively market and sell OCA in the United States and Europe; and
negotiating and securing reimbursement from third-party payors for OCA.

While we are conducting pre-commercial activities, such as patient profiling, to better understand how physicians care for PBC patients, PBC is a rare disease in which no new therapy has been approved in approximately 20 years. As such, there is significant uncertainty in the degree of market acceptance OCA will have in PBC. Even if we receive marketing approvals for OCA in PBC and commence our commercial launch, we do not expect to generate significant revenues in PBC in 2016. We cannot foresee if OCA will ever be accepted as a therapy in PBC eventually resulting in sustained revenues and it may take the passage of a significant amount of time to generate significant sustained revenues even if OCA becomes accepted as a therapy in PBC.

If OCA or any of our other product candidates fails in clinical trials or does not gain regulatory approval, or if our product candidates do not achieve market acceptance, we may never become profitable. Our net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders equity and working capital. Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.

We are currently advancing OCA through clinical development for multiple indications and other product candidates through preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. In June 2015, we completed our filings for marketing approval of OCA in PBC in the United States under the FDA s accelerated approval pathway. In August 2015, the FDA accepted for review our New Drug Application, or NDA, and granted priority review for OCA in PBC. The FDA set a target date of May 29, 2016 to take action under PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. We are also currently in the regulatory review process with the EMA. If we receive marketing approval from the FDA on the PDUFA date, we plan to initiate the commercial launch of OCA in PBC in the United States in June 2016. In June 2015, we also received notice of the acceptance of the Marketing Authorization Application, or MAA, for review by the EMA for use of OCA in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned

commercial launches thereafter in certain European countries. We also plan to apply for marketing approval of OCA in PBC in other markets such as Australia and Canada.

We have incurred and expect to incur additional costs associated with operating as a public company and further plan on expanding our operations in the United States, Europe and in other countries such as Canada and Australia. In addition, subject to obtaining regulatory approval of any of our product candidates, we

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, i

TABLE OF CONTENTS

expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We anticipate incurring significant expenses as we prepare for the potential commercialization of OCA in PBC, including significant expenses relating to our sales, marketing and distribution capabilities and increasing our drug manufacturing activities. As part of our longer-term strategy, we also anticipate incurring significant expenses in connection with our planned increase in our product development, scientific, commercial and administrative personnel and expansion of our facilities and infrastructure in the United States and abroad.

As of December 31, 2015, we had $628.1 million in cash, cash equivalents and investment securities. We currently project adjusted operating expenses in the range of $360 million to $400 million in the fiscal year ending December 31, 2016, which excludes stock-based compensation and other non-cash items. These expenses are planned to support the continued clinical development program for OCA in PBC, NASH and PSC, increased OCA manufacturing activities, the continued development of INT-767 and other preclinical pipeline programs, as well as pre-commercial and commercial activities. We believe that the build out of our U.S. commercial infrastructure for the PBC commercial launch is mostly complete with the hiring of our U.S. territory business managers and other field personnel in October 2015. We also significantly expanded our commercial and other infrastructure internationally in 2015, and plan on making additional investments over 2016 should key regulatory milestones be achieved on a timely basis. Our adjusted operating expense estimate for 2016 is higher than our adjusted operating expenses for 2015 reflecting the increase in headcount that occurred in the latter part of 2015 and the anticipated increases in commercialization and research and development expenses. Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds required to complete the research and development and commercialization of our products under development.

Adjusted operating expense is a financial measure not calculated in accordance with U.S. generally accepted accounting principles, or GAAP. We anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded in adjusted operating expenses as compared to operating expenses under GAAP. See Non-GAAP Financial Measures for more information.

Due to the many variables inherent to the development and commercialization of novel therapies, such as the risks described in this Risk Factors section of our Annual Report on Form 10-K, and our rapid growth and expansion, we currently cannot accurately or precisely predict the duration beyond 2016 over which we expect our cash and cash equivalents to be sufficient to fund our operating expenses and capital expenditure requirements. However, we currently believe that our cash and cash equivalents will be sufficient for us to:

- continue and expand our clinical development programs for OCA in PBC, NASH and PSC, such as continuing, but not completing, our planned Phase 3 clinical program for OCA in NASH, including the REGENERATE trial, our ongoing AESOP trial for OCA in PSC, and our ongoing COBALT confirmatory clinical outcomes trial of OCA in PBC;
- advance the continued development of INT-767, including the completion of a recently initiated Phase 1 clinical trial, and our preclinical compounds, but not completing the clinical or preclinical development needed, as the case may be, for INT-767 or our preclinical compounds;
- increase OCA manufacturing activities, including investing in supply chain and product development, preparing for our PBC commercial launch and planning for the continuation of our clinical program in NASH, but not manufacture the supply needed for any potential commercial launch of OCA in NASH;
- prepare for and, if we obtain marketing approval on a timely basis, initiate the commercial launch of OCA in PBC in both the United States and certain European countries, but not commercially launch OCA in PBC in other countries across the world; and

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, i

expand, if necessary, our clinical, regulatory, medical affairs and commercial infrastructure through the time we initiate such planned commercial launch of OCA in PBC in both the United States and certain European countries, but not expand such infrastructure as may be required in the longer term.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, i

TABLE OF CONTENTS

Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds required to complete the research and development and commercialization of our products under development.

The amount and timing of our future funding requirements will depend on many factors, including:

the willingness of the FDA and EMA to accept the POISE trial, which is our completed Phase 3 clinical trial for PBC, as well as our other clinical and preclinical studies and other work, as the basis for review and marketing approval of OCA for PBC;
the progress, costs, results of and timing of our COBALT confirmatory clinical outcomes trial of OCA for the treatment of PBC, the completion of which we expect will not be a condition to the receipt of marketing approval in the United States or the European Union;
the progress, costs, results of and timing of the Phase 3 program and other supporting trials and studies necessary to support anticipated filings for marketing approval in NASH, including the sufficiency of the REGENERATE trial to be accepted as the sole pivotal trial for marketing approval or the acceptability of a surrogate endpoint for accelerated approval of OCA for the treatment of NASH;
the progress, costs, results of and timing of clinical development of OCA for other indications, including our Phase 2 AESOP trial of OCA in PSC and our Phase 2 CARE trial of OCA in biliary atresia;
the significant expansion of our operations, personnel and the size of our company and our need to continue to expand in the longer term;
the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
the number and characteristics of product candidates that we pursue, including INT-767 which is in a Phase 1 clinical trial, and our product candidates in preclinical development such as INT-777;
the ability of our product candidates to progress through preclinical and clinical development successfully and in a timely manner;
the expansion of our research and development activities;
the costs and timing of commercialization activities, including product sales, marketing and distribution, for any of our product candidates that receive marketing approval;
the costs associated with securing and establishing manufacturing capabilities and procuring the materials necessary for our product candidates;
market acceptance of our product candidates, which may be affected by the reimbursement that our products receive from payors;
the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;
our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
our need and ability to hire and retain additional management, scientific and medical, commercial and other qualified personnel and the substantial cost of retaining such additional personnel;
the effect of competing technological and market developments;

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, i

TABLE OF CONTENTS

our need to implement and maintain internal systems, software and infrastructure, including those to assist in our financial and reporting, clinical development and commercialization efforts and to support our personnel and operations as our business evolves; and

the economic and other terms, timing of and success of our existing licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future.

We have no committed external sources of funding. We may seek additional funding through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail our planned activities, including research and development programs and commercialization activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us.

Our revenues to date have been generated through our collaboration agreements and we may not receive any additional revenues under such agreements.

To date, our sources of revenue have been the payments received under our collaboration and license agreements with Sumitomo Dainippon and Servier. Additional payments under each of the Sumitomo Dainippon and Servier agreements are based on the exercise of optional rights held by our collaborators under the agreements or the achievement of various research, development, regulatory and commercial sales milestones and royalty payments based on the sales of the products covered by such agreements. Future payments from Sumitomo Dainippon and Servier under their respective collaboration and license agreements are uncertain because Sumitomo Dainippon or Servier, as the case may be, may choose not to exercise their optional rights under the agreements or continue research or development activities for the product candidates under license in their licensed territory, the product candidates may not be approved for the proposed indications or, even if any product candidate is approved for one or more indications, it may not be commercially successful. If we are unable to develop and commercialize one or more of our product candidates, either alone or with collaborators, or if revenues from any such collaboration product candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we achieve profitability, we may not be able to sustain or increase profitability.

We have a limited operating history and we expect a number of factors to cause our operating results to fluctuate on a quarterly and annual basis, which may make it difficult to predict our future performance.

We are a development stage biopharmaceutical company with a limited operating history. Our operations to date have been limited to developing our technology and undertaking preclinical studies and clinical trials of our product candidates and engaging in pre-commercial activities for OCA in PBC. Although the FDA set a target date of May 29, 2016 to take action under PDUFA, we have not yet obtained regulatory approvals for any of our product candidates. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or approved products on the market. Our financial condition and operating results have

varied significantly in the past and are expected to continue to significantly fluctuate from quarter-to-quarter or year-to-year due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include:

- any delays in regulatory review and approval of our product candidates in clinical development, including our ability to receive approval from the FDA and the EMA for OCA for the treatment of PBC based on our POISE trial, and our other clinical and preclinical studies and other work, as the basis for review and approval of OCA for PBC;
- delays in the commencement, enrollment and timing of clinical trials;

TABLE OF CONTENTS

difficulties in identifying and treating patients suffering from our target indications, including those due to PBC and PSC being rare diseases and NASH currently requiring an invasive liver biopsy for diagnosis;
the success of our clinical trials through all phases of clinical development, such as the success of our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis;
potential side effects of our product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
the required timeframe for us to receive and analyze data from our clinical trials;
our ability to identify and develop additional product candidates;
market acceptance of our product candidates, which may be affected by the reimbursement that our products receive from payors;
our ability to establish and maintain an effective sales and marketing infrastructure directly or through collaborations with third parties;
competition from existing products or new products that may emerge;
the ability of patients or healthcare providers to obtain coverage or reimbursement for our products and the extent to which such coverage or reimbursement will be provided;
our ability to adhere to clinical trial requirements directly or with third parties such as contract research organizations, or CROs;
our dependency on third-party manufacturers to manufacture our products and key ingredients;
our ability to establish or maintain collaborations, licensing or other arrangements;
the costs to us, and our ability and our third-party collaborators ability to obtain, maintain and protect our intellectual property rights;
costs related to and outcomes of potential intellectual property, securities and other litigation;
our ability to adequately support future growth;
our ability to attract and retain key personnel to manage our business effectively;
our ability to build and improve our company s infrastructure, systems and controls;
potential product liability claims; and
our ability to obtain and maintain adequate insurance coverage.

Risks Related to Regulatory Review and Approval of Our Product Candidates

We cannot be certain that OCA or any of our other product candidates will receive regulatory approval and the timeline of any such approval. Without regulatory approval we will not be able to market and commercialize our product candidates.

We are initially developing OCA for the treatment of patient populations with non-viral, progressive liver diseases, with a current principal focus on PBC, NASH and PSC, and our business currently depends entirely on the successful development and commercialization of OCA.

Our ability to generate revenue related to product sales, if ever, will depend on the successful development and regulatory approval of OCA, particularly for the treatment of PBC and NASH, and our other product candidates.

We currently have no products approved for sale and we cannot guarantee that we will ever have marketable products. The development of a product candidate and issues relating to its approval and marketing are subject to extensive

regulation by the FDA in the United States, the EMA in Europe and regulatory authorities in other countries, with regulations differing from country to country. We are not

We cannot be certain that OCA or any of our other product candidates will receive regulatory approval and the time

TABLE OF CONTENTS

permitted to market our product candidates in the United States or Europe until we receive approval of an NDA from the FDA or an MAA from the EMA, respectively. While we have completed the submissions of our NDA and MAA for OCA in PBC, we have not yet received marketing authorization from either the FDA or EMA for any of our product candidates.

NDAs and MAAs must include extensive preclinical and clinical data and supporting information to establish the product candidate s safety and effectiveness for each desired indication. NDAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA or an MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is never guaranteed. Even after the submission of an NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We completed our filing the NDA with the FDA and the MAA with the EMA in June 2015. In August 2015, the FDA accepted our NDA for filing and granted Priority Review for OCA for the treatment of PBC. The target date for the FDA to take action under PDUFA was initially set for February 29, 2016. In December 2015, our PDUFA action date was extended to May 29, 2016 due to an information request from the FDA that resulted in the submission of additional clinical data analyses. As part of the regulatory review process, the FDA and EMA will continue to review our submission package and conduct regulatory inspections of us and our vendors. We have provided responses as to many of the issues that have been identified in the regulatory review process and continue to respond with respect to others. We may be requested to provide further information, which may impact our regulatory review process. It remains possible that one or more of the issues identified to date, or other issues that may be identified by the FDA or EMA as the review process continues, may result in the FDA and/or the EMA not approving these marketing applications or delaying approval. As a result, we cannot be certain that our applications will be reviewed in a timely manner or approved.

Approvals may also be conditional upon the completion of one or more clinical trials. In addition, delays in approvals or rejections of marketing applications in the United States, Europe or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding our product candidates or other products. Regulatory approval is also dependent on successfully passing regulatory inspection of our company, our clinical sites and key vendors and to ensure compliance with applicable good clinical, laboratory and manufacturing practices regulation. Critical findings could jeopardize or delay the approval of the NDA or MAA.

Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications or uses for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Also, regulatory approval for any of our product candidates may be withdrawn. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country.

We have completed a randomized, placebo-controlled Phase 3 trial of OCA in PBC patients, which we refer to as the POISE trial, and two randomized, placebo-controlled Phase 2 trials of OCA in PBC patients, one with OCA in combination with ursodiol and one with OCA as monotherapy. Following discussions with the FDA and EMA, we are also conducting our COBALT clinical outcomes confirmatory trial of OCA in PBC, which must be completed on a post-approval basis. Furthermore, we will need to complete a number of clinical trials and other studies for the continued development of OCA in indications other than PBC. For example, we initiated our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis in September 2015 and initiated our Phase 2

We cannot be certain that OCA or any of our other product candidates will receive regulatory approval and the time

CONTROL trial to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients in December 2015. We also intend to complete our planning for a Phase 2 program in NASH patients with cirrhosis in 2016. In each of these cases, our ability to obtain the approvals necessary to commercialize our

We cannot be certain that OCA or any of our other product candidates will receive regulatory approval and the time

TABLE OF CONTENTS

product candidates will depend on our ability to conduct and complete these additional trials as well as assemble various other data to complete our regulatory filings for OCA in the relevant indication or patient population.

There can be no assurance that we will be able to receive marketing approval for OCA in PBC or that we will be able to complete our regulatory filings for any other indication on a timely basis or at all. We cannot predict whether our trials and studies as to NASH or any other indication or patient population will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date or require us to conduct additional studies or trials. For example, while OCA received breakthrough therapy designation from the FDA in January 2015 for the treatment of NASH patients with liver fibrosis, we do not know if one pivotal clinical trial will be sufficient for marketing approval or if regulators will ultimately agree to a surrogate endpoint for accelerated approval of OCA for the treatment of NASH. While the interim histological endpoint is similar to that in the Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health, our Phase 3 REGENERATE trial has different trial designs. For example, the REGNERATE trial will include the following interim co-primary endpoints which are intended to serve as the basis for seeking marketing approvals in the United States, Europe and other countries: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. The REGENERATE trial will also remain blinded after the interim analysis and continue to follow patients until the occurrence of a pre-specified number of adverse liver-related clinical events, including progression to cirrhosis, to confirm clinical benefit on a post-marketing basis.

Furthermore, the Phase 2 dose ranging trial of OCA in 200 adult NASH patients in Japan conducted by our collaborator, Sumitomo Dainippon, did not meet its primary endpoint with statistical significance. In this trial, there was a dose dependent, although not statistically significant, increase in the percentage of OCA treated patients compared to placebo who achieved the primary endpoint (p=0.053). In addition, no difference was seen in fibrosis improvement in the OCA groups compared to placebo. The baseline characteristics between the patients in the Japanese Phase 2 trial conducted by Sumitomo Dainippon were distinct in a number of ways from those of the Western patients included in the Phase 2b FLINT trial conducted by NIDDK. For example, differences were observed among the patient population at baseline in relation to gender mix and metabolic factors like weight, diabetes status, dyslipidemia and hypertension. While our REGENERATE trial was designed based on the results of the FLINT trial and is anticipated to enroll a predominantly Western NASH patient population, the results of the FLINT trial may not be replicated in our REGENERATE trial. Although Sumitomo Dainippon has informed us that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan, the results may not be an improvement as compared to those from the Phase 2 trial on Japanese NASH patients.

If we are unable to obtain approval from the FDA, the EMA or other regulatory agencies for OCA and our other product candidates, or if, subsequent to approval, we are unable to successfully commercialize OCA or our other product candidates, we will not be able to generate sufficient revenue to become profitable or to continue our operations.

We are developing product candidates for the treatment of rare diseases or diseases for which there are no or limited therapies and for some of which there is little clinical experience, and our development approach involves new endpoints and methodologies. As a result, there is increased risk that we will not be able to gain agreement with regulatory authorities regarding an

acceptable development plan, the outcome of our clinical trials will not be favorable or that, even if favorable, regulatory authorities may not find the results of our clinical trials to be sufficient for marketing approval.

Currently, there are no approved therapies for NASH or PSC. As a result, the design and conduct of clinical trials for these diseases and other indications we may pursue will be subject to increased risk.

The FDA generally requires two pivotal clinical trials to approve an NDA. Furthermore, for full approval of an NDA, the FDA requires a demonstration of efficacy based on a clinical benefit endpoint. Under Subpart

We are developing product candidates for the treatment of rare diseases or diseases for which there are li

 or limite

TABLE OF CONTENTS

H regulations, the FDA can grant accelerated approval based on a surrogate reasonably likely to predict clinical benefit. The POISE primary endpoint is a surrogate endpoint that we believe is reasonably likely to predict clinical benefit, therefore meeting the FDA s Subpart H requirements for consideration under its accelerated approval regulation. In August 2015, the FDA accepted our NDA for filing and granted Priority Review for OCA for the treatment of PBC. A target date of May 29, 2016 has been set to take action under PDUFA, after giving effect to a 90 day extension. It is unlikely we will receive definitive written guidance from the FDA prior to formal review of our NDA as to the acceptability of the POISE trial surrogate endpoint to support an approval of OCA for the treatment of PBC. Although the results from our POISE trial are highly significant and supported by two controlled Phase 2 trials, our POISE trial and our regulatory submissions package may nonetheless not be sufficient to support approval in the United States. In addition, it is possible that the FDA may not complete its review of our NDA by the specified PDUFA action date, may seek to delay our PDUFA date through a major amendment as it did in December 2015 for our NDA for OCA in PBC or may provide a complete response letter denying our application for marketing authorization. We anticipate that similar risks will apply to other indications for which we intend to seek marketing approval for our product candidates under accelerated approval regulations. For example, we will face these risks for OCA for the treatment of NASH because of our plan to seek accelerated approval based on the REGENERATE trial which incorporates interim co-primary surrogate endpoints.

In order to support the clinical utility of the surrogate endpoint for OCA as a treatment for PBC, we have sponsored an independent study pooling and analyzing long-term PBC patient data from a number of leading PBC academic centers, which we refer to as the Global PBC Study Group. Furthermore, an academic consortium in the United Kingdom has published the results of another large observational study in PBC patients in the United Kingdom. Although we believe the results of both studies are supportive of the clinical utility of our surrogate endpoint for the use of OCA in PBC, the supporting data may still not be accepted by the FDA in its consideration of the adequacy of our surrogate endpoint under an NDA for OCA for the treatment of PBC. In addition to the risk around the acceptability of the surrogate biochemical endpoint to support accelerated approval, there are quality assurance risks around the data supporting assessment of the biochemical endpoint. It is possible that key parameters such as the validation of the assay and consistency across laboratories will not be acceptable to FDA and could delay or jeopardize approval of the NDA.

The FDA has also informed us that, even if it provides us an accelerated approval for OCA, we will be required to conduct a post-approval clinical outcomes trial to confirm the clinical benefit of OCA in PBC by demonstrating the correlation of biochemical therapeutic response in patients taking OCA with a significant reduction in adverse clinical outcomes over time. Following discussions with the FDA, we initiated our COBALT clinical outcomes confirmatory trial in December 2014. There can be no assurance that our COBALT trial will confirm that the surrogate endpoints used for accelerated approval will eventually show an adequate correlation with clinical outcomes. If the COBALT trial fails to show such adequate correlation, we may not be able to maintain our previously granted marketing approval for OCA in PBC.

Likewise, while we completed our filing of the MAA with the EMA in June 2015, we will not receive definitive feedback from the EMA prior to formal review of our MAA as to the acceptability of the POISE trial endpoint to support a marketing authorization of OCA for the treatment of PBC. It is also possible that any marketing authorization we receive from the EMA for OCA for the treatment of PBC could be conditional on post-approval studies and not considered a full approval. Our ability to obtain and maintain conditional marketing authorization in the European Union will be limited to specific circumstances and subject to several conditions and obligations, if obtained at all, including the completion of a clinical outcomes trial to confirm the clinical benefit of OCA in PBC. Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under European Union law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to

provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the

TABLE OF CONTENTS

conditional marketing authorization. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions.

Our Phase 3 REGENERATE trial of OCA in non-cirrhotic NASH patients with liver fibrosis, which was initiated in September 2015, incorporates interim co-primary surrogate endpoints that may serve as the basis for a supplemental NDA filing for accelerated approval in the United States and approval in Europe. Accelerated approval in the United States and conditional approval in the European Union for OCA in NASH are subject to similar risks as discussed above in relation to OCA for PBC. The primary endpoint in the Phase 2b FLINT trial of OCA in NASH patients was based on liver biopsy and was defined as an improvement of two or more points in the NAFLD activity score (a system of scoring the histopathological features in the liver), or NAS, with no worsening of liver fibrosis and the co-primary endpoints for our REGENERATE trial are: (i) the proportion of OCA-treated patients relative to placebo achieving at least one stage of liver fibrosis improvement with no worsening NASH and (ii) the proportion of OCA-treated patients relative to placebo achieving NASH resolution with no worsening of liver fibrosis. Currently, other biopharmaceutical companies are enrolling or have initiated trials in certain subpopulations of NASH patients based on different endpoints from those in the FLINT and REGENERATE trials. Although the FDA acknowledged at recent workshops the possibility of granting accelerated approval for NASH therapies using surrogate endpoints, with potential examples including histological improvement, using the NAS or another scoring system, histological resolution of NASH, or improvements in fibrosis in pre-cirrhotic patients with NASH, the FDA did not provide any formal regulatory guidance on approvable endpoints and may not accept a surrogate endpoint for OCA for the treatment of NASH.

The FDA generally requires two pivotal clinical trials to approve an NDA. Therefore, even if we achieve favorable results in a single Phase 3 clinical trial, the FDA may not accept this one trial as an adequate basis for approval and require that we conduct and complete a second Phase 3 clinical trial before considering an NDA for any of the indications for which we may seek marketing approval for our product candidates. Our NDA for OCA for the treatment of PBC patients who have an inadequate response to or are intolerant of ursodiol will be based on the results of three clinical trials the POISE trial and two Phase 2 trials. It is possible that our final NDA submission for regulatory approval will not be accepted by the FDA for review or, even if it is accepted for review, that there may be delays in the FDA s review process and that the FDA may determine that our NDA does not merit the approval of OCA for the treatment of PBC, in particular because we have only conducted a single Phase 3 clinical trial of OCA for the treatment of PBC, in which case the FDA may require that we conduct and/or complete additional clinical trials and preclinical studies before it will reconsider our application for approval. A similar risk applies if we seek marketing approval of OCA for non-cirrhotic NASH patients with liver fibrosis based on the interim results of our REGENERATE trial. Our regulatory pathway for OCA for the treatment of NASH will depend upon our discussions with the FDA and EMA. As a result, we may face difficulty in designing an acceptable registration strategy around REGENERATE or any other trials in different subpopulations of NASH patients. In addition, since the design of the REGENERATE trial deviates from that of the FLINT trial, there is an increased risk that the results of the REGENERATE trial would differ from the FLINT results.

The EMA and regulatory authorities in other countries in which we may seek approval for, and market, OCA or our other product candidates may require additional preclinical studies and/or clinical trials prior to granting approval. It may be expensive and time consuming to conduct and complete additional preclinical studies and clinical trials that the FDA, EMA and other regulatory authorities may require us to perform. As such, any requirement by the FDA, EMA or other regulatory authorities that we conduct additional preclinical studies or clinical trials could materially and adversely affect our business, financial condition and results of operations. Furthermore, even if we receive regulatory approval of OCA for the treatment of any of our targeted indications, the labeling for our product candidates in the United States, Europe or other countries in which we seek approval may include limitations that

could impact the commercial success of our product candidates.

We are developing product candidates for the treatment of rare diseases or diseases for which there are no or limite

TABLE OF CONTENTS

Delays in the commencement, enrollment and completion of clinical trials could result in increased costs to us and delay or limit our ability to obtain regulatory approval for OCA and our other product candidates.

Delays in the commencement, enrollment and completion of clinical trials could increase our product development costs or limit the regulatory approval of our product candidates. We initiated our COBALT clinical outcomes confirmatory trial of OCA in PBC in December 2014, our Phase 2 AESOP trial of OCA in PSC in December 2014, our REGENERATE trial in September 2015, our Phase 2 CARE trial of OCA in biliary atresia in October 2015 and our Phase 2 CONTROL trial to assess the lipid metabolic effects of OCA and the effects of concomitant statin administration in NASH patients in December 2015. The results from these trials may not be available when we expect or we may be required to conduct additional clinical trials or preclinical studies not currently planned to receive approval for OCA as a treatment for the related indication, in which case we would require additional funding. In addition, our clinical programs are subject to a number of variables and contingencies, such as the results of other trials or regulatory interactions that may result in a change in timing. As such, we do not know whether any future trials or studies of our other product candidates, including our COBALT trial, will begin on time or will be completed on schedule, if at all.

The commencement, enrollment and completion of clinical trials can be delayed or suspended for a variety of reasons, including:

inability to obtain sufficient funds required for a clinical trial or lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions;

inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;

discussions with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials;

inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indications targeted by our product candidates;

the delay in receiving results from or the failure to achieve the necessary results in other clinical trials;

inability to obtain approval from institutional review boards, or IRBs, to conduct a clinical trial at their respective sites;

severe or unexpected drug-related adverse effects experienced by patients or any determination that a clinical trial presents unacceptable health risks;

a breach of the terms of any agreement with, or for any other reason by, current or future collaborators that have responsibility for the clinical development of any of our product candidates, including Sumitomo Dainippon and Servier or investigators leading clinical trials on our product candidates;

inability to timely manufacture sufficient quantities of the product candidate required for a clinical trial;

difficulty recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our trial, the risks of procedures that may be required as part of the trial, such as a liver biopsy, and competition from other clinical trial programs for the same indications as our product candidates; and

inability to retain enrolled patients after a clinical trial is underway.

Delays in the commencement, enrollment and completion of clinical trials could result in increased costs to us and d

TABLE OF CONTENTS

For example, in the past, we experienced delays in our Phase 2 clinical trial of OCA given as a monotherapy to patients with PBC because we were unable to find and enroll a sufficient number of trial patients who met the specific enrollment criteria in accordance with our anticipated trial schedule.

Changes in regulatory requirements and guidance may also occur and we or any of our collaborators may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us or any of our collaborators to resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

In addition, if we or any of our collaborators are required to conduct additional clinical trials or other preclinical studies of our product candidates beyond those contemplated, our ability to obtain regulatory approval of these product candidates and generate revenue from their sales would be similarly harmed.

Clinical failure can occur at any stage of clinical development. The results of earlier clinical trials are not necessarily predictive of future results and any product candidate we, Sumitomo Dainippon, Servier or our potential future collaborators advance through clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Clinical failure can occur at any stage of our clinical development. Clinical trials may produce negative or inconclusive results, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Success in preclinical studies and early clinical trials does not ensure that subsequent clinical trials will generate the same or similar results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in Phase 3 clinical trials and at other stages of clinical development, even after seeing promising results in earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. We may be unable to design and execute a clinical trial to support regulatory approval. Further, clinical trials of potential products often reveal that it is not practical or feasible to continue development efforts. If OCA or our other product candidates are found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for them, the prospects for approval of OCA would be materially and adversely affected and our business would be harmed.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes or differences in trial protocols, differences in composition of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our collaborators may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates. If we are unable to bring any of our current or future product candidates to market, or to acquire any marketed, previously approved products, our ability to create long-term stockholder value will be limited.

We believe that the results of our POISE trial and our long-term safety extension trials in PBC patients, which include

patients who currently have been on OCA therapy for more than four years, demonstrate that OCA produces a durable therapeutic response. We completed our filings for marketing approval of OCA in PBC in the United States and the European Union in June 2015. In August 2015, the FDA accepted our NDA for filing and granted Priority Review for OCA for the treatment of PBC. The target date for the FDA to take action under PDUFA was initially set for February 29, 2016. In December 2015, our PDUFA action date was extended to May 29, 2016 due to an information request from the FDA that resulted in the submission of additional clinical data analyses. We cannot assure you that our POISE trial results will result in our receiving marketing approval for OCA in PBC or that our ongoing COBALT clinical outcomes confirmatory trial of OCA in PBC will demonstrate a correlation of biochemical therapeutic response in patients taking OCA with a significant reduction in adverse clinical events over time. In addition, it is possible that the FDA may not

Clinical failure can occur at any stage of clinical development. The results of earlier clinical trials are not necessarily

TABLE OF CONTENTS

complete its review of our NDA by the specified PDUFA action date, may seek to delay our PDUFA date through a major amendment or may provide a complete response letter denying our application for marketing authorization.

In December 2014, we received comprehensive datasets from the FLINT trial, which met its primary endpoint with statistical significance. In October 2015, we announced that the Phase 2 dose ranging trial of OCA in the Sumitomo Dainippon Phase 2 trial did not meet its primary endpoint with statistical significance. In this trial, there was a dose dependent, although not statistically significant, increase in the percentage of OCA treated patients compared to placebo who achieved the primary endpoint (p=0.053). In addition, no difference was seen in fibrosis improvement in the OCA groups compared to placebo. The Phase 2 trial in NASH conducted in Japan by our collaborator Sumitomo Dainippon involved different doses of OCA being administered to the trial subjects than those utilized in FLINT. Furthermore, the baseline characteristics between the patients in the Japanese Phase 2 trial conducted by Sumitomo Dainippon were distinct in a number of ways from those of the Western patients included in FLINT. While our REGENERATE trial was designed based on the results of the FLINT trial and is anticipated to enroll a predominantly Western NASH patient population, the results of the FLINT trial may not be replicated in our REGENERATE trial. In addition, since the design of the REGENERATE trial deviates from that of the FLINT trial, there is an increased risk that the results of the REGENERATE trial would differ from the FLINT results. Even though OCA has been granted breakthrough therapy designation by the FDA, we do not know if one pivotal clinical trial will be sufficient for marketing approval or if regulators will agree to a surrogate endpoint for accelerated approval of OCA for the treatment of NASH. As a result, it may take longer than anticipated to initiate and complete the Phase 3 REGENERATE trial or our Phase 3 program in NASH for other patient subpopulations.

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require our product candidates to be taken off the market, require them to include safety warnings or otherwise limit their sales.

A substance that binds to a receptor of a cell and triggers a response by that cell is called an agonist. OCA has been shown to be a potent agonist of the farnesoid X receptor, or FXR. With the exception of the endogenous human bile acid CDCA and cholic acid, there are no approved FXR agonists and the adverse effects from long-term exposure to this drug class are unknown. Unforeseen side effects from any of our product candidates could arise either during clinical development or, if approved, after the approved product has been marketed.

The most common side effects observed in clinical trials of OCA in PBC were pruritus, or itching, fatigue, headaches, nausea, constipation and diarrhea. In our Phase 2 PBC clinical trial of OCA in combination with ursodiol, approximately 8% of the patients enrolled in the 10 mg and 25 mg dose groups withdrew from the trial due to severe pruritus. At the 50 mg dose, approximately 25% of the patients withdrew from the trial due to severe pruritus. In our POISE trial, pruritus, generally mild to moderate, was the most frequently reported adverse event associated with OCA treatment and was observed in 38% of patients on placebo, 68% of patients in the 10 mg OCA group and 56% of patients in the OCA titration group (5 mg to 10 mg). Eight patients discontinued due to pruritus, of whom none were in the placebo group, seven (10%) patients were in the 10 mg OCA group and one (1%) patient was in the OCA titration group (in a patient who had titrated up to 10 mg). Pruritus also has been observed in other clinical trials of OCA.

Based on information in the manuscript for the FLINT trial published in November 2014, pruritus occurred more frequently in the OCA treatment group than in the placebo treatment group (23% vs. 6%, $p < 0.001$) and at a higher grade (predominately moderate pruritus), but resulted in only one patient discontinuation in the OCA treatment group. In the FLINT trial, OCA treatment was associated with changes in serum lipid levels, including increases in total

cholesterol and LDL cholesterol and a decrease in HDL cholesterol, that were observed within 12 weeks of initiating treatment, peaked and then decreased in magnitude while on treatment, and reversed further during the 24-week post-treatment period. As previously disclosed, these changes in cholesterol levels, along with achieving the pre-defined efficacy criteria, played a role in the decision of the FLINT data and safety monitoring board to terminate the treatment phase of FLINT, and the publication of the FLINT results has noted the need for further study of these changes. In December 2015, we initiated CONTROL, a Phase 2 trial characterizing the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients. There were two patient

TABLE OF CONTENTS

deaths in the FLINT trial that were previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2013, and neither death was considered related to OCA treatment.

Additional or unforeseen side effects from these or any of our other product candidates could arise either during clinical development or, if approved, after the approved product has been marketed. If new side effects are found during the development of OCA for any indication, if known side effects are shown to be more severe than previously observed or if OCA is found to have other unexpected characteristics, we may need to abandon our development of OCA for PBC, NASH, PSC, biliary atresia and other potential indications.

The range and potential severity of possible side effects from systemic therapies is significant. The results of future clinical trials may show that our product candidates cause undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, or result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings.

In addition, our drug candidates are being developed as potential treatments for severe, life threatening diseases and, as a result, our trials will necessarily be conducted in a patient population that will be more prone than the general population to exhibit certain disease states or adverse events. It may be difficult to discern whether certain events or symptoms observed during our trials were due to our drug candidates or placebo, resulting in our company and our development programs being negatively affected even if such events or symptoms are ultimately determined to be unlikely related to our drug candidates. We further cannot assure you that additional or more severe adverse side effects with respect to OCA will not develop in future clinical trials, which could delay or preclude regulatory approval of OCA or limit its commercial use.

If any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;
we may be subject to limitations on how we may promote the product;
sales of the product may decrease significantly;
regulatory authorities may require us to take our approved product off the market;
we may be subject to litigation or product liability claims; and
our reputation may suffer.

Any of these events could prevent us, Sumitomo Dainippon, Servier or our potential future collaborators from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of our products.

Breakthrough therapy designation for OCA may not lead to faster development or regulatory processes nor does it increase the likelihood that OCA will receive marketing approval for NASH.

If a drug is intended for the treatment of a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically

significant endpoints, such as substantial treatment effects observed early in clinical development, the FDA may grant a breakthrough therapy designation. Breakthrough therapy designation is intended to facilitate the development, and expedite the review of such drugs, but the breakthrough therapy designation does not assure any such qualification or ultimate marketing approval by the FDA.

In January 2015, we received breakthrough therapy designation for OCA in the treatment of NASH patients with fibrosis. However, there is no guarantee that the receipt of breakthrough therapy designation will result in a faster development process, review or approval for OCA in fibrotic NASH patients or increase the likelihood that OCA will be granted marketing approval for fibrotic NASH patients. Likewise, any future

TABLE OF CONTENTS

breakthrough therapy designation for any other potential indication of OCA neither guarantees a faster development process, review or approval nor improves the likelihood of the grant of marketing approval by FDA for any such potential indication of OCA compared to drugs considered for approval under conventional FDA procedures. In addition, the FDA may withdraw any breakthrough therapy designation at any time. We may seek a breakthrough therapy designation for other of our product candidates, but the FDA may not grant this status to any of our proposed product candidates.

We may not be able to obtain or maintain orphan drug exclusivity for our product candidates, if approved, which would cause our revenues to suffer.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. In addition, it is possible that orphan drug designation in Europe will not be maintained following approval if the EMA determines that the product does not satisfy the requisite criteria including demonstration of significant clinical benefit. In November 2015, the European Commission set forth a consultation document and a notice detailing proposed amendments to the rules governing orphan medicinal products which may make it more difficult to demonstrate significant clinical benefit at the time of marketing authorization. The result of this process may impact our ability to maintain orphan drug designation in Europe.

The failure to maintain orphan status may impact our ability to receive a premium price for OCA or our other products and may subject us to mandatory price discounts in Europe. In addition, our ability to launch in Europe may be delayed and we may lose other benefits such as tax exemptions for sales. As such, the loss of orphan drug status may have a negative effect on our ability to successfully commercialize our products, earn revenues and achieve profitability.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA and EMA can subsequently approve the later product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance of our product candidates, if approved. If there is not sufficient reimbursement for our products or they are not covered

at all, it is less likely that they will be widely used.

Market acceptance and sales of OCA or any other product candidates that we develop, if approved, will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. We cannot be certain that reimbursement will be available for OCA or any other product candidates that we develop. Also, reimbursement policies could reduce the demand for, or the price paid for, our products. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize OCA or any other product candidates that we develop.

Reimbursement decisions by third-party payors may have an adverse effecton pricing and market acceptance of ou

TABLE OF CONTENTS

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. Any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, ACA, became law in the United States. The goal of ACA is to reduce the cost of health care and substantially change the way health care is financed by both governmental and private insurers. The ACA requires discounts under the Medicare drug benefit program and increased the rebates paid by pharmaceutical companies on drugs covered by Medicaid. The ACA also imposes an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers.

In addition, third-party payors attempt to contain health care costs by demanding price discounts or rebates and limiting both the types and variety of drugs that they will cover and the amounts that they will pay for drugs. As a result, they may not cover or provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products or any other future products to such payors satisfaction. Such studies might require us to commit a significant amount of management s time and our financial and other resources. Our products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Reimbursement in the European Union and many other territories must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The timing to complete the negotiation process in each country is highly uncertain, and in some countries we expect that it may exceed 12 months. Even after a price is negotiated, countries frequently request or require adjustments to the price and other concessions over time. Reimbursement agencies in Europe are often more conservative than those in the United States and the reimbursement process is often slower since reimbursement decisions are made on a country-by-country basis.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of OCA and any other products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws, commonly referred to as fraud and abuse laws, have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. Other jurisdictions such as Europe have similar laws and are enacting more stringent regulations. These laws include false claims and anti-kickback statutes. If we market our products and our products are paid for by governmental programs, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price

TABLE OF CONTENTS

other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service covered by Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers or formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Most states also have statutes or regulations similar to the federal anti-kickback law and federal false claims laws, which apply to items and services covered by Medicaid and other state programs, or, in several states, apply regardless of the payor. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

Over the past few years, a number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates.

If the FDA and EMA and other regulatory agencies do not approve the manufacturing facilities of our future contract manufacturers for commercial production on a timely basis or at all, we may not be able to commercialize any of our product candidates or commercialization of our product candidates could be delayed.

We do not intend to manufacture the pharmaceutical products that we plan to sell. We currently have agreements with a contract manufacturer for the production of the active pharmaceutical ingredients and the formulation of sufficient quantities of drug product for the COBALT clinical outcomes confirmatory trial of OCA in PBC and the long-term safety extension phase of the POISE trial for OCA in PBC, our Phase 3 NASH program for OCA, including the REGENERATE trial, and the certain other trials and preclinical studies that we plan to conduct prior to and after seeking regulatory approval. If our contract manufacturer should cease to provide services to us for any reason, we likely would experience delays in advancing our clinical trials while we identify and qualify one or more replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us.

We do not have agreements for commercial supplies of OCA or any of our other product candidates. We currently obtain these supplies and services from our third-party contract manufacturers on a purchase order basis. We are currently seeking to contract to qualify one or more back-up API manufacturers. While we have procured sufficient supplies for the commercial launch of OCA, we may not be able to reach agreements with these or other contract manufacturers for sufficient supplies to continue commercial sales of OCA on a long-term basis.

Additionally, the facilities used by any contract manufacturer to manufacture OCA or any of our other product candidates must be the subject of a satisfactory inspection before the FDA or the regulators in other jurisdictions approve the product candidate manufactured at that facility. We are completely dependent on these third-party manufacturers for compliance with the requirements of U.S. and non-U.S. regulators for the manufacture of our finished products. If our manufacturers cannot successfully manufacture material that conform to our specifications and current good manufacturing practice requirements of any governmental agency whose jurisdiction to which we are subject, our product candidates will not be approved or, if already approved, may be subject to recalls.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates, including:

the possibility that we are unable to enter into a manufacturing agreement with a third party to manufacture our product candidates;

If the FDA and EMA and other regulatory agencies do not approve the manufacturing facilities of our future contract

TABLE OF CONTENTS

the possible breach of the manufacturing agreements by the third parties because of factors beyond our control; and the possibility of termination or nonrenewal of the agreements by the third parties before we are able to arrange for a qualified replacement third-party manufacturer.

Any of these factors could cause the delay of approval or commercialization of our product candidates, cause us to incur higher costs, prevent us from commercializing our product candidates successfully or disrupt the supply of our products after commercial launch. Furthermore, if any of our product candidates are approved and contract manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for our products and could lose potential revenue. It may take several years to establish an alternative source of supply for our product candidates and to have any such new source approved by the government agencies that regulate our products.

Even if our product candidates receive regulatory approval, we will still be subject to strict regulatory requirements governing manufacturing and marketing of our products and, as a result, we could face future development and regulatory difficulties.

Our product candidates, if approved, will also be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. In addition, approved products, manufacturers and manufacturers facilities are required to comply with extensive FDA and EMA requirements and requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMPs. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and EMA and other similar agencies and to comply with certain requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product s approved label. Accordingly, we may not promote our approved products, if any, for indications or uses for which they are not approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters;

mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;

require us or our collaborators to enter into a consent decree or permanent injunction, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;

impose other administrative or judicial civil or criminal penalties;

withdraw regulatory approval;

refuse to approve pending applications or supplements to approved applications filed by us, Sumitomo Dainippon, Servier or our potential future collaborators;

impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products.

Even if our product candidates receive regulatory approval, we will still be subject to strict regulatory requirements g

TABLE OF CONTENTS

Risks Related to the Commercialization of Our Products

Even if approved, our product candidates may not achieve broad market acceptance among physicians, patients and healthcare payors, and as a result our revenues generated from their sales may be limited.

Our NDA and MAA for OCA in PBC has been undergoing regulatory review with the FDA and EMA, respectively. If we receive marketing approval from the FDA on the PDUFA date, we plan to initiate the commercial launch of OCA in PBC in the United States in June 2016. Furthermore, if we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned commercial launches thereafter in certain European countries.

The commercial success of OCA or our other product candidates, if approved, will depend upon their acceptance among the medical community, including physicians, healthcare payors and patients. For PBC, the current standard of care is ursodeoxycholic acid, which is available generically as ursodiol. In order for OCA to be commercially successful, we will need to demonstrate that it is safe and effective for the treatment of patients who have an inadequate response to or who are unable to tolerate ursodiol, referred to as second line treatment, and is more effective than any other alternatives that may be developed as a second line treatment for PBC, particularly given the much higher price that we anticipate charging for OCA compared to the price of generically available ursodiol. In NASH and PSC, since there are currently no approved therapies, we do not know the degree to which OCA will be accepted as a therapy, even if approved.

The degree of market acceptance of our product candidates will depend on a number of factors, including:

limitations or warnings contained in our product candidates FDA or EMA-approved labeling;
changes in the standard of care or availability of alternative therapies at similar or lower costs for the targeted indications for any of our product candidates, such as ursodiol for the treatment of PBC;
limitations in the approved clinical indications for our product candidates;
demonstrated clinical safety and efficacy compared to other products;
lack of significant adverse side effects;
sales, marketing and distribution support;
availability of reimbursement from managed care plans and other third-party payors;
timing of market introduction and perceived effectiveness of competitive products;
the degree of cost-effectiveness;
availability of alternative therapies at similar or lower cost, including generics and over-the-counter products;
the extent to which our product candidates are approved for inclusion on formularies of hospitals and managed care organizations;
whether our product candidates are designated under physician treatment guidelines for the treatment of the indications for which we have received regulatory approval;
adverse publicity about our product candidates or favorable publicity about competitive products;
convenience and ease of administration of our product candidates; and
potential product liability claims.

In addition, the potential market opportunity for our product candidates is difficult to precisely estimate. While ursodiol is the established standard of care for PBC, a majority of patients while on therapy remain at ALP levels

above the upper limit of normal, or ULN. According to our analysis of industry data in PBC, approximately 70% of patients treated with ursodiol experience elevated ALP levels, with 35% of patients experiencing ALP levels greater than 1.67 times ULN. In addition, a small minority of PBC patients (estimated at approximately 3%) are intolerant to ursodiol therapy. Our estimates of the potential market

Even if approved, our product candidates may not achieve broad market acceptance among physicians, patients ar

TABLE OF CONTENTS

opportunity for OCA for the treatment of PBC include a number of key assumptions related to prevalence rates, patients access to healthcare, diagnosis rates and patients response to or tolerance of OCA, which are based on available literature and epidemiology research in PBC, our industry knowledge gained through market research and other methods, industry publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of these assumptions prove to be inaccurate, then the actual market for OCA could be smaller than our estimates of our potential market opportunity. If the actual market opportunity for our product candidates is smaller than we expect, our product revenue may be limited.

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

We have no sales, marketing or distribution experience and we will have to invest significant additional resources to develop those capabilities or enter into acceptable third-party sales and marketing arrangements.

We have no sales, marketing or distribution experience and have only recently started the build out of our internal commercial organization. We plan to commercialize OCA for PBC in the United States and Europe ourselves with a targeted sales force if and when it is approved and may utilize the services of third-party collaborators in certain jurisdictions. To develop internal sales, distribution and marketing capabilities, we have invested and will continue to invest significant additional amounts of financial and management resources, some of which will be committed prior to any confirmation that OCA or any of our other product candidates will be approved. For example, in October 2015, we hired our territory business managers who are anticipated to constitute our sales force upon approval. Recruiting and training a commercial organization is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel.

For product candidates where we decide to perform sales, marketing and distribution functions ourselves or through third parties, we could face a number of additional risks, including:

we or our third-party sales collaborators may not be able to attract and build an effective marketing or sales force;
the cost of securing or establishing a marketing or sales force may exceed the revenues generated by any products; and
our direct sales and marketing efforts may not be successful.

We have entered into an agreement with Sumitomo Dainippon for the development and commercialization of OCA in Japan, China, South Korea and potentially other Asian countries, if approved, and have entered into an agreement with Servier to assist in the development and commercialization of certain of our earlier stage agonists of a dedicated bile acid receptor called TGR5 outside of the United States and Japan, if approved, and may elect to seek additional strategic collaborators for our product candidates. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

If any of our current strategic collaborators fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated and our business could be substantially harmed.

We currently have strategic collaborations in place relating to certain of our product candidates. We entered into an exclusive license agreement with Sumitomo Dainippon regarding the development and commercialization of OCA for PBC and NASH in Japan, China and South Korea and provided Sumitomo

TABLE OF CONTENTS

Dainippon with an option to extend its exclusive license to different indications as well as certain other Asian countries. We entered into a strategic collaboration with Servier initially focused on the identification and optimization of novel TGR5 agonists for the treatment of type 2 diabetes and other associated disorders. These strategic collaborations may not be scientifically or commercially successful due to a number of important factors, including the following:

Sumitomo Dainippon and Servier have significant discretion in determining the efforts and resources that each will apply to their strategic collaboration with us. The timing and amount of any cash payments, milestones and royalties that we may receive under such agreements will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of our product candidates by Sumitomo Dainippon and Servier under their respective agreements;

Our agreement with Servier provides it with wide discretion in deciding which novel compounds to advance through the preclinical and clinical development process. It is possible for Servier to reject certain compounds at any point in the research, development and clinical trial process without triggering a termination of their agreement with us;

Our agreement with Sumitomo Dainippon restricts it from developing or commercializing any FXR agonist to treat PBC or NASH during the term of the agreement other than pursuant to the Sumitomo Dainippon agreement and our agreement with Servier restricts it from developing or commercializing any TGR5 receptor agonist during the term of the agreement other than pursuant to the Servier agreement. Subject to these restrictions, it is possible that Sumitomo Dainippon or Servier may develop and commercialize, either alone or with others, or be acquired by a company that has, products that are similar to or competitive with the product candidates that they license from us;

Sumitomo Dainippon or Servier may change the focus of their development and commercialization efforts or pursue higher-priority programs;

Sumitomo Dainippon or Servier may, under specified circumstances, terminate their strategic collaborations with us on short notice and for circumstances outside of our control, which could make it difficult for us to attract new strategic collaborators or adversely affect how we are perceived in the scientific and financial communities;

Sumitomo Dainippon and Servier have, under certain circumstances, the right to maintain or defend our intellectual property rights licensed to them in their territories, and, although we may have the right to assume the maintenance and defense of our intellectual property rights if our strategic collaborators do not, our ability to do so may be compromised by our strategic collaborators acts or omissions;

Sumitomo Dainippon or Servier may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability; and

Sumitomo Dainippon or Servier may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If either Sumitomo Dainippon or Servier fails to develop or effectively commercialize OCA or any TGR5 compounds, respectively, we may not be able to replace them with another collaborator. For example, although Sumitomo Dainippon has informed us that it is exploring the initiation of a Phase 3 clinical trial for OCA in NASH patients intended to support the registration of this indication in Japan, Sumitomo Dainippon may ultimately decide not to pursue such a trial or cease continuing development despite commencing the trial. We may also be unable to obtain, on terms acceptable to us, a license from such strategic collaborator to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

If any of our current strategic collaborators fails to perform its obligations or terminates its agreement with us, the de

TABLE OF CONTENTS

We may not be successful in establishing and maintaining development and commercialization collaborations, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results.

Because developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, expanding manufacturing capabilities and marketing approved products are expensive, we have entered into, and may seek to enter into, collaborations with companies that have more experience and resources than we have. For example, we have entered into collaborations with Sumitomo Dainippon for OCA and Servier for our earlier stage TGR5 program. We may establish additional collaborations for development and commercialization of OCA in territories outside of those licensed by Sumitomo Dainippon or for our earlier stage TGR5 program in the United States or Japan and for other product candidates and research programs, including INT-767 and INT-777. Additionally, if any of our product candidates receives marketing approval, we may enter into sales and marketing arrangements with third parties with respect to our unlicensed territories. If we are unable to maintain our existing arrangements or enter into any new such arrangements on acceptable terms, if at all, we may be unable to effectively market and sell our products in our target markets. We expect to face competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements for the development of our product candidates.

When we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. For example, Sumitomo Dainippon has the exclusive rights to OCA in Japan, China and South Korea and a right of first refusal to license OCA in several other Asian countries. Our collaboration partner may not devote sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization. The terms of any collaboration or other arrangement that we establish may not be favorable to us. In addition, any collaboration that we enter into, including our collaborations with Sumitomo Dainippon and Servier, may be unsuccessful in the development and commercialization of our product candidates. In some cases, we may be responsible for continuing preclinical and initial clinical development of a product candidate or research program under a collaboration arrangement, and the payment we receive from our collaboration partner may be insufficient to cover the cost of this development. If we are unable to reach agreements with suitable collaborators for our product candidates, we would face increased costs, we may be forced to limit the number of our product candidates we can commercially develop or the territories in which we commercialize them and we might fail to commercialize products or programs for which a suitable collaborator cannot be found. If we fail to achieve successful collaborations, our operating results and financial condition will be materially and adversely affected.

If we fail to develop OCA for additional indications, our commercial opportunity will be limited.

To date, we have focused the majority of our development efforts on the development of OCA for the second line treatment of PBC. Among our other product candidates, only INT-767, which is undergoing Phase 1 clinical trials, is currently in clinical development. One of our strategies is to pursue clinical development of OCA for other orphan and more common indications, to the extent that we have sufficient funding.

PBC is a rare disease for which we plan to seek marketing approval for OCA as a second-line treatment and, as a result, the market size for treatments of PBC is limited. Furthermore, because a significant proportion of PBC patients

do not exhibit any symptoms at the time of diagnosis, PBC may be left undiagnosed for a significant period of time. Due to these factors, our ability to grow revenues will be dependent on our ability to successfully develop and commercialize OCA for the treatment of additional indications, including NASH. In particular, we believe that our future success will depend in large part on the results of our development of OCA for the treatment of NASH. Although NASH is believed to be one of the most prevalent chronic liver diseases worldwide, NASH may be left undiagnosed for a long time and a definitive diagnosis of NASH is currently based on a histological assessment of a liver biopsy, which impacts the ability to easily identify patients. Furthermore, even if we are successful in developing and obtaining marketing approval of OCA for the treatment of NASH, we may not be able to commercialize OCA successfully.

TABLE OF CONTENTS

The completion of development, securing of approval and commercialization of OCA for additional indications will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully advance any of these indications through the development process. Even if we receive FDA or EMA approval to market OCA for the treatment of any of these additional indications, we cannot assure you that any such additional indications will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize OCA for these additional indications, our commercial opportunity will be limited and our business prospects will suffer.

Risks Related to Our Business and Strategy

We face competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in the United States, Europe and other jurisdictions, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies and universities and other research institutions. Many of our competitors have greater financial and other resources, such as larger research and development staff and more experienced marketing and manufacturing organizations. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater research, sales and marketing capabilities and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA or EMA approval or discovering, developing and commercializing drugs for the diseases that we are targeting before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Some of the pharmaceutical and biotechnology companies we expect to compete with include Albireo AB, Akarna Therapeutics Ltd., AstraZeneca plc, Biotie Therapies Corp. (acquired by Acorda Therapeutics, Inc.), Boehringer Ingelheim GmbH, Bristol-Myers Squibb Company, Conatus Pharmaceuticals Inc., Dr. Falk Pharma GmbH, Durect Corporation, Eli Lilly, Enanta Pharmaceuticals, Inc., ENYO Pharma SAS, Exelixis, Inc., FibroGen, Inc., FF Pharmaceuticals BV, Galectin Therapeutics Inc., Galmed Medical Research Ltd., Genfit SA, Genkyotex SA, Gilead Sciences, Inc., GlaxoSmithKline, Immuron Ltd., Islet Sciences, Inc., Medivation, Inc., MiNA Therapeutics, NGM Biopharmaceuticals, Nitto Denko Corporation, Novartis International AG, Novo Nordisk A/S, NuSirt Biopharma, Inc., Protalix Biotherapeutics, Shire plc, Tobira Therapeutics, Inc., Viking Therapeutics, Inc. and Zydus Pharmaceuticals Inc. Ongoing Phase 3 clinical trials for the treatment of PBC include an investigator-sponsored trial of bezafibrate, a fibrate that has not been approved for commercialization by the FDA and is only available outside of the United States, and a combination of ursodiol and budesonide, a steroid, sponsored by Dr. Falk Pharma GmbH. Genfit SA has an ongoing Phase 3 clinical trial of GFT505, a dual PPAR alpha/delta agonist, in NASH. Gilead Sciences, Inc. is conducting multiple Phase 2 clinical trials in NASH patients of various disease severity with both simtuzimab, an anti-body against the lysyl oxidase-like 2 enzyme, and GS-4997, an inhibitor of the apoptosis signal-regulating kinase 1. Gilead Sciences, Inc. is also studying an FXR agonist (GS-9674) for the treatment of NASH. A number of companies have trials in PBC, NASH and other liver diseases we are targeting.

In addition, many universities and private and public research institutes may become active in our target disease areas. The results from our POISE and FLINT trials have brought more attention to our targeted indications and bile acid chemistry. As a result, we believe that additional companies and organizations may seek to compete with us in the future. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, technologies and drug products that are more effective or less costly than OCA or any other product candidates that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive.

TABLE OF CONTENTS

Off-label uses of other potential treatments may limit the commercial potential of our product candidates, especially given the anticipated pricing for our product candidates. For example, while fibrates are not approved for use in PBC, off-label use of fibrate drugs has been reported, though many fibrates are specifically contraindicated for use in PBC due to potential concerns over acute and long-term safety in this patient population. In NASH, a number of treatments, including vitamin E (an antioxidant), insulin sensitizers (such as metformin), antihyperlipidemic agents (such as gemfibrozil), pentoxifylline and ursodiol, are used off-label. Although none of these treatments have been clearly shown in clinical trials to alter the course of the disease, in a previous study conducted by the NASH Clinical Research Network, similar improvements to those observed with OCA in the FLINT trial in certain histological measures of NASH were reported with vitamin E and pioglitazone. Various other treatments, both approved and unapproved, have been used in the other indications we are targeting.

We believe that our ability to successfully compete will depend on, among other things:

the results of our and our strategic collaborators clinical trials and preclinical studies;
our ability to recruit and enroll patients for our clinical trials;
the efficacy, safety and reliability of our product candidates;
the speed at which we develop our product candidates;
our ability to design and successfully execute appropriate clinical trials;
our ability to maintain a good relationship with regulatory authorities;
the timing and scope of regulatory approvals, if any;
our ability to commercialize and market any of our product candidates that receive regulatory approval;
the price of our products;
adequate levels of reimbursement under private and governmental health insurance plans, including Medicare;
our ability to protect intellectual property rights related to our products;
our ability to manufacture and sell commercial quantities of any approved products to the market; and
acceptance of our product candidates by physicians and other health care providers.

If our competitors market products that are more effective, safer or less expensive than our future products, if any, or that reach the market sooner than our future products, if any, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

We depend on third-party contractors for a substantial portion of our operations and may not be able to control their work as effectively as if we performed these functions ourselves.

We outsource and plan to continue to outsource substantial portions of our operations to third-party service providers, including the conduct of preclinical studies and clinical trials, collection and analysis of data and manufacturing. We will likely use the services of third-party vendors in relation to our commercialization activities, including product sales, marketing and distribution. Our agreements with third-party service providers are on a study-by-study and/or project-by-project basis. Typically, we may terminate the agreements with notice and are responsible for the supplier s previously incurred costs. In addition, a number of third-party service providers that we retain will be subject to the FDA s and EMA s regulatory requirements and similar standards outside of the United States and Europe and we do not have control over compliance with these regulations by these providers. Consequently, if these providers do not adhere to applicable

We depend on third-party contractors for a substantial portion of our operations and may not be able to control their

TABLE OF CONTENTS

governing practices and standards, the development and commercialization of our product candidates could be delayed or stopped, which could severely harm our business and financial condition.

Because we have relied on third parties, our internal capacity to perform these functions is limited to management oversight. Outsourcing these functions involves the risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. Several years ago, we experienced difficulties with a third-party contract manufacturer for OCA, including delays in receiving adequate clinical trial supplies as requested within the requested time periods. We subsequently replaced this manufacturer with other third-party contract manufacturers for OCA. It is possible that we could experience similar difficulties in the future. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. There are a limited number of third-party service providers that specialize or have the expertise required to achieve our business objectives. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. Despite our recent growth, we currently have a small number of employees, which limits the internal resources we have available to identify and monitor third-party service providers. To the extent we are unable to identify, retain and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. We may further be subject to the imposition of civil or criminal penalties if their conduct of clinical trials violates applicable law.

Our third-party service providers generally are not prohibited from providing their services to other biopharmaceutical companies, including companies that currently or may in the future compete with us. For example, certain of our third-party service providers and consultants may be able to develop intellectual property to which we are not entitled under our agreements which may eventually be used to develop products that compete with our products. Although we generally have confidentiality and non-disclosure agreements in place with our third-party service providers and consultants, such third parties may be able to provide services to other companies without violating the terms of our agreements. In addition, although we may seek to enter into non-compete arrangements with our key third-party service providers, such arrangements are difficult to negotiate and we may be unable to successfully enter into such arrangements.

A variety of risks associated with our international business operations and our planned international business relationships could materially adversely affect our business.

We have recently formed a wholly-owned subsidiary in the United Kingdom which we anticipate will serve as our headquarters for our operations in Europe and anticipate building out our European operations. We also currently have an Italian subsidiary that acts as our legal representative for our clinical trials in the European Union to satisfy European Union regulatory requirements. We have also formed a number of other wholly-owned subsidiaries in Europe and Canada in preparation for the anticipated commercial launch of OCA in PBC. In addition, we have entered into an agreement with Sumitomo Dainippon for the development of OCA and with Servier for our earlier stage TGR5 program, and we may enter into agreements with other third parties for the development and commercialization of OCA or our other product candidates in international markets. Our international operations and business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- differing regulatory requirements for drug approvals internationally;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights in countries outside of the United States;

the potential for so-called parallel importing, which is what occurs when a local seller, e.g., a pharmacy, faced with relatively high local prices, opts to import goods from another jurisdiction with relatively low prices, rather than buying them locally;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;

compliance with tax, employment, immigration and labor laws for employees traveling abroad;

A variety of risks associated with our international business operations and our planned international business relati

TABLE OF CONTENTS

taxes in other countries;
foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
workforce uncertainty in countries where labor unrest is more common than in the United States;
production shortages resulting from events affecting raw material supply or manufacturing capabilities abroad; and
business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

Changes in our effective income tax rate could adversely affect our results of operations.

We are subject to income taxes in the United States and various foreign jurisdictions. Various factors may have favorable or unfavorable effects on our effective income tax rate. These factors include, but are not limited to, interpretations of existing tax laws, changes in tax laws and rates, the accounting for stock options and other stock-based compensation, changes in accounting standards, future levels of research and development spending, changes in the mix and level of pre-tax earnings by taxing jurisdiction, the outcome of examinations by the U.S. Internal Revenue Service and regulators of other jurisdictions, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets, or by changes to our ownership or capital structure. The impact on our effective income tax rate resulting from the above-mentioned factors and others may be significant and could adversely affect our results of operations.

We have been significantly expanding our operations and the size of our company and will need to continue our expansion to support our NASH program. We may experience difficulties in managing our significant growth.

From December 31, 2014 to December 31, 2015, our employee base has grown from 136 to 405 employees. Of the 405 employees as of December 31, 2015, 216 employees were in our drug development operations, 117 employees were in our commercial group and 72 employees were in our corporate group. At December 31, 2015, 309 employees were based in the United States, 89 employees were based in Europe and 7 employees were based in Canada. As we advance our programs for OCA in NASH and other potential indications and our other product candidates, seek regulatory approval in the United States and elsewhere, increase the number of ongoing product development programs and advance our product candidates through preclinical studies and clinical trials, we will need to increase our product development, scientific and administrative headcount to manage these programs. We will also need to grow our commercial capabilities, which will require us to hire additional personnel, both for our ongoing pre-commercial activities and for the launch and ongoing marketing and sale of any product candidate for which we obtain marketing approval. In addition, in order to continue to meet our obligations as a public company and to support the anticipated longer-term growth in the other functions at our company, we will need to increase our general and administrative capabilities. We are also expanding our operations geographically and formed a number of wholly-owned subsidiaries outside of the United States, including our wholly-owned subsidiary in the United Kingdom. We also opened an office in London, United Kingdom which serves as our headquarters for our operations in Europe, Canada and Australia. In the longer term, we may further expand our geographical footprint. Our management, personnel and systems currently in place may not be adequate to support this future growth.

Our need to effectively manage our operations, growth and various projects requires that we:

successfully attract and recruit new employees or consultants with the expertise and experience we will require in the United States, Europe and in other jurisdictions;

manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites across the world, and advance our other development efforts;

develop and expand our marketing and sales infrastructure; and

continue to improve our operational, financial and management controls, reporting systems and procedures

We have been significantly expanding our operations and the size of ourcompany and will need to continue our exp

TABLE OF CONTENTS

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

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

We may not be able to attract or retain qualified personnel and consultants across our organization due to the intense competition for qualified personnel and consultants among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercial objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Mark Pruzanski, our co-founder and president and chief executive officer; David Shapiro, our chief medical officer; and our other key employees and consultants. If we lose one or more of our executive officers, or key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees or consultants may terminate their employment at any time. Replacing executive officers, key employees and consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel and consultants.

We have scientific and clinical advisors and consultants, such as our co-founder Professor Roberto Pellicciari, who assist us in formulating our research, development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us and typically they will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Failure to establish and maintain adequate finance infrastructure and accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002, and the related rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting expense and expend significant management efforts. Our testing, or the testing by our

independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner so as to be able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act each year. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner each year, we could be subject to sanctions or investigations by the Securities and Exchange Commission, the NASDAQ Stock Market or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

TABLE OF CONTENTS

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with health care fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations in the United States and abroad intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a global code of business conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for a product candidate and may have to limit its commercialization.

The use of our product candidates in clinical trials and the sale of any products for which we may obtain marketing approval expose us to the risk of product liability claims. Product liability claims may be brought against us or our collaborators by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against any such claims, we would incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

withdrawal of clinical trial participants;
termination of clinical trial sites or entire trial programs;
costs of related litigation;
substantial monetary awards to patients or other claimants;
decreased demand for our product candidates and loss of revenues;
impairment of our business reputation;
diversion of management and scientific resources from our business operations; and
the inability to commercialize our product candidates or the withdrawal of our products from the market.

We have obtained limited product liability insurance coverage for our clinical trials in the United States and in selected other jurisdictions where we are conducting clinical trials. Our product liability insurance coverage for clinical trials in the United States is currently limited to an aggregate of $10 million and outside of the United States we have coverage for amounts that vary by country. As such, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to product liability. We intend to expand our insurance coverage

for products to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful

We face potential product liability exposure, and if successful claims arebrought against us, we may incur substanti

TABLE OF CONTENTS

product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash resources and adversely affect our business.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers compensation, products liability and directors and officers insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations. Furthermore the increased volatility of our stock price may result in us being required to pay substantially higher premiums for our directors and officers insurance than those to which we are currently subject, and may even lead a large number of underwriters to be unwilling to cover us.

If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.

From time to time we have considered, and we will continue to consider in the future, strategic business initiatives intended to further the expansion and development of our business. These initiatives may include acquiring businesses, technologies or products or entering into a business combination with another company. If we pursue such a strategy, we could, among other things:

issue equity securities that would dilute our current stockholders percentage ownership;
incur substantial debt that may place strains on our operations;
spend substantial operational, financial and management resources to integrate new businesses, technologies and products;
assume substantial actual or contingent liabilities;
reprioritize our development programs and even cease development and commercialization of our product candidates; or
merge with, or otherwise enter into a business combination with, another company in which our stockholders would receive cash and/or shares of the other company on terms that certain of our stockholders may not deem desirable.

Although we intend to evaluate and consider acquisitions, reorganizations and business combinations in the future, we have no agreements or understandings with respect to any acquisition, reorganization or business combination at this time.

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

Despite the implementation of security measures and policies, our internal information technology systems, as well as those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs, damage to our reputation and/or monetary damages. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and

significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Our information security systems are subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, the Health Insurance Portability and Accountability Act, or HIPAA, and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security

TABLE OF CONTENTS

of personal health information. In addition to HIPAA, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and storage of personal information. Various foreign countries where we may process personal information also have, or are developing, laws governing the collection, use, disclosure and storage of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues that may affect our business. We have in the past relied on adherence to the U.S.-EU Safe Harbor Framework as agreed to and set forth by the U.S. Department of Commerce and the European Commission as a means to legitimize certain transfers of personal information from the European Economic Area, or EEA, to the United States. However, a recent opinion of the European Union Court of Justice, or ECJ, deemed the U.S.-EU Safe Harbor Framework an invalid method of protecting the transfer of personal information from the EEA to the United States. While we are engaging in efforts to address the implications of the ECJ opinion and actively employing other means to legitimize the transfer of personal information from the EEA to the United States, we may be unsuccessful in these efforts. Failure to comply with laws regarding data protection could expose us to risk of enforcement actions and the potential for significant penalties as well as the loss of access to certain data from the EU. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and can generate negative publicity, which could harm our business.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business, possibly materially.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently own or may own in the future, or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, derivation, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to develop a platform similar to, or better than, ours in a way that is not covered by the claims of our patents;
- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by our pending patent applications;

It is difficult and costly to protect our proprietary rights, and we may not beable to ensure their protection.If our pate

TABLE OF CONTENTS

we might not have been the first to file patent applications for these inventions;
others may independently develop similar or alternative technologies or duplicate any of our technologies;
any patents that we obtain may not provide us with any competitive advantages;
we may not develop additional proprietary technologies that are patentable; or
the patents of others may have an adverse effect on our business.

As of December 31, 2015, we were the owner of record of over 110 issued or granted U.S. and non-U.S. patents relating to OCA with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds, and methods of using these compounds in various indications. We were also the owner at that date of record of 53 pending U.S. and non-U.S. patent applications relating to OCA in these areas.

In addition, as of December 31, 2015, we were the owner of record of over 160 issued or granted U.S. and non-U.S. patents relating to our product candidates other than OCA, with claims directed to pharmaceutical compounds, pharmaceutical compositions, methods of making these compounds and methods of using these compounds in various indications. We were also the owner of record of over 90 pending U.S. and non-U.S. patent applications relating to such other product candidates in these areas.

Patents covering the composition of matter of OCA expire in 2022 at the soonest and 2033 at the latest if the appropriate maintenance renewal, annuity, or other government fees are paid. We expect that the other patents in the OCA portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2033. We expect the issued INT-767 composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2029. We expect the other patents in the INT-767 portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2027 to 2029. We expect the issued INT-777 composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2030. We expect the other patents in the INT-777 portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2028 to 2030.

We have received assignments of rights to the INT-767 patent portfolio from all inventors, with the exception of one inventor. That inventor is contractually obligated to provide an assignment to us. Thus, we believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the patent assignments we have received. By virtue of the patent assignments we have received and other contractual obligations owed to us, we believe we are the owner of the INT-777 patent portfolio.

Without patent protection on the composition of matter of our product candidates, our ability to assert our patents to stop others from using or selling our product candidates in a non-pharmaceutically acceptable formulation may be limited.

Due to the patent laws of a country, or the decisions of a patent examiner in a country, or our own filing strategies, we may not obtain patent coverage for all of our product candidates or methods involving these candidates in the parent patent application. We plan to pursue divisional patent applications or continuation patent applications in the United States and other countries to obtain claim coverage for inventions which were disclosed but not claimed in the parent patent application.

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by e

Depending upon the timing, duration and specifics of FDA marketing approval of OCA and our other product candidates, if any, one or more of our U.S. patents may be eligible for limited extension of patent term under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits an extension of patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by e

TABLE OF CONTENTS

deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. In the event that we are unable to obtain any patent term extensions, the issued composition of matter patents for OCA are expected to expire in 2022 at the soonest and 2033 at the latest, assuming they withstand any challenge. We expect that the other patents for the OCA portfolio, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2033.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

If we choose to go to court to stop another party from using the inventions claimed in any patents we obtain, that individual or company has the right to ask the court to rule that such patents are invalid, not infringed, or should not be enforced against that third party. These lawsuits are expensive and would consume time and resources and divert the attention of managerial and scientific personnel even if we were successful in stopping the infringement of such patents. In addition, there is a risk that the court will decide that such patents are not valid or not infringed, and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of such patents is upheld, the court will refuse to stop the other party on the ground that such other party s activities do not infringe our rights to such patents. In addition, the U.S. Supreme Court has recently modified some tests used by the U.S. Patent and Trademark Office, or USPTO, in granting patents over the past 20 years, which may decrease the likelihood that we will be able to obtain patents and increase the likelihood of challenge of any patents we obtain or license.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. We cannot guarantee that our products, or manufacture or use of our product candidates, will not infringe third-party patents. Furthermore, a third party may claim that we or our manufacturing or commercialization collaborators are using inventions covered by the third party s patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our product candidates. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and scientific personnel. There is a risk that a court would decide that we or our commercialization collaborators are infringing the third party s patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our commercialization collaborators may not have a viable way around the patent and may need to halt commercialization of the relevant product. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages for having violated the other party s patents. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not

infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management s time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to

TABLE OF CONTENTS

a successful conclusion. In addition, if we fail to obtain a license, develop or obtain non-infringing technology or defend an infringement action successfully, or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent the technology, because:

some patent applications in the United States may be unpublished or otherwise maintained in secrecy until the patents are issued;

patent applications in the United States are typically not published until 18 months after the priority date; and

publications in the scientific literature often lag behind actual discoveries.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications, and such patent applications may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

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

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

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and products could be significantly diminished.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

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

TABLE OF CONTENTS

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA s disclosure policies may change in the future, if at all. Moreover, the EMA has already adopted a policy of general transparency both in relation to requests under EU freedom of information legislation for access to pre-clinical and clinical research data once marketing authorizations are granted and through proactive disclosure of clinical data on its website. This policy coupled with imminent requirements for public disclosure of clinical research data under a new EU Clinical Trial Regulation, means that public disclosure will ordinarily be made of substantial research data that previously would have been considered commercially confidential. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

We have applied for a number of trademarks and service marks to further protect the proprietary position of our products. We have approximately 280 pending trademark and service mark applications in the United States and abroad. Our trademark applications may not be allowed for registration or our registered trademarks may not be maintained or enforced. During prosecution of applications for trademark registration, we may receive rejections or refusals. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Trademark protection varies in accordance with local law, and continues in some countries as long as the trademark is used and in other countries as long as the trademark is registered. Trademark registrations generally are for fixed but renewable terms. We cannot provide any assurances that any trademarks or service marks will be sufficient to prevent competitors from adopting similar names. The adoption of similar names by competitors could impede our ability to build brand identity and lead to customer confusion, which could adversely affect our sales or profitability.

In addition, we have not yet received final approval from regulatory authorities for a proprietary name for any of our product candidates, including OCA, in any jurisdiction. Any proprietary name we propose to use with OCA in the United States and Europe must be approved by the FDA and EMA, respectively, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA and EMA typically conduct a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or EMA objects to our proposed proprietary product names, we may be required to expend significant additional resources in

an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the regulatory agencies.

We have not yet registered all of our trademarks and failure to secure those registrations could adversely affect our

TABLE OF CONTENTS

Risks Related to Ownership of Our Common Stock

An active trading market in our common stock may not be maintained.

The trading market in our common stock has been extremely volatile. The quotation of our common stock on The NASDAQ Global Select Market does not assure that a meaningful, consistent and liquid trading market will exist. We cannot predict whether an active market for our common stock will be maintained in the future. An absence of an active trading market could adversely affect our stockholders ability to sell our common stock at current market prices in short time periods, or possibly at all. Additionally, market visibility for our common stock may be limited and such lack of visibility may have a depressive effect on the market price for our common stock. As of December 31, 2015, approximately 40.04% of our outstanding shares of common stock was held by our officers, directors, beneficial owners of 5% or more of our securities (other than FMR LLC, Carmignac Gestion, Capital World Investors, Ameriprise Financial, Inc. and their respective affiliates) and their respective affiliates, which adversely affects the liquidity of the trading market for our common stock, in as much as federal securities laws restrict sales of our shares by these stockholders. If our affiliates continue to hold their shares of common stock, there will be limited trading volume in our common stock, which may make it more difficult for investors to sell their shares or increase the volatility of our stock price.

We are currently subject to securities class action litigation and may be subject to similar or other litigation in the future, which may divert management s attention.

On February 21, 2014 and February 28, 2014, purported shareholder class actions, styled *Scot H. Atwood v. Intercept Pharmaceuticals, Inc. et al.* and *George Burton v. Intercept Pharmaceuticals, Inc. et al.*, respectively, were filed in the United States District Court for the Southern District of New York, naming us and certain of our officers as defendants. These lawsuits were filed by stockholders who claim to be suing on behalf of anyone who purchased or otherwise acquired our securities between January 9, 2014 and January 10, 2014.

The lawsuits allege that we made material misrepresentations and/or omissions of material fact in our public disclosures during the period from January 9, 2014 to January 10, 2014, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The alleged improper disclosures relate to our January 9, 2014 announcement that the FLINT trial had been stopped early based on a pre-defined interim efficacy analysis. Specifically, the lawsuits claim that the January 9, 2014 announcement was misleading because it did not contain information regarding certain lipid abnormalities seen in the FLINT trial in OCA-treated patients compared to placebo.

On April 22, 2014, two individuals each moved to consolidate the cases and a lead plaintiff was subsequently appointed by the Court. On June 27, 2014, the lead plaintiff filed an amended complaint on behalf of the putative class as contemplated by the order of the Court. On August 14, 2014, the defendants filed a motion to dismiss the complaint. Oral arguments on the motion to dismiss were held on February 24, 2015. On March 4, 2015, the defendants motion to dismiss was denied by the Court. The defendants answered the amended complaint on April 13, 2015. On July 15, 2015, the plaintiff moved for class certification and appointment of class representatives and class counsel. On September 14, 2015, the defendants opposed the plaintiff s class certification motion. The plaintiff filed its reply to the defendants opposition on October 14, 2015, to which the defendants filed a sur-reply on November 10, 2015. Oral arguments on the class certification motion were held on January 20, 2016. No decision has been made by the Court on the class certification motion. The parties are currently undergoing discovery in relation to this matter.

Dispositive motions are due on September 16, 2016.

The lead plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including attorneys fees.

While we believe we have valid defenses to the claims in the lawsuit, have denied liability and intend to defend ourselves vigorously, we cannot predict the outcome of the lawsuit. There may be additional suits or proceedings brought in the future. Monitoring and defending against legal actions, whether or not meritorious, is time-consuming for our management and detracts from our ability fully to focus our internal resources on our business activities, and we cannot predict how long it may take to resolve these matters. In addition, we

We are currently subject to securities class action litigation and may besubject to similar or other litigation in the futu

TABLE OF CONTENTS

may incur substantial legal fees and costs in connection with litigation. Although we have insurance, coverage could be denied or prove to be insufficient. We are not currently able to estimate the possible cost to us from these lawsuits, and we cannot be certain how long it may take to resolve these lawsuits or the possible amount of any damages that we may be required to pay. We have not established any reserves for any potential liability relating to these lawsuits. It is possible that we could, in the future, incur judgment or enter into settlement of claims for monetary damages. A decision adverse to our interests on either of these lawsuits could result in the payment of substantial damages and could have a material adverse effect on our business, results of operations and financial condition. In addition, the uncertainty of the currently pending lawsuits could lead to more volatility in our stock price.

Our stock price has been and may in the future be volatile, which could cause purchasers of our common stock to incur substantial losses.

The trading price of our stock price has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Since our initial public offering which occurred in October 2012, the price of our common stock on The NASDAQ Global Select Market has ranged from $17.96 per share to $497.00 per share. In addition to the other factors discussed in this Risk Factors section, these factors include:

adverse results or delays in our clinical trials;
inability to obtain additional funding;
any delay in filing an IND, NDA, MAA or comparable submission for any of our product candidates and any adverse development or perceived adverse development with respect to the regulatory review of such submission;
failure to successfully develop and commercialize OCA and any of our other product candidates;
failure to maintain our existing strategic alliances or enter into new alliances;
inability to obtain adequate product supply for OCA and our future product candidates or the inability to do so at acceptable prices;
results of clinical trials of our competitors products;
regulatory actions with respect to our products or our competitors products;
changes in laws or regulations applicable to our future products;
failure to meet or exceed financial projections we may provide to the public;
failure to meet or exceed the estimates and projections of the investment community;
actual or anticipated fluctuations in our financial condition and operating results;
actual or anticipated changes in our growth rate relative to our competitors;
actual or anticipated fluctuations in our competitors operating results or changes in their growth rate;
competition from existing products or new products that may emerge;
announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
issuance of new or updated research or reports by securities analysts;
fluctuations in the valuation of companies perceived by investors to be comparable to us;
share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
additions or departures of key management or scientific personnel;
disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

TABLE OF CONTENTS

announcement or expectation of additional financing efforts;
significant lawsuits, including patent or stockholder litigation, involving us;
sales of our common stock by us, our insiders or our other stockholders;
failure to adopt appropriate information security systems, including any systems that may be required to support our growing and changing business requirements;
market conditions for biopharmaceutical stocks in general; and
general economic, industry and market conditions.

Furthermore, the stock markets in general and the market for biotechnology companies in particular have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations may negatively impact the market price of shares of our common stock, regardless of our actual operating performance. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We are currently subject to class action securities lawsuits and may be the target of this type of litigation in the future, which could result in substantial costs and divert our management s attention from other business concerns, which could seriously harm our business. As a result of this volatility, our stockholders could incur substantial losses.

We have a significant stockholder, which will limit your ability to influence corporate matters and may give rise to conflicts of interest.

Genextra S.p.A., together with its affiliates, whom we refer to collectively as Genextra, is our largest stockholder. As of December 31, 2015, Genextra owned 6,454,953 shares of our common stock. The shares of common stock owned by Genextra represented approximately 26.5% of our outstanding common stock as of December 31, 2015. Accordingly, Genextra exerts and will continue to exert significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors and amendments to our organizational documents, such as increases in our authorized shares of common stock and approval of significant corporate transactions. This concentration of voting power makes it less likely that any other holder of common stock or directors of our business will be able to affect the way we are managed and could delay or prevent an acquisition of us on terms that other stockholders may desire.

Furthermore, the interests of Genextra may not always coincide with your interests or the interests of other stockholders, and Genextra may act in a manner that advances its best interests and not necessarily those of other stockholders, including seeking a premium value for its common stock, and might affect the prevailing market price for our common stock. Our board of directors, which consists of nine directors, including two affiliated with Genextra, has the power to set the number of directors on our board from time to time.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosure due to error or fraud may occur and not be detected.

TABLE OF CONTENTS

You may experience future dilution as a result of future equity offerings.

In the future, we may offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock in order to raise additional capital. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share you paid for our shares. Investors purchasing shares or other securities in the future could have rights, preferences or privileges senior to those of existing stockholders and you may experience dilution. You may incur additional dilution upon the exercise of any outstanding stock options or vesting of restricted stock units or awards.

If securities or industry analysts cease publishing research or reports about us, our business or our market, or if they publish inaccurate or unfavorable reports about our stock, the price of our stock and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about our company. We do not have any control over these analysts, and there can be no assurance that analysts will continue to cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of the analysts covering us fail to regularly publish reports on us, demand for our common stock could decline, which could cause our stock price and trading volume to decline.

Anti-takeover provisions in our restated certificate of incorporation and our restated by-laws, as well as provisions of Delaware law, might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our restated certificate of incorporation and restated bylaws, as well as provisions of Delaware law, contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Our corporate governance documents include provisions:

authorizing the issuance of blank check convertible preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;

prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders, to the extent that no stockholder, together with its affiliates, holds more than 50% of our voting stock;

eliminating the ability of stockholders to call a special meeting of stockholders;

permitting our board of directors to accelerate the vesting of outstanding equity awards upon certain transactions that result in a change of control; and

establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, as a Delaware corporation, we are subject to provisions of Delaware law, including Section 203 of the Delaware General Corporation Law, or DGCL, which prevents some stockholders holding more than 15% of our outstanding common stock from engaging in certain business combinations without approval of the holders of

substantially all of our outstanding common stock. Any provision of our restated certificate of incorporation or restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

The existence of the foregoing provisions and anti-takeover measures may also frustrate or prevent any attempts by our stockholders to replace or remove our current management or members of our board of directors and could limit the price that investors might be willing to pay in the future for shares of our

Anti-takeover provisions in our restated certificate of incorporation and ourrestated by-laws, as well as provisions of

TABLE OF CONTENTS

common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful stockholder claims against us and may reduce the amount of money available to us.

As permitted by Section 102(b)(7) of the DGCL, our restated certificate of incorporation limits the liability of our directors to the fullest extent permitted by law. In addition, as permitted by Section 145 of the DGCL, our restated certificate of incorporation and restated bylaws provide that we shall indemnify, to the fullest extent authorized by the DGCL, each person who is involved in any litigation or other proceeding because such person is or was a director or officer of our company or is or was serving as an officer or director of another entity at our request, against all expense, loss or liability reasonably incurred or suffered in connection therewith. Our restated certificate of incorporation provides that the right to indemnification includes the right to be paid expenses incurred in defending any proceeding in advance of its final disposition, provided, however, that such advance payment will only be made upon delivery to us of an undertaking, by or on behalf of the director or officer, to repay all amounts so advanced if it is ultimately determined that such director is not entitled to indemnification. If we do not pay a proper claim for indemnification in full within 60 days after we receive a written claim for such indemnification, except in the case of a claim for an advancement of expenses, in which case such period is 20 days, our restated certificate of incorporation and our restated bylaws authorize the claimant to bring an action against us and prescribe what constitutes a defense to such action.

Section 145 of the DGCL permits a corporation to indemnify any director or officer of the corporation against expenses (including attorney s fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action (i.e., one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

The rights conferred in the restated certificate of incorporation and the restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons. We have entered into indemnification agreements with each of our officers and directors.

The above limitations on liability and our indemnification obligations limit the personal liability of our directors and officers for monetary damages for breach of their fiduciary duty as directors by shifting the burden of such losses and expenses to us. Although we have increased the coverage under our directors and officers liability insurance, certain liabilities or expenses covered by our indemnification obligations may not be covered by such insurance or the coverage limitation amounts may be exceeded. As a result, we may need to use a significant amount of our funds to satisfy our indemnification obligations, which could severely harm our business and financial condition and limit the funds available to stockholders who may choose to bring a claim against our company.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2015 and 2014, we had net operating loss carryforwards, or NOLs, for federal income tax purposes of $454.4 million and $221.2 million, respectively, which expire between 2024 and 2035. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code. The limitations apply if an ownership change, as defined by

TABLE OF CONTENTS

Section 382 of the Internal Revenue Code, occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points over their lowest ownership percentage in a testing period (typically three years). We have evaluated whether one or more ownership changes as defined under Section 382 of the Internal Revenue Code have occurred since our inception and have determined that there have been at least two such changes. Although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to utilize these NOLs may be limited due to future ownership changes or for other reasons. Additionally, tax laws limit the time during which NOLs and certain other tax attributes may be utilized against future taxes. As a result, we may not be able to take full advantage of our carryforwards for federal, state, and foreign tax purposes.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters and clinical development operations are located in New York, New York and San Diego, California, where we lease and occupy approximately 20,626 and 47,000 square feet of space, respectively.

In February 2015, we entered into an underlease with Merck Sharp & Dohme Limited for our new office in the King s Cross area of London, United Kingdom. The lease provides us with approximately 6,000 rentable square feet in London for office space. The lease term is anticipated to end in June 2019.

On January 22, 2016, Intercept Pharma Europe Ltd., or IPEL, our wholly owned subsidiary, entered into an underlease with Performing Right Society, Ltd. for additional office space in the Kings Cross area of London, United Kingdom. We are the guarantor to the underlease. The underlease provides IPEL with an additional 8,549 square feet of office space. The lease term is anticipated to end on May 31, 2024.

On February 23, 2016, we entered into a sublease for an additional 10,785 square feet of office space in New York, New York. The lease term is anticipated to end on July 31, 2021.

Item 3. Legal Proceedings

See Item 1. Business Legal Proceedings of this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures

Not applicable.

TABLE OF CONTENTS

PART II

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

Market Information

Our common stock began trading on the NASDAQ Global Market on October 11, 2012 under the symbol ICPT . The following table sets forth, for the quarterly periods indicated, the high and low sales prices per share of our common stock as reported on the NASDAQ Global Select Market for each quarter in the years ended December 31, 2015 and 2014.

Year Ended December 31, 2015	High	Low
First quarter	$ 308.28	$ 144.79
Second quarter	314.88	232.19
Third quarter	285.00	150.00
Fourth quarter	217.99	137.28

Year Ended December 31, 2014	High	Low
First quarter	$ 497.00	$ 65.22
Second quarter	339.67	209.00
Third quarter	349.08	208.00
Fourth quarter	264.92	128.50

Stockholders

As of January 31, 2016, there were 390 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers.

Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock from October 11, 2012 through December 31, 2015 to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on October 10, 2012 in our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index and it assumes the reinvestment of dividends, if any. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

TABLE OF CONTENTS

Comparison of Cumulative Total Return* Among Intercept Pharmaceuticals, Inc., the NASDAQ Composite Index and the NASDAQ Biotechnology Index

* $100 invested on 10/10/2012 in stock or index. Fiscal Year ending December 31, 2015.

The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Form 10-K into any filing under the Securities Act of 1933, as amended, or Securities Act, or the Securities Exchange Act of 1934, as amended, or Exchange Act, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Recent Sales of Unregistered Securities

Except as previously disclosed in our Quarterly Reports during 2015, we did not sell any securities that were not registered under the Securities Act.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

TABLE OF CONTENTS

Item 6. Selected Financial Data

The selected financial data set forth below is derived from our audited consolidated financial statements. The following selected consolidated financial data should be read in conjunction with Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the notes thereto included elsewhere in this Annual Report on Form 10-K. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of our future results.

	Years Ended December 31,				
	2015	2014	2013	2012	2011
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Licensing revenues	$2,782	$1,742	$1,622	$2,446	$1,805
Operating expenses:					
Research and development	128,193	80,311	27,941	16,183	11,426
General and administrative	103,745	34,601	13,132	5,177	4,209
Total operating expenses	231,938	114,912	41,073	21,360	15,635
Loss from operations	(229,156)	(113,170)	(39,451)	(18,914)	(13,830)
Total other income (expense), net	2,727	(170,056)	(28,341)	(24,729)	1,093
Net loss	$(226,429)	$(283,226)	$(67,792)	$(43,643)	$(12,737)
Dividend on preferred stock, not declared				(2,630)	(3,000)
Net loss attributable to common stockholders	$(226,429)	$(283,226)	$(67,792)	$(46,273)	$(15,737)
Net loss per share, basic and diluted	$(9.56)	$(13.63)	$(3.76)	$(7.36)	$(4.73)
Weighted average shares outstanding, basic and diluted	23,694,244	20,784,438	18,028,731	6,283,238	3,329,666

	December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$628,056	$239,724	$144,832	$110,194	$17,707
Total assets	655,758	254,149	150,319	112,179	19,470
Accounts payable, accrued expenses and other liabilities	45,591	13,459	7,260	3,746	1,504
Warrant liability			50,112	30,359	5,836
Deferred revenue	8,017	9,799	10,541	12,162	14,608
Common and preferred stock	24	21	19	17	31
Additional paid-in capital	1,300,008	700,355	268,302	184,100	72,134
Accumulated deficit	(695,630)	(469,202)	(185,976)	(118,183)	(74,540)
Total stockholders equity (deficit)	602,149	230,891	82,406	65,912	(2,560)

TABLE OF CONTENTS

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this Annual Report on Form 10-K, including those set forth under Item 1A. Risk Factors and under Forward-Looking Statements in this Annual Report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat non-viral, progressive liver diseases. Our product candidates have the potential to treat orphan and more prevalent liver diseases for which there currently are limited therapeutic solutions.

Our lead product candidate, obeticholic acid, or OCA, is a bile acid analog, a chemical substance that has a structure based on a naturally occurring human bile acid, that selectively binds to and activates the farnesoid X receptor, or FXR, which we believe has broad liver-protective properties. OCA has been tested in five placebo-controlled clinical trials, including a Phase 3 clinical trial in patients with primary biliary cirrhosis, recently renamed primary biliary cholangitis, or PBC, and two Phase 2 clinical trials in patients with nonalcoholic fatty liver disease, or NAFLD, and nonalcoholic steatohepatitis, or NASH. OCA met the primary efficacy endpoint in each of these trials with statistical significance. In addition, in October 2015, we announced results from a Phase 2 dose ranging trial of OCA in 200 patients with NASH in Japan conducted by our collaborator, Sumitomo Dainippon Pharma Co., Ltd., or Sumitomo Dainippon.

In January 2015, OCA received breakthrough therapy designation from the U.S. Food and Drug Administration, or FDA, for the treatment of NASH patients with liver fibrosis. OCA has also been granted fast track designation by the FDA for the treatment of patients with PBC who have an inadequate response to or are intolerant of ursodiol. OCA has received orphan drug designation in the United States and the European Union for the treatment of PBC and primary sclerosing cholangitis, or PSC.

Our most advanced development program for OCA is for PBC as a second line treatment for patients who have an inadequate response to or who are unable to tolerate standard of care therapy and therefore need additional treatment. PBC is a chronic autoimmune liver disease that, if inadequately treated, may eventually lead to cirrhosis, liver failure and death. In March 2014, we completed a Phase 3 clinical trial, known as the POISE trial, in which OCA achieved the primary endpoint for the treatment of PBC. We intend to use these results, along with two previously completed randomized Phase 2 clinical trials of OCA in PBC, as the basis for seeking the first regulatory approvals to market OCA in the United States, Europe, Australia and Canada.

In June 2015, we completed our filings for marketing approval of OCA in PBC in the United States under the FDA s accelerated approval pathway. In August 2015, the FDA accepted our New Drug Application, or NDA, for filing and granted Priority Review for OCA for the treatment of PBC. The FDA set a target date of May 29, 2016 to take action under the Prescription Drug User Fee Act, or PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. If we receive marketing approval from the FDA on the PDUFA date, we plan to initiate the commercial launch of OCA in PBC in the United States in June 2016.

In June 2015, we also received notice of the acceptance of the Marketing Authorization Application, or MAA, for review by the European Medicines Agency, or EMA, for use of OCA in PBC. If we are successful in the EMA review process, we anticipate receiving marketing approval in late 2016, with planned commercial launches thereafter in certain European countries. We also plan to apply for marketing approval of OCA in PBC in other markets across the world such as Australia and Canada.

OCA achieved the primary endpoint in a Phase 2b clinical trial for the treatment of NASH, known as the FLINT trial, which was sponsored by the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, a part of the National Institutes of Health. The FLINT trial was completed in late July 2014. We initiated our Phase 3 clinical trial in non-cirrhotic NASH patients with liver fibrosis, known as

TABLE OF CONTENTS

the REGENERATE trial, in September 2015. In December 2015, we initiated a Phase 2 clinical trial, known as the CONTROL trial, to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients.

In addition to PBC and NASH, we plan to continue our research on OCA in patient populations suffering from other liver diseases, as we believe that FXR has broad therapeutic potential. In December 2014, we initiated an international Phase 2 clinical trial, known as the AESOP trial, in patients with PSC to evaluate the effects of 24 weeks of treatment with varying doses of OCA compared to placebo. In October 2015, we initiated a Phase 2 clinical trial, known as the CARE trial, of OCA in pediatric patients with biliary atresia. This trial will evaluate the effects of 11 weeks of OCA treatment where patients with biliary atresia will be randomized to varying doses of OCA or a control group receiving only their current treatment. As part of our development program, in November 2015, we initiated a Phase 1 clinical trial of our second product candidate to enter clinical development, called INT-767, a dual FXR and TGR5 agonist, in healthy volunteers. We are currently evaluating our future development strategy for OCA in other indications, for INT-767 and for our pre-clinical candidates.

Our net losses were approximately $226.4 million, $283.2 million and $67.8 million for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, we had an accumulated deficit of approximately $695.6 million. Substantially all our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations and from the mark-to-market of our previously outstanding liability-classified warrants.

We have devoted substantially all of our resources to our development efforts relating to our product candidates, including expansion of our clinical, regulatory and medical affairs infrastructure, conducting clinical trials of our product candidates, expansion of our manufacturing activities, providing general and administrative support for our operations, engaging in pre-commercialization activities and building our commercial infrastructure and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. From our inception until December 31, 2015, we have funded our operations primarily through the private and public sales of preferred stock, common stock, convertible notes and warrants to purchase common stock and payments received under our collaboration agreements totaling $623.2 million (net of issuance costs of $33.7 million). In February 2015, we completed a public offering of 1,150,000 shares of our common stock pursuant to a registration statement on Form S-3. After underwriting discounts and commissions and offering expenses, we received net proceeds of approximately $191.6 million. In April 2015, we completed a public offering of 1,330,865 shares of its common stock pursuant to a registration statement on Form S-3. After underwriting discounts and commissions and offering expenses, we received net proceeds of approximately $367.1 million.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially as we:

complete the development of our lead product candidate, OCA, for the treatment of PBC, and continue the development of OCA in NASH, PSC and other patient populations;

seek to obtain regulatory approvals for OCA for PBC, NASH, PSC and other potential patient populations;

prepare for the potential commercialization of OCA in PBC, including enhancing our sales, marketing and distribution capabilities and increasing our drug manufacturing activities;

continue development of our other product candidates, such as INT-767, and engage in other research and development activities;

maintain, expand and protect our intellectual property portfolio;

increase our product development, scientific, commercial and administrative personnel and expand our facilities and operations in the United States and abroad; and

operate as a public company.

TABLE OF CONTENTS

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain marketing approval for one or more of our product candidates, which is subject to significant uncertainty. Even if we receive marketing approvals for OCA in PBC and commence our commercial launch, we do not expect to generate significant revenues in PBC in 2016. Accordingly, we anticipate that we will need to raise additional capital to commercialize OCA on a worldwide basis and continue our research and development activities in relation to OCA and our other pipeline candidates. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our operating activities through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our product candidates.

Our principal executive offices are in New York, New York. We also have administrative offices in San Diego, California and London, United Kingdom.

Financial Overview

Revenue

To date, we have not generated any revenue from the sale of products. If we are successful with our regulatory approval process for OCA in PBC, we expect to generate sales revenue starting in June 2016 in the United States and in 2017 in certain European countries. We do not expect to generate any meaningful sales revenues until 2017 at the earliest.

All of our revenue has been derived from our collaborative agreements for the development and commercialization of certain of our product candidates. We have entered into an exclusive licensing agreement with Sumitomo Dainippon for the development of OCA in Japan, China and Korea. Under the terms of the agreement, we have received up-front payments of $16.0 million, including $1.0 million upon the exercise by Sumitomo Dainippon of its option to add Korea to its licensed territories, and may be eligible to receive up to approximately $300 million in additional payments for development, regulatory and commercial sales milestones for OCA in the licensed territories. As of December 31, 2015, we have achieved $1.0 million of the development milestones.

For accounting purposes, the up-front payments are recorded as deferred revenue and amortized over time and milestone payments are recognized once earned. We recognized $2.8 million, $1.7 million and $1.6 million in license revenue for the years ended December 31, 2015, 2014 and 2013 respectively. For the year ended December 31, 2015, $1.8 million resulted from the amortization of the up-front payments under the collaboration agreement and $1.0 million resulted from the milestone achieved in the period. All of the revenue recognized in the years ended December 31, 2014 and 2013 related to the amortization of the up-front payments under the collaboration agreement. We anticipate that we will recognize revenue of approximately $1.8 million per year through 2020, for the amortization of the relevant up-front collaboration payments from Sumitomo Dainippon. We did not receive any milestone payments during 2012, 2013 or 2014 related to our collaboration agreements. In the future, we may generate revenue from a combination of license fees and other up-front payments, research and development payments, milestone payments, product sales and royalties in connection with our collaborations. We expect that any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing of our achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of our products are approved and successfully commercialized by us or our collaboration partners. If our

collaboration partners fail to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

TABLE OF CONTENTS

Research and Development Expenses

Since our inception, we have focused our resources on our research and development activities, including conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for our product candidates. We recognize research and development expenses as they are incurred. Our research and development expenses consist primarily of direct costs, personnel costs and indirect costs such as the following:

Direct costs:

fees paid to consultants and clinical research organizations, or CROs, including in connection with our preclinical and clinical trials, and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work, clinical trial database management, clinical trial material management and statistical compilation and analysis;

costs related to activities associated with acquiring and manufacturing OCA;

costs associated with discovery and early stage research initiatives; and

costs related to compliance with regulatory requirements.

Personnel costs:

salaries and related benefit expenses for personnel in research and development functions; and

costs related to stock compensation granted to personnel in research and development functions.

Indirect costs:

rent and other facilities-related costs; and

product-related legal costs.

We plan to increase our research and development expenses for the foreseeable future as we continue the development of OCA for the treatment of PBC, NASH and PSC and other indications and to further advance the development of our other product candidates, subject to the availability of additional funding.

The table below summarizes our direct research and development expenses by program for the periods indicated. We do not allocate personnel and indirect costs related to our research and development function to specific product candidates. Those expenses are included in personnel costs and indirect research and development expense in the table below.

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Direct research and development expense by program:			
OCA	$ 58,906	$ 51,316	$ 16,467
Research and discovery initiatives	6,043		
INT-767	6,265	1,527	534
INT-777			49
Total direct research and development expense	71,214	52,843	17,050
Personnel costs	48,057	23,525	9,852
Indirect research and development expense	8,922	3,943	1,039
Total research and development expense	$ 128,193	$ 80,311	$ 27,941

Personnel costs include stock-based compensation expense associated with stock options, restricted stock units, or RSUs, and restricted stock awards, or RSAs, granted to employees and non-employees of $17.9 million, $11.7 million

and $4.7 million for the years ended December 31, 2015, 2014 and 2013, respectively. For the year ended December 31, 2015, we had a net increase of 66 research and development personnel in support of our expansion in activities.

Indirect costs:

TABLE OF CONTENTS

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash inflows from these product candidates, including OCA, may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

the scope, rate of progress and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;

future clinical trial results; and

the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. We may also face delays in the regulatory review process, as we did with OCA in PBC where the target date for the FDA to take action under PDUFA, was extended from February 29, 2016 until May 29, 2016.

OCA

During 2015, the majority of our research and development resources were focused on completing our NDA and MAA filings for OCA for the treatment of PBC, which were completed during June 2015. In August 2015, the FDA accepted our NDA for filing and granted priority review for OCA for the treatment of PBC. The FDA set a target date of May 29, 2016 to take action under PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. In addition to the review by the FDA, we are undergoing our regulatory review process with the EMA.

In relation to OCA, we have incurred and expect to continue to incur significant expenses in connection with these efforts, including:

Continuing the long-term safety extension phase of our Phase 3 POISE trial of OCA in PBC potentially through 2019.
Continuing our COBALT clinical outcomes confirmatory trial for OCA in PBC which we expect to complete on a postmarketing basis.
Contracting with third-party manufacturers to increase OCA manufacturing activities, including investing in supply chain and product development, preparing for our PBC commercial launch and planning for the continuation of our clinical program in NASH, and working to secure second manufacturers as part of our strategy to secure more than one approved supplier of OCA in the future. We are building commercial supplies, including supplies of the starting material for manufacturing OCA.
Contracting with and planning to engage a number of consultants and other third party vendors in relation to our seeking of regulatory approval and implementing various electronic software and systems in relation to our regulatory activities.
In addition, we are evaluating OCA in non-viral, progressive liver diseases other than PBC, particularly NASH, PSC and biliary atresia. We initiated our Phase 3 REGENERATE trial in non-cirrhotic NASH patients with liver fibrosis in September 2015, the Phase 2 CONTROL trial to characterize the lipid metabolic effects of OCA and cholesterol management effects of concomitant statin administration in NASH patients in December 2015, the Phase 2 AESOP trial of OCA in patients with PSC in December 2014, and the Phase 2

82

TABLE OF CONTENTS

CARE trial of OCA in patients with biliary atresia in October 2015. As a result, we expect that our expenditures in connection with our NASH, PSC and biliary atresia programs will increase significantly in future periods.

INT-767 and INT-777

We intend to continue to develop INT-767 (a dual FXR/TGR5 agonist) and INT-777 (a selective TGR5 agonist). We initiated a Phase 1 clinical trial of INT-767 in healthy volunteers in November 2015. We also intend to conduct additional preclinical work on INT-777 to further characterize its therapeutic potential and to invest in product development in anticipation of further clinical trials.

Other than OCA, our product development programs are at an early stage, and successful development of OCA and our future product candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to maintain or enter into new strategic alliances with respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, as well as ongoing assessments as to each future product candidate s commercial potential. We will need to raise additional capital and may seek additional strategic alliances in the future in order to advance our various programs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive and operational functions, including sales and marketing, finance, information technology, legal and human resources. Other significant general and administrative expenses include stock-based compensation expenses, expenses related to our OCA pre-commercialization activities, facilities costs, and other expense of operating as a public company.

Our general and administrative expenses have increased and will continue to increase as we operate as a public company and due to the potential commercialization of our product candidates. We further plan on expanding our operations both in the United States and Europe, which will increase our general and administration expenses. We believe that these activities will result in increased costs related to the hiring of significant additional personnel, increased fees for outside consultants, lawyers and accountants and the addition of facilities. We have also incurred and may continue to incur increased costs to comply with corporate governance, internal controls and similar requirements applicable to public companies with expanding operations and biopharmaceutical companies seeking to commercialize its product candidates.

Other Income, Net

Other income, net primarily consists of interest income earned on our cash, cash equivalents and investment securities, offset by management fees, capital base, franchise and real estate taxes.

Revaluation of Warrants

In conjunction with various financing transactions prior to our initial public offering, we issued warrants to purchase shares of our common stock. As of December 31, 2014, all of the warrants were exercised or expired in accordance with their terms. Certain of the warrants that were outstanding during 2014 included a provision that provided for a reduction in the warrant exercise price upon subsequent issuances of additional shares of common stock for

consideration per share less than the applicable per share warrant exercise price. The warrants containing this provision were deemed to be derivative instruments and as such, were recorded as a liability and marked-to-market at each reporting period. The fair value estimates of these warrants were determined using a Black-Scholes option-pricing model and were based, in part, on subjective assumptions. Non-cash changes in the fair value of the common stock warrant liability from the prior period were recorded as a component of other income and expense for the years ended December 31, 2014 and 2013.

Critical Accounting Policies and Estimates

Our management s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial

TABLE OF CONTENTS

statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in note 3 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

We recognize revenue when the following criteria are met: persuasive evidence that an arrangement exists, services have been rendered, the price is fixed or determinable and collectability is reasonably assured.

We have entered into collaboration agreements with Sumitomo Dainippon and other collaborators. The terms of these agreements include nonrefundable up-front licensing fees, in addition to potential milestone payments and royalties on any future product sales developed by the collaborators under our licenses. We assess these multiple elements in order to determine whether particular components of the arrangement represent separate units of accounting.

We recognize up-front license payments as revenue upon delivery of the license only if the license has stand-alone value. The underlying performance obligations are accounted for separately as the obligations are fulfilled. If the license is considered as not having stand-alone value, the arrangement is accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever we determine that an arrangement should be accounted for as a single unit of accounting, we determine the period over which the performance obligations will be performed and revenue will be recognized. If we cannot reasonably estimate the timing and the level of effort to complete our performance obligations under the arrangement, then we recognize revenue under the arrangement on a straight-line basis over the period that we expect to complete our performance obligations.

Our collaboration agreements also provide for potential milestone payments to us. As of December 31, 2015, we achieved $1.0 million of the development milestones under our collaboration agreement with Sumitomo Dainippon. Revenues from milestone payments, if they are non-refundable and considered substantive, are recognized upon successful accomplishment of the milestones. If milestones are not considered substantive, milestone payments are initially deferred and recognized over the remaining performance obligation.

To date, we have not received any royalty payments and accordingly have not recognized any related revenue. We will recognize royalty revenue upon the sale of the related products, provided we have no remaining performance obligations under the arrangement.

We record deferred revenue when payments are received in advance of the culmination of the earnings process. This revenue is recognized in future periods when the applicable revenue recognition criteria have been met.

Valuation of Stock-Based Compensation and Warrant Liability

Stock-Based Compensation

We record the fair value of stock options, restricted stock units, or RSUs, and restricted stock awards, or RSAs, issued to employees as of the grant date as compensation expense. We recognize compensation expense over the requisite service period, which is the vesting period. For non-employees, we also record stock options, RSUs and RSAs at their fair value as of the grant date. We then periodically re-measure the awards

TABLE OF CONTENTS

to reflect the current fair value at each reporting period until the non-employee completes the performance obligation or the date on which a performance commitment is reached. Expense is recognized over the related service period.

Stock-based compensation expense has been reported in our statements of operations as follows:

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
General and administrative	$ 16,223	$ 8,418	$ 4,723
Research and development	17,966	11,709	4,723
Total stock-based compensation	$ 34,189	$ 20,127	$ 9,446

We calculate the fair value of stock-options using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of assumptions, including stock price volatility, the expected life of stock options, risk free interest rate and the fair value of the underlying common stock on the date of grant. Our key assumptions are:

The expected volatility was estimated based upon the historical volatility information of peer companies for each respective reporting period. We calculated expected volatility based on reported data for selected reasonably similar publicly traded companies for which the historical information is available. For the purpose of identifying peer companies, we consider characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status.

The assumed dividend yield is based on our expectation of not paying dividends for the foreseeable future.

We determine the average expected life of stock options based on the simplified method in accordance with the Securities and Exchange Commission Staff Accounting Bulletin Nos. 107 and 110. We expect to use the simplified method until we have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term.

We determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant.

We estimate forfeitures based on our historical analysis of actual stock option forfeitures.

We expect the impact of stock-based compensation to grow in future periods due to the potential increases in the value of our common stock, increased headcount and additional stock option and other equity grants.

We are required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. For 2015, 2014 and 2013, we used a forfeiture rate of five percent. There were no significant forfeitures through December 31, 2015.

TABLE OF CONTENTS

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar Change	% Change
	2015	2014		
		(in thousands)		
Licensing revenue	$ 2,782	$ 1,742	$ 1,040	60 %
Operating expenses:				
Research and development	128,193	80,311	47,882	60 %
General and administrative	103,745	34,601	69,144	200 %
Loss from operations	(229,156)	(113,170)	(115,986)	102 %
Warrant revaluation expense		(170,832)	170,832	(100)%
Other income, net	2,727	776	1,951	251 %
Net loss	$ (226,429)	$ (283,226)	$ 56,797	(20)%

Licensing Revenue

Licensing revenue was $2.8 million and $1.7 million for the years ended December 31, 2015 and 2014, respectively. For years ended December 31, 2015, $1.8 million resulted from the amortization of the up-front payments under the collaboration agreement with Sumitomo Dainippon and $1.0 million resulted from the development milestone achieved in the period. All of the revenue recognized in the year ended December 31, 2014 related to the amortization of the up-front payments under the collaboration agreement.

Research and Development Expenses

Research and development expenses were $128.2 million and $80.3 million for the years ended December 31, 2015 and 2014, respectively. The net increase in research and development expenses was $47.9 million. This increase in research and development expense primarily reflects:

additional personnel on our development team to manage the increased activities around our OCA development program, resulting in increased compensation and related benefits costs of approximately $18.4 million;
increased OCA regulatory expenses, research expenses and clinical development-related expenses of approximately $7.5 million;
increased stock-based compensation expense of approximately $6.2 million;
increased expenses related to our preclinical programs of approximately $6.0 million;
increased indirect expenses of approximately $5.1 million; and
increased expenses of approximately $4.7 million associated with our INT-767 program.

General and Administrative Expenses

General and administrative expenses were $103.7 million and $34.6 million for the years ended December 31, 2015 and 2014, respectively. The increase in general and administrative expenses of $69.1 million was primarily due to:

increased expenses of approximately $34.4 million related to pre-commercialization activities, which include marketing and public relations;

additional personnel to manage our increased operational activities, resulting in increased compensation and related benefit costs of approximately $19.7 million;

increased stock-based compensation expense of approximately $7.8 million; and

increased operating costs such as legal, facilities and technology-related expenses of approximately $7.2 million.

TABLE OF CONTENTS

Warrant Revaluation Expense

Our previously outstanding warrants were deemed to be derivative instruments that required liability classification and mark-to-market accounting. As such, at the end of each period, the fair values of the warrants were determined using a Black-Scholes option-pricing model, resulting in the recognition of losses of $170.8 million for the year ended December 31, 2014. These fluctuations in value were primarily due to the increase in the price of the common stock underlying the warrants offset by declines in the estimated life of the warrants and the changes in volatility of the shares of common stock underlying the warrants.

Other Income, Net

Other income, net was primarily attributable to interest income earned on cash, cash equivalents and investment securities, which increased compared to the prior year period as a result of the increase in the investment balances from our April 2014, February 2015, and April 2015 equity financings, offset primarily by the increases in cash used in operations.

Comparison of the Years Ended December 31, 2014 and 2013

The following table summarizes our results of operations for the years ended December 31, 2014 and 2013, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar Change	% Change
	2014	2013		
		(in thousands)		
Licensing revenue	$ 1,742	$ 1,622	$ 120	7 %
Operating expenses:				
Research and development	80,311	27,941	52,370	187 %
General and administrative	34,601	13,132	21,469	163 %
Loss from operations	(113,170)	(39,451)	(73,719)	187 %
Warrant revaluation expense	(170,832)	(28,441)	(142,391)	501 %
Other income, net	776	100	676	676 %
Net loss	$ (283,226)	$ (67,792)	$ (215,434)	318 %

Licensing Revenue

For the years ended December 31, 2014 and 2013, we recorded a total of $1.7 million and $1.6 million respectively, of licensing revenue, consisting of the up-front payments from our collaboration agreements with Sumitomo Dainippon.

Research and Development Expenses

Research and development expenses were $80.3 million and $27.9 million for the years ended December 31, 2014 and 2013, respectively. The net increase in research and development expenses was $52.4 million. This increase in research and development expense primarily reflects:

increased direct clinical trial costs for OCA of approximately $22.9 million;

additional personnel on our development team to manage the increased activities around our OCA development program, resulting in increased compensation and related benefits costs of approximately $6.7 million;

increased non-cash stock-based compensation expense of approximately $7.0 million;

increased OCA manufacturing activities of approximately $6.4 million to support our commercial scale manufacturing and investment in clinical trial materials;

TABLE OF CONTENTS

increased regulatory-related expenses, research-related expenses and clinical development-related expenses of approximately $5.5 million; and

increased expenses related to our research and preclinical programs of approximately $3.9 million.

General and Administrative Expenses

General and administrative expenses were $34.6 million and $13.1 million for the years ended December 31, 2014 and 2013, respectively. The increase in general and administrative expenses of $21.5 million was mainly due to:

increased expenses related to pre-commercialization activities of approximately $6.8 million;

additional personnel to manage our increased operational activities, resulting in increased compensation and related benefit costs of approximately $5.8 million;

increased operating costs such as legal, facilities and technology-related expenses of approximately $5.1 million; and

increased non-cash stock-based compensation expense of approximately $3.7 million.

Warrant Revaluation Expense

Our previously outstanding warrants were deemed to be derivative instruments that required liability classification and mark-to-market accounting. As such, at the end of each period, the fair values of the warrants were determined using a Black-Scholes option-pricing model, resulting in the recognition of losses of $170.8 million and $28.4 million for the years ended December 31, 2014 and 2013, respectively. These fluctuations in value were primarily due to the increase in the price of the common stock underlying the warrants offset by declines in the estimated life of the warrants and the changes in volatility of the shares of common stock underlying the warrants.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2015, we had an accumulated deficit of $695.6 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may seek to obtain through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

We have funded our operations primarily through the sale of common stock, preferred stock, convertible notes and warrants and payments received under our collaboration agreements totaling $623.2 million (net of issuance costs of $33.7 million), including $29.7 million in net proceeds from our Series C financing in August 2012, $78.7 million in net proceeds from our initial public offering in October 2012, $61.2 million in net proceeds from our follow-on public offering in June 2013, $183.5 million in net proceeds from a follow-on public offering in April 2014, $191.6 million in net proceeds from a follow-on public offering in February 2015, $367.1 million in net proceeds from the follow-on offering in April 2015 and the receipt of $17.4 million in up-front payments under our licensing and collaboration agreements with Sumitomo Dainippon and Servier. As of December 31, 2015, we had cash, cash equivalents and investment securities of $628.1 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our funds are held in cash and money market bank accounts and investments, all of which have maturities of less than two years.

TABLE OF CONTENTS

Cash Flows

The following table sets forth the significant sources and uses of cash for the periods set forth below:

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Net cash provided by (used in):			
Operating activities	$(162,902)	$(87,738)	$(28,006)
Investing activities	(389,472)	(96,585)	(70,214)
Financing activities	565,469	190,983	66,072
Effect of exchange rate changes	(376)		
Net increase (decrease) in cash and cash equivalents	$12,719	$6,660	$(32,148)

Operating Activities. Net cash used in operating activities of $163.0 million for the year ended December 31, 2015 was primarily a result of our $226.4 million net loss and net changes in operating assets and liabilities of $22.5 million, $34.2 million for stock-based compensation, $1.7 million for depreciation and the amortization of investment premium of $6.3 million.

Net cash used in operating activities of $87.7 million for the year ended December 31, 2014 was primarily a result of our $283.2 million net loss and net changes in operating assets and liabilities of $699,000 offset by the add-back of non-cash expense of $170.8 million for warrant liability revaluation, $20.1 million for stock-based compensation, $443,000 for depreciation and the amortization of interest premium of $3.4 million.

Net cash used in operating activities of $28.0 million for the year ended December 31, 2013 was primarily a result of our $67.8 million net loss and net changes in operating assets and liabilities of $200,000 offset by the add-back of non-cash expense of $28.4 million for warrant liability revaluation, $9.4 million for stock-based compensation, $106,000 for depreciation and the amortization of interest premium of $1.6 million.

Investing Activities. For the year ended December 31, 2015, net cash used in investing activities primarily reflects the net investment of the proceeds from the February 2015 public offering of $191.6 million and the April 2015 public offering of $367.1 million, offset by expenditures for leasehold improvements of $5.9 million primarily for our King s Cross, London facility and the expansion of our New York headquarters.

For the year ended December 31, 2014, net cash used in investing activities reflects the net investment of the proceeds from the April 2014 public offering of $183.5 million and expenditures for leasehold improvements of $4.6 million as a result of the relocation of our San Diego facility.

For the year ended December 31, 2013, net cash used in investing activities reflects the net investment of the proceeds from the June 2013 public offering of $61.2 million and expenditures for leasehold improvements of $1.6 million as a result of the relocation of our New York headquarters.

Financing Activities. Net cash provided by financing activities in the year ended December 31, 2015 consisted primarily of net proceeds of the February 2015 public offering of $191.6 million and the April 2015 public offering of $367.1 million and $6.7 million from the exercise of options to purchase common stock.

Net cash provided by financing activities in the year ended December 31, 2014 consisted primarily of net proceeds of

$183.5 million from the completion of our April 2014 public offering and $7.5 million from the exercise of options and warrants to purchase common stock.

Net cash provided by financing activities in the year ended December 31, 2013 consisted primarily of net proceeds of $61.2 million from the completion of our June 2013 public offering and $4.8 million from the exercise of options and warrants to purchase common stock.

Future Funding Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize OCA or any of our other product

TABLE OF CONTENTS

candidates. Even if we receive marketing approvals for OCA in PBC and commence our commercial launch, we do not expect to generate significant revenues in PBC in 2016.

At the same time, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates. In June 2015, we completed our filings for marketing approval of OCA in PBC in the United States and Europe. In August 2015, the FDA accepted for review our NDA and granted priority review for OCA in PBC. The FDA set a target date of May 29, 2016 to take action under PDUFA, after giving effect to a 90 day extension. The FDA has also publicly announced a planned advisory committee meeting date of April 7, 2016. We are also currently in the regulatory review process with the EMA.

We have incurred and expect to incur additional costs associated with operating as a public company and further plan on expanding our operations in the United States, Europe and in other countries such as Canada and Australia. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. As part of our longer-term strategy, we also anticipate incurring significant expenses in connection with our planned increase in our product development, scientific, commercial and administrative personnel and expansion of our facilities and infrastructure in the United States and abroad.

As of December 31, 2015, we had $628.1 million in cash, cash equivalents and investment securities. Our adjusted operating expenses for the year ending December 31, 2015 was below our previously provided guidance of $240 million, driven primarily by the timing of hiring of personnel, certain clinical trial and related expenses, market and medical research expenses and manufacturing related purchases for OCA. We currently project adjusted operating expenses in the range of $360 million to $400 million in the fiscal year ending December 31, 2016, which excludes stock-based compensation and other non-cash items. These expenses are planned to support the continued clinical development program for OCA in PBC, NASH and PSC, increased OCA manufacturing activities, the continued development of INT-767 and other preclinical pipeline programs, as well as pre-commercialization activities commercial activities. We believe that the build out of our U.S. commercial infrastructure is mostly complete with the recent hiring of the U.S. territory business managers and other field personnel in October 2015. We also significantly expanded our commercial and other infrastructure internationally in 2015, and plan on making additional investments over 2016 should key regulatory milestones be achieved on a timely basis. Our adjusted operating expense estimate for 2016 is higher than our adjusted operating expenses for 2015 reflecting the increase in headcount that occurred in the latter part of 2015 and the anticipated increases in commercialization and research and development expenses.

Adjusted operating expense is a financial measure not calculated in accordance with U.S. generally accepted accounting principles, or GAAP. We anticipate that stock-based compensation expense will represent the most significant non-cash item that is excluded in adjusted operating expenses as compared to operating expenses under GAAP. See Non-GAAP Financial Measures for more information.

Due to the many variables inherent to the development and commercialization of novel therapies and our rapid growth and expansion, we currently cannot accurately and precisely predict the duration beyond 2016 over which we expect our cash and cash equivalents to be sufficient to fund our operating expenses and capital expenditure requirements. However, we currently believe that our cash and cash equivalents will be sufficient for us to:

continue and expand our clinical development programs for OCA in PBC, NASH and PSC, such as continuing, but not completing, our planned Phase 3 clinical program for OCA in NASH, including the REGENERATE trial, our ongoing AESOP trial for OCA in PSC, and our ongoing COBALT confirmatory clinical outcomes trial of OCA in PBC;

advance the continued development of INT-767, including the completion of a recently initiated Phase 1 clinical trial, and our preclinical compounds, but not completing the clinical or preclinical development needed, as the case may be, for INT-767 or our preclinical compounds;

TABLE OF CONTENTS

increase OCA manufacturing activities, including investing in supply chain and product development, preparing for our PBC commercial launch and planning for the continuation of our clinical program in NASH, but not manufacture the supply needed for any potential commercial launch of OCA in NASH;
prepare for and, if we obtain marketing approval on a timely basis, initiate the commercial launch of OCA in PBC in both the United States and certain European countries, but not commercially launch OCA in PBC in other countries across the world; and
expand, if necessary, our clinical, regulatory, medical affairs and commercial infrastructure through the time we initiate such planned commercial launch of OCA in PBC in both the United States and certain European countries, but not expand such infrastructure as may be required in the longer term.

Accordingly, we will continue to require substantial additional capital in connection with our continuing operations, including continuing our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds required to complete the research and development and commercialization of our products under development.

The amount and timing of our future funding requirements will depend on many factors, including:

the willingness of the FDA and EMA to accept the POISE trial, which is our completed Phase 3 clinical trial for PBC, as well as our other clinical and preclinical studies and other work, as the basis for review and marketing approval of OCA for PBC;
the progress, costs, results of and timing of our COBALT confirmatory clinical outcomes trial of OCA for the treatment of PBC, the completion of which we expect will not be a condition to the receipt of marketing approval in the United States or the European Union;
the progress, costs, results of and timing of the Phase 3 program and other supporting trials and studies necessary to support anticipated filings for marketing approval in NASH, including the sufficiency of the REGENERATE trial to be accepted as the sole pivotal trial for marketing approval or the acceptability of a surrogate endpoint for accelerated approval of OCA for the treatment of NASH;
the progress, costs, results of and timing of clinical development of OCA for other indications, including our Phase 2 AESOP trial of OCA in PSC and our Phase 2 CARE trial of OCA in biliary atresia;
the significant expansion of our operations, personnel and the size of our company and our need to continue to expand in the longer term;
the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
the number and characteristics of product candidates that we pursue, including INT-767 which is in a Phase 1 clinical trial, and our product candidates in preclinical development such as INT-777;
the ability of our product candidates to progress through preclinical and clinical development successfully and in a timely manner;
the expansion of our research and development activities;
the costs and timing of commercialization activities, including product sales, marketing and distribution, for any of our product candidates that receive marketing approval;
the costs associated with securing and establishing manufacturing capabilities and procuring the materials necessary for our product candidates;
market acceptance of our product candidates, which may be affected by the reimbursement that our products receive from payors;

TABLE OF CONTENTS

the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;

our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;

our need and ability to hire and retain additional management, scientific and medical, commercial and other qualified personnel and the substantial cost of retaining such additional personnel;

the effect of competing technological and market developments;

our need to implement and maintain internal systems, software and infrastructure, including those to assist in our financial and reporting, clinical development and commercialization efforts and to support our personnel and operations as our business evolves; and

the economic and other terms, timing of and success of our existing licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future.

We have no committed external sources of funding. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

Our long-term contractual obligations include commitments and estimated purchase obligations entered into in the normal course of business. The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2015 and the effects such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due By Period				
	Total	Less than 1 year	1 3 years	3-5 years	More than 5 years
	(in thousands)				
Operating leases	$ 21,329	$ 3,453	$ 6,851	$ 4,443	$ 6,582
Purchase obligations	20,576	15,143	1,345	1,345	2,743
Total	$ 41,905	$ 18,596	$ 8,196	$ 5,788	$ 9,325

We lease general and administrative office space in New York, New York, San Diego, California and Kings Cross, United Kingdom, pursuant to operating leases that expire in 2024, 2019 and 2024, respectively. In October 2013, we entered into a lease agreement in New York City for our corporate headquarters, providing 11,124 square feet of space. We leased an additional 9,502 square feet in December 2014. The lease for our New York City office will expire in July 2024.

In May 2014, we entered into a lease agreement with The Irvine Company LLC for approximately 47,000 square feet in San Diego for office space. The lease ends in September 2019; however, we have an option to further extend the lease for an additional five year term at market rates prevailing at such time.

TABLE OF CONTENTS

In February 2015, we entered into an underlease with Merck Sharp & Dohme Limited for our new office in the King s Cross area of London, United Kingdom. The lease provides us with approximately 6,000 rentable square feet in London for office space. The lease term is anticipated to end in June 2019.

On January 22, 2016, Intercept Pharma Europe Ltd., or IPEL, our wholly owned subsidiary, entered into an underlease with Performing Right Society, Ltd. for additional office space in the King s Cross area of London, United Kingdom. We are the guarantor to the underlease. The underlease provides IPEL with an additional 8,549 square feet of space. The lease term is anticipated to end on May 31, 2024. The annual rent is approximately £0.7 million (or approximately US$1.0 million), payable quarterly. IPEL is also required to pay VAT on the rent. IPEL will be responsible for a portion of the insurance, certain service charges and taxes for the building based on the floor area rented by them. As security for the underlease, IPEL has provided the landlord a rent deposit in an amount equal to 12 months rent, plus applicable VAT. The underlease is subject to an upwards only open market rent review of the current market rent with review to take place on June 4, 2019.

On February 23, 2016, we entered into a sublease with Restoration Hardware, Inc. for additional office space in New York City. The sublease provides us with an additional 10,785 square feet of office space. The lease term is anticipated to end on July 31, 2021. The annual rent is approximately $1.0 million payable monthly. We are also responsible for our proportionate share of increases in operating expenses beginning January 2017 as well as our proportionate share of increases in real estate taxes over the average of the 2015/2016 and 2016/2017 fiscal years. As security for the sublease, we must deliver a letter of credit in the amount of approximately $0.3 million in favor of the sublandlord within forty-five (45) days of execution of the sublease. While the letter of credit is pending, we provided the sublandlord with a temporary security deposit of $75,000 in cash which will be returned to us upon delivery of the letter of credit to the sublandlord.

We are a party to license and research and development agreements with universities and other third parties, as well as patent assignment agreements, under which we have obtained rights to patents, patent applications and know-how. We enter into contracts in the normal course of business with contract research organizations, or CROs, for clinical trials, clinical and commercial supply manufacturing, with vendors for preclinical research studies and for other services and products for operating purposes. Our agreements generally provide for termination within 90 days of notice. Such agreements are cancelable contracts and not included in the table of contractual obligations and commitments. We have included as purchase obligations our commitments under agreements to the extent they are quantifiable and are not cancelable.

Under our agreement with Sumitomo Dainippon, we are required to use our commercially reasonable efforts to develop OCA outside of the territories in which Sumitomo Dainippon has a license under the agreement. As these amounts are not quantifiable, they are not included in the table above.

Income Taxes

No income tax expense or benefit was recognized in the accompanying consolidated financial statements. Our deferred tax assets are comprised primarily of net operating loss carryforwards. We maintain a full valuation allowance on our deferred tax assets since we have not yet achieved sustained profitable operations. As a result, we have not recorded any income tax benefit since our inception.

Net Operating Losses

As of December 31, 2015 and 2014, we had net operating loss carryforwards, or NOLs, for federal income tax purposes of $454.4 million and $221.2 million, respectively, which expire between 2024 and 2035. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code. The limitations apply if an ownership change, as defined by Section 382 of the Internal Revenue Code, occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points over their lowest ownership percentage in a testing period (typically three years). We have evaluated whether one or more ownership changes as defined under Section 382 of the Internal Revenue Code have occurred since our inception and have determined that there have been at least two such changes. Although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to utilize these NOLs may be limited due to future ownership changes or for other reasons. Additionally,

TABLE OF CONTENTS

tax laws limit the time during which NOLs and certain other tax attributes may be utilized against future taxes. As a result, we may not be able to take full advantage of our carryforwards for federal, state, and foreign tax purposes.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under Securities and Exchange Commission rules.

Recent Accounting Pronouncements

In August 2015, the Financial Accounting Standards Board (FASB) Accounting Standards Update No. 2015-14 Revenue from Contracts with Customers (Topic 606) Deferral of Effective Date. The FASB decided to defer the effective date of the guidance in Update 2014-09 by one year for public business entities. The core principle of the guidance is that an entity should recognized revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchanges for those goods or services. Public business entities will apply this guidance to annual reporting periods beginning after December 15, 2017. We are evaluating the implications of this update.

In November 2015, the FASB issued Accounting Standards update No. 2015-17 Income Taxes (Topic 740) to simplify the presentation of deferred income taxes. The update requires that deferred tax liabilities and assets and associated valuation allowance be classified as noncurrent in a classified statement of financial position. This update is effective for the financial statements issued for annual periods beginning after December 15, 2016 and interim periods within those annual periods. The adoption is not expected to have an impact on our consolidated financial statements.

In January 2016, the FASB issued Accounting Standards Update No. 2016-01 Financials Instruments Overall (Subtopic 825-10) Recognition and Measurement of Financial Assets and Financial Liabilities. The objective in the update was to enhance the reporting model for financial instruments to provide users of financial statements with more decision-useful information. The amendments in this update address certain aspects of recognition, measurement, presentation and disclosure of financial instruments. The amendments in this update are effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. We are evaluating the implications of this update.

Basic and Diluted Net Loss Attributable to Common Stockholders per Share of Common Stock

Our Series A, B and C preferred stock represented participating securities. However, since we have operated at a loss since inception, and losses are not allocated to the preferred stock, the two class method did not affect our calculation of earnings per share. Upon the closing of our initial public offering, all outstanding shares of our preferred stock were converted into an aggregate of 7,403,817 shares of common stock.

Dilutive common stock equivalents would include the dilutive effect of convertible securities, common stock options, RSUs and warrants to purchase common stock. Potentially dilutive common stock equivalents totaled approximately 1,541,164 shares, 1,495,254 shares and 2,511,287 shares for the years ended December 31, 2015, 2014 and 2013, respectively. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. We currently do not hedge interest rate exposure. Because of the short-term maturities of our cash equivalents and investment securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investment securities. If a 10% change in interest rates were to have occurred on December 31, 2015, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

We do not believe that our cash and cash equivalents and available for sale investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and available for sale investments do

TABLE OF CONTENTS

not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

We contract with CROs and investigational sites in Europe, Canada and Australia. We are therefore subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during 2015, 2014 or 2013.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our principal executive officer and principal financial officer evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2015. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2015, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were adequate and effective.

Management s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company s principal executive and principal financial officers and effected by the company s board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP and includes those policies and procedures that: (i) pertain to the

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

TABLE OF CONTENTS

Internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements prepared for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2015. In making this assessment, our management used the criteria set forth in the *Internal Control Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2015 based on those criteria.

Attestation Report of Independent Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2015 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report which is included in this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act), identified in connection with the evaluation of such internal control, that occurred during the three months ended December 31, 2015 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On February 23, 2016, we entered into a sublease with Restoration Hardware, Inc. for additional office space in New York City. The sublease provides us with an additional 10,785 square feet of office space. The lease term is anticipated to end on July 31, 2021. The annual rent is approximately $1.0 million payable monthly. We are also responsible for our proportionate share of increases in operating expenses beginning January 2017 as well as our proportionate share of increases in real estate taxes over the average of the 2015/2016 and 2016/2017 fiscal years. As security for the sublease, we must deliver a letter of credit in the amount of approximately $0.3 million in favor of the sublandlord within forty-five (45) days of execution of the sublease. While the letter of credit is pending, we provided the sublandlord with a temporary security deposit of $75,000 in cash which will be returned to us upon delivery of the letter of credit to the sublandlord.

TABLE OF CONTENTS

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2016 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation

The information required by this Item 11 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2016 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item 12 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2016 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item 13 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2016 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this Item 14 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2016 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

TABLE OF CONTENTS

SIGNATURES

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

INTERCEPT PHARMACEUTICALS, INC.

By:

/s/ Mark Pruzanski, M.D.

Date: February 29, 2016

Mark Pruzanski
President and Chief Executive Officer
(Principal Executive Officer)

By:

/s/ Barbara Duncan

Date: February 29, 2016

Barbara Duncan
Chief Financial Officer
(Principal Financial and Accounting Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities indicated below and on the dates indicated:

Signature	Title	Date
/s/ Mark Pruzanski Mark Pruzanski	President, Chief Executive Officer and Director (Principal Executive Officer)	February 29, 2016
/s/ Barbara Duncan Barbara Duncan	Chief Financial Officer (Principal Financial and Accounting Officer)	February 29, 2016
/s/ Paolo Fundaro Paolo Fundaro	Chairman of the Board of Directors	February 29, 2016
/s/ Srinivas Akkaraju Srinivas Akkaraju	Director	February 29, 2016
/s/ Luca Benatti Luca Benatti	Director	February 29, 2016
/s/ Gino Santini Gino Santini	Director	February 29, 2016
	Director	February 29, 2016

/s/ Glenn Sblendorio Glenn Sblendorio		
/s/ Jonathan Silverstein Jonathan Silverstein	Director	February 29, 2016
/s/ Klaus Veitlinger Klaus Veitlinger	Director	February 29, 2016
/s/ Dan Welch Dan Welch	Director	February 29, 2016

TABLE OF CONTENTS

INTERCEPT PHARMACEUTICALS, INC.

Index to Consolidated Financial Statements

TABLE OF CONTENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Intercept Pharmaceuticals, Inc.:

We have audited the accompanying consolidated balance sheets of Intercept Pharmaceuticals, Inc. and subsidiaries as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, changes in stockholders equity, and cash flows for each of the years in the three-year period ended December 31, 2015. These consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Intercept Pharmaceuticals, Inc. and subsidiaries as of December 31, 2015 and 2014, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Intercept Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated February 29, 2016 expressed an unqualified opinion on the effectiveness of Intercept Pharmaceuticals, Inc. s internal control over financial reporting.

/s/ KPMG LLP

New York, New York
February 29, 2016

TABLE OF CONTENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Intercept Pharmaceuticals, Inc.:

We have audited Intercept Pharmaceuticals, Inc. and subsidiaries internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Intercept Pharmaceuticals, Inc. and subsidiaries management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management s Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company s internal control over financial reporting based on our audit.

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

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

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

In our opinion, Intercept Pharmaceuticals, Inc. and subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Intercept Pharmaceuticals, Inc. and subsidiaries as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, changes in stockholders equity, and cash flows for each of the years in the three-year period ended December 31, 2015 and our report dated February

29, 2016 expressed an unqualified opinion on those consolidated financial statements.

/s/ KPMG LLP

New York, New York
February 29, 2016

TABLE OF CONTENTS

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	December 31,	
	2015	2014
	(in thousands)	
Assets		
Current assets:		
Cash and cash equivalents	$32,742	$ 20,023
Investment securities, available-for-sale	595,313	219,701
Prepaid expenses and other current assets	13,638	6,104
Total current assets	641,693	245,828
Fixed assets, net	10,047	5,852
Security deposits	4,018	2,469
Total assets	$655,758	$ 254,149
Liabilities and Stockholders Equity		
Current liabilities:		
Accounts payable, accrued expenses and other liabilities	$45,591	$ 13,459
Short-term portion of deferred revenue	1,782	1,782
Total current liabilities	47,373	15,241
Long-term liabilities:		
Long-term portion of deferred revenue	6,236	8,017
Total liabilities	$53,609	$ 23,258
Stockholders equity:		
Common stock 35,000,000 shares authorized; 24,391,430, and 21,415,243 shares issued and outstanding as of December 31, 2015 and December 31, 2014, respectively; par value $0.001 per share	24	21
Additional paid-in capital	1,300,008	700,355
Accumulated other comprehensive loss, net	(2,253)	(284)
Accumulated deficit	(695,630)	(469,202)
Total stockholders equity	602,149	230,891
Total liabilities and stockholders equity	$655,758	$ 254,149

See accompanying notes to consolidated financial statements.

TABLE OF CONTENTS

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Operations

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Licensing revenue	$ 2,782	$ 1,742	$ 1,622
Costs and expenses:			
Research and development	128,193	80,311	27,942
General and administrative	103,745	34,601	13,132
Total costs and expenses	231,938	114,912	41,073
Other income (expense):			
Revaluation of warrants		(170,832)	(28,441)
Other income, net	2,727	776	100
	2,727	(170,056)	(28,341)
Net loss	$ (226,429)	$ (283,226)	$ (67,792)
Net loss attributable to common stockholders	$ (226,429)	$ (283,226)	$ (67,792)
Net loss per share, basic and diluted	$ (9.56)	$ (13.63)	$ (3.76)
Weighted average shares outstanding, basic and diluted	23,694	20,784	18,029

See accompanying notes to consolidated financial statements.

TABLE OF CONTENTS

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Net loss	$(226,429)	$(283,226)	$(67,792)
Other comprehensive loss:			
Unrealized gains (losses) on securities:			
Unrealized holding gains (losses) arising during the period	(1,628)	(369)	81
Reclassification for recognized gains on marketable investment securities during the period recognized in other income, net	3	25	
Net unrealized gains (losses) on marketable investment securities	$(1,625)	$(344)	$81
Foreign currency translation adjustments	(347)		
Comprehensive loss	$(228,401)	$(283,570)	$(67,711)

See accompanying notes to consolidated financial statements.

TABLE OF CONTENTS

INTERCEPT PHARMACEUTICALS, INC.

Consolidated Statements of Changes in Stockholders Equity
For the Years Ended December 31, 2015, 2014, and 2013
(in thousands)