INTERCEPT PHARMACEUTICALS INC
Form 10-K
April 01, 2013

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, 2012

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.)
18 Desbrosses Street New York, NY (Address of Principal Executive Offices)	10013 (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 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 o No x

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 o Accelerated filer o Non-accelerated filer x 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 March 15, 2013 was $232,642,790. The registrant has provided this information as of March 15, 2013 because its common stock was not publicly traded as of the last business day of its most recently completed second fiscal quarter.

As of March 15, 2013, there were 16,614,165 shares of common stock, $0.001 par value per share, outstanding.

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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, and any related restrictions, limitations, and/or warnings in the label of any approved product candidates;
our plans to research, develop and commercialize our future product candidates;
our collaborators election to pursue research, development and commercialization activities;
our ability to attract collaborators with development, regulatory and commercialization expertise;
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;
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 ability to obtain additional financing;
our use of the proceeds from our recently completed initial public offering;
our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
the accuracy of our estimates regarding expenses, future revenues, capital requirements and the need for additional financing; 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.

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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.

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PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to Intercept the Company, we, us, and our refer to Intercept Pharmaceuticals, Inc. and its consolidated subsidiary.

Item 1. Business

Overview

We are a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat chronic liver diseases utilizing our proprietary bile acid chemistry. 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. OCA is a first-in-class product candidate that selectively binds to and induces activity in the farnesoid X receptor, or FXR, which we believe has broad liver-protective properties. We are developing OCA initially for primary biliary cirrhosis, or 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. We are conducting a Phase 3 clinical trial of OCA in PBC, which we call the POISE trial, that we anticipate will serve as the basis for seeking regulatory approval in the United States and Europe. As of December 19, 2012, we have completed enrollment of the POISE trial with 217 patients, exceeding the originally targeted number of patients by approximately 20%. We currently expect results from the POISE trial to be available in the second quarter of 2014. OCA has received orphan drug designation in the United States and Europe for the treatment of PBC. We own worldwide rights to OCA outside of Japan and China, where we have exclusively licensed the compound to Dainippon Sumitomo Pharma, or DSP, and granted it an option to exclusively license OCA in certain other Asian countries.

If the POISE trial is successful, we intend to submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for approval of OCA for the treatment of PBC in the United States and a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for approval in Europe. Based on written scientific advice from the EMA, we believe that the EMA will accept our current clinical program as the basis for considering approval of OCA for PBC. With respect to the FDA, we intend to request an accelerated approval of OCA based on the acceptance of the POISE trial primary endpoint as a surrogate endpoint that is reasonably likely to predict clinical benefit. If the FDA grants an accelerated approval of OCA, we will be required to conduct one or more additional clinical trials post-approval to verify and confirm the clinical benefit predicted by the surrogate endpoint. This clinical outcomes trial must satisfy FDA s definition of an adequate and well-controlled trial and would have to be substantially underway at the time of the NDA submission and would be completed after accelerated approval. We are in discussions with the FDA about the design of the clinical outcomes trial and plan to initiate it as early as the second half of 2013.

We are sponsoring an independent study involving more than ten leading PBC centers in North America and Europe, or collectively the Global PBC Study Group, that are pooling their long-term patient data to evaluate the relationship between biochemical and clinical endpoints. We anticipate final data from at least 4,000 patients will be collected and analyzed as part of this study. Initial results for more than 2,100 patients have been accepted as a poster presentation

at the annual meeting of the European Association for the Study of the Liver, or EASL, to be held in April 2013. The data confirms that the POISE trial primary endpoint has a highly statistically significant correlation with liver transplant-free survival. We anticipate that final results will be available by the end of 2013 and will support what we believe is an emerging consensus among PBC opinion leaders concerning the clinical utility of our selected surrogate endpoint.

An academic consortium in the United Kingdom has recently published data from a large observational study of over 2,300 PBC patients recruited from every hospital in the UK into a PBC research cohort. The results show that there is a highly statistically significant correlation between ALP, both alone and together with other biochemical parameters such as bilirubin, and clinical outcomes. Several different threshold values

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of ALP were tested and it was demonstrated that reductions in ALP levels down through to less than 1.5 times upper limit normal (ULN) are strongly predictive of clinical benefit.

In addition to PBC, we are pursuing other indications in our OCA development program, including portal hypertension, nonalcoholic steatohepatitis, or NASH, and primary bile acid diarrhea, or PBAD. The pipeline chart below shows the current stage of development of OCA for these indications, as well as the preclinical programs for our other product candidates.

* An agonist is a substance that binds to a receptor of a cell and triggers a response by that cell.

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 bile acid chemistry therapeutic field. Through a longstanding collaboration with Professor Roberto Pellicciari, Ph.D., one of our co-founders, and certain scientists in the medicinal chemistry group at the University of Perugia, we have gained the capability to rationally design compounds that bind selectively and potently to FXR and other bile acid receptors. Starting with OCA, which was invented by Professor Pellicciari and, together with its underlying patents, was assigned to us under our agreements with him and the University of Perugia, our collaboration has resulted in a pipeline of bile acid analogs in addition to OCA, which target both FXR and a second dedicated bile acid receptor called TGR5, a target of interest for the treatment of type 2 diabetes and associated metabolic diseases. We intend to continue developing these and other product candidates as we advance our pipeline, in some cases subject to the procurement of additional funding or through strategic collaborations.

Our Strategy

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

complete the development of OCA for its lead indication, PBC;
obtain regulatory 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 in other orphan and more prevalent liver and other diseases; and
advance the development of earlier stage product candidates in our pipeline.

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We may enter into strategic collaborations to implement our strategy.

Overview of Liver Function, Bile Acids and Chronic Liver Diseases

The liver performs many essential 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 up 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 the past decade, we have learned that 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 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 and other mechanisms that are necessary for the normal regeneration of the liver. 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) for PBC

Primary Biliary Cirrhosis

Our current clinical focus is on the development of OCA, a novel, orally administered, first-in-class 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.

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 cause 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 the fifth most common cause of liver transplant and accounts for approximately two percent of deaths attributed to cirrhosis. 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 by far 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 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, an enzyme that is released by liver cells

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in response to the bile acid mediated toxicity and that is a key biomarker of the disease pathology. ALP is routinely measured in blood tests and, in the earlier stages of PBC, it is often the only abnormally elevated liver enzyme, rising to between two to ten times higher than normal values. It is closely monitored in PBC patients as an indicator of treatment response and prognosis. 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 but usually is relatively slow, 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 traditional Asian medicine, ursodiol obtained from bears has been used for centuries as a liver tonic for any disease or condition associated with liver malfunction. In humans, 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.

Although 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.

Our PBC Opportunity

While ursodiol s mechanism of action at therapeutic doses is to dilute more detergent bile acids, it has no known pharmacological effects mediated by FXR or other bile acid receptors. Although ursodiol is the established standard of care for the treatment of PBC, studies have shown that up to 50% of PBC patients fail to respond adequately to treatment. Patients typically need to take approximately one gram of ursodiol daily in divided doses, which we believe presents a compliance challenge for some patients.

The outlook and treatment options for end-stage PBC patients who fail to respond to ursodiol 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 disease recurrence rate is as high as 18% at five years and up to 30% at ten years after liver transplant.

According to industry data, there are approximately 300,000 people with PBC in developed countries, of whom we believe approximately 60,000 have been diagnosed and are on ursodiol therapy. Based on this estimate, we believe there are up to 30,000 PBC patients who may currently be eligible for treatment with OCA. With increasing identification of PBC through routine liver function testing in primary care, we believe that there may be significantly more patients who will potentially be eligible for, and be interested in, receiving a new therapy if it becomes available on the market. While ursodiol is the standard of care for the treatment of PBC, given the limitations of its efficacy and compliance with the dosing regimen discussed above, we believe that there is a significant unmet need for a novel second line therapy in PBC.

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Our Solution: OCA for PBC

Overview

Our lead product candidate, OCA, is a bile acid analog and first-in-class 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. We are initially developing OCA for the second line treatment of PBC for patients with an inadequate therapeutic response to ursodiol or who are unable to tolerate ursodiol. OCA has received orphan drug designation in the United States for the treatment of PBC and a related disease called primary sclerosing cholangitis, or PSC. OCA also has orphan designation in Europe for PBC. We submitted an Investigational New Drug Application, or IND, to the FDA for OCA for the treatment of PBC in 2006. We believe we are the first company to have advanced an FXR agonist into clinical trials and have completed enrollment of our Phase 3 POISE trial to evaluate the safety and efficacy of OCA as a novel treatment in PBC. We own worldwide rights to OCA outside of Japan and China, where we have exclusively licensed the compound to DSP, which also has an option to exclusively license OCA in certain additional Asian countries.

We have 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. The first trial enrolled 165 patients to evaluate the addition of OCA to ursodiol in patients with an inadequate response to ursodiol therapy, and the second trial enrolled 59 patients to evaluate OCA given as monotherapy. Both trials showed that, over a 12-week period, single daily doses of OCA at the lowest dose of 10 mg met the primary and secondary endpoints of those trials, producing statistically significant reductions in levels of ALP of greater than 20% and other important liver enzymes. We consider reductions in ALP levels of greater than 10% to be a clinically meaningful improvement. Further, long-term open label extension phases of these trials have demonstrated that the majority of patients taking OCA for at least 12 months, with some on therapy for more than 3 years, maintained a durable treatment response. Pruritus, or itching, a very common symptom in PBC patients, was the most common adverse event reported in our Phase 2 trials, with severity increasing with dose.

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 trials, the data also demonstrated that 80% of OCA-treated patients across our Phase 2 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. Furthermore, our analysis of the data for those Phase 2 patients who would have met the entry criteria for our POISE trial demonstrated that after 12 weeks of treatment approximately 40% to 45% of OCA-treated patients would have met the POISE trial primary endpoint, as compared to 5% to 9% of the placebo-treated patients.

Pharmacological Activity. Unlike ursodiol, which has no FXR-agonistic 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 damage caused by progressive fibrosis. Our Phase 2 trials have demonstrated that most patients taking OCA also have significant reductions in immunoglobulin M, or IgM, and, in the combination trial with ursodiol, C-reactive protein, or CRP, common indicators of autoimmune activity. We believe that this demonstrates 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 at a dose of a single 10 mg tablet each day, which is approximately one percent of the amount of ursodiol that a patient is typically prescribed.

Phase 3 PBC Program for OCA

We are currently conducting our Phase 3 POISE trial, which has been designed to study the safety and efficacy of OCA in PBC patients with an inadequate therapeutic response to ursodiol or who are unable to tolerate ursodiol. In this trial, eligible PBC patients continue their ursodiol treatment, except for those patients unable to

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tolerate ursodiol, and were randomized into one of three trial arms of approximately 72 patients each, adding either: 10 mg of OCA; 5 mg of OCA increasing over the course of the trial to 10 mg of OCA; or a placebo. The double-blind phase of the trial will be 12 months in duration, and patients completing this phase will have the option to continue in an open label, long-term safety extension phase for another five years, during which all patients will receive OCA treatment with daily doses ranging from 5 mg to 25 mg a day, as clinically indicated. In March 2013, we enrolled our first patient into the long-term safety extension phase of our POISE trial.

The primary endpoint of the 12 month double-blind portion of the POISE trial is the achievement of both a reduction in ALP level to below a threshold of 1.67 times upper limit normal, or ULN, with a minimum of 15% reduction in ALP level from baseline, and a normal bilirubin level, a biomarker of liver function, as compared to placebo after 12 months of therapy. ULN is the uppermost level of a specified parameter that is considered normal in healthy people. Patients with ALP and bilirubin levels within these thresholds have been shown in long-term studies to be at significantly lower risk of progressing to liver transplant and death. In order to be eligible to enter the POISE trial, patients must have previously met the diagnostic criteria for PBC and have been taking a therapeutic dose of ursodiol for at least 12 months or, if unable to tolerate ursodiol, patients must not have been on therapy for at least three months prior to entering the trial. In addition, patients must have ALP levels of at least 1.67 times ULN and/or bilirubin levels of one to two times ULN. The POISE trial was designed to enroll 180 patients across approximately 60 clinical sites in North America and Europe. We completed enrollment of the POISE trial in December 2012 with 59 participating clinical sites in North America and Europe. The trial has enrolled 217 patients, approximately 20% more than the 180 patients we had originally targeted. The demographics and baseline disease characteristics of the patients enrolled are similar to those seen in our Phase 2 trial of OCA as combination therapy in PBC patients. As of March 15, 2013, the discontinuation rate due to pruritus, even if attributed solely to the OCA dose groups, is lower than that seen in the 10mg OCA dose group in our Phase 2 combination study.

We are advancing a once daily 10 mg dose of OCA in the POISE trial as our potential approvable dose. The chart below shows an analysis of the extracted intention to treat data for the 10 mg dose groups in our two Phase 2 trials based on patients who would have met the inclusion criteria for entry in the POISE trial. The analysis demonstrates that after 12 weeks of treatment, approximately 40% to 45% of OCA-treated patients in our Phase 2 trials would have met the POISE trial primary endpoint as compared to 5% to 9% of the placebo-treated patients. In addition, 80% of OCA-treated patients across our Phase 2 trials had a reduction in ALP levels of at least 10%, as compared to 13% of placebo-treated patients.

If the POISE trial is successful, we intend to submit an NDA to the FDA for approval of OCA for the treatment of PBC in the United States and an MAA to the EMA for approval in Europe. Based on written scientific advice from the EMA, we believe that the EMA will accept our current clinical program as the basis for considering approval of OCA for PBC. With respect to the FDA, we intend to request an accelerated

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approval of OCA based on the acceptance of the POISE trial primary endpoint as a surrogate endpoint that is reasonably likely to predict clinical benefit. If the FDA grants an accelerated approval of OCA, we will be required to conduct one or more additional clinical trials post-approval to verify and confirm the clinical benefit predicted by the surrogate endpoint. This clinical outcomes trial must satisfy FDA s definition of an adequate and well-controlled trial and would have to be substantially underway at the time of the NDA submission and would be completed after accelerated approval. We are in discussions with the FDA about the design of the clinical outcomes trial and plan to initiate it as early as the second half of 2013.

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 potential acceptance of our POISE trial primary endpoint as a basis for approval will be the result of additional analysis of the already available PBC clinical outcomes data.

We are sponsoring the Global PBC Study Group, which involves more than ten leading academic PBC centers in Europe and North America, that are pooling their long-term patient data to evaluate the relationship between biochemical and clinical endpoints. We anticipate final data from at least 4,000 patients will be collected and analyzed as part of the study. Initial results for more than 2,100 patients have been accepted as a poster presentation at the EASL annual meeting, to be held in April 2013. The data confirms that the POISE trial primary endpoint has a highly statistically significant correlation with liver transplant-free survival. We anticipate that final results will be available by the end of 2013 and will support what we believe is an emerging consensus among PBC opinion leaders concerning the clinical utility of our selected surrogate endpoint.

An academic consortium in the UK has recently published data from a large observational study of over 2,300 PBC patients recruited from every hospital in the UK into a PBC research cohort. The results show that there is a highly statistically significant correlation between ALP, both alone and together with other biochemical parameters such as bilirubin, and clinical outcomes. Several different threshold values of ALP were tested and it was demonstrated that reductions in ALP levels down through to less than 1.5 times ULN are strongly predictive of clinical benefit.

We believe that the Global PBC Study Group and UK-based PBC research cohort represent the largest PBC clinical datasets ever assembled to analyze the correlation of biochemical therapeutic response with clinical outcomes in PBC patients. We further believe that the analyses already available confirm the results recently published, or made available to us, by four different members of the Global PBC Study Group (the University of Toronto, Mayo Clinic, University of Paris and Erasmus MC (Rotterdam)). These groups have independently corroborated that the achievement of an ALP level of less than 1.67 times ULN, together with a normal bilirubin level, correlate with a statistically significant reduction of risk of adverse clinical outcomes such as liver transplant and death.

Summary of additional preclinical and clinical studies required for regulatory submissions

Based on our interactions with the FDA and EMA, we believe that, in addition to the successful completion of the POISE trial, we will need to complete the following clinical studies prior to our planned NDA and MAA filings:

long-term safety extension studies, for which we expect to submit approximately 650 patient cumulative years of safety data across all clinical trials;
a study to evaluate the potential effects and clinical significance of OCA on the lipid profile of patients with PBC;
a Phase 1 clinical trial in healthy volunteers to evaluate the effect of OCA on the heart s electrical cycle, known as the QT interval; and

additional clinical pharmacology trials, including, but not limited to, drug interactions, the effects of food and drug-disease interaction studies.

In addition, other nonclinical studies that we will need to complete are carcinogenicity studies in two rodent species, which were initiated in early 2012, and reproductive toxicology studies. Finally, before we

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submit an NDA to the FDA, we believe that we will need to be substantially underway with a clinical outcomes trial to confirm clinical benefit at the time of NDA submission. We are in discussions with the FDA about the design of the clinical outcomes trial and plan to initiate it as early as the second half of 2013. It is possible that the FDA may require that we conduct and/or complete additional clinical trials and preclinical studies before it will consider our NDA for approval.

Summary of Completed OCA PBC Clinical Trials

Phase 2 Trial: OCA as Combination Therapy in PBC Patients

We have completed a double-blind, placebo-controlled Phase 2 clinical trial of OCA in 165 patients with PBC. The trial evaluated the effects of adding one of three doses of OCA (10 mg, 25 mg and 50 mg) or placebo to ursodiol therapy in patients with ALP levels of higher than 1.5 times ULN who had not responded adequately to ursodiol therapy alone. Patients continued their prior ursodiol dose throughout the trial. The trial was comprised of a 12-week treatment period, with a two-week follow up. At the end of the 12-week treatment period, all three doses of OCA added to ursodiol therapy produced statistically significant reductions in ALP levels as compared with patients receiving placebo plus ursodiol therapy, the primary endpoint. OCA-treated patients demonstrated a mean reduction of 21% to 25% in ALP levels, as compared to patients receiving placebo plus ursodiol therapy, who exhibited a mean reduction of less than 3%. At trial entry, the baseline mean ALP value for all the patient groups was approximately 2.4 times ULN. In addition, patients who received OCA experienced similar significant decreases in other clinically relevant liver enzymes such as gamma glutamyl transferase, or GGT, aspartate transaminase, or AST, alanine transaminase, or ALT, and bilirubin. Furthermore, serum markers of inflammation and immune response also improved as seen in reductions of CRP and IgM, which are closely associated with autoimmune dysfunction in PBC.

With the exception of a higher incidence of pruritus in the two highest OCA dose groups and a higher incidence of severe pruritus in all OCA dose groups, the Phase 2 clinical trial data showed that adverse events were generally similar across all groups, including the placebo group. Pruritus was dose dependent, with the ursodiol plus placebo incidence at 50%, ursodiol plus 10 mg of OCA at 47%, ursodiol plus 25 mg of OCA at 85% and ursodiol plus 50 mg of OCA at 80%. However, the severity of pruritus and the discontinuation rate due to severe pruritus increased with OCA dose and was worse than seen with placebo. There were no other statistically significant side effects observed over the placebo group, except for mild nausea.

Open Label Long-Term Safety and Efficacy Trial for OCA as Combination Therapy

Following the completion of the double-blind portion of the Phase 2 combination trial described above, 78 patients were enrolled in an open label long-term safety and efficacy extension study, or LTSE. Of these patients, 19 subsequently discontinued their participation in the LTSE, ten due to pruritus, one due to elevated bilirubin and eight due to other adverse events or for other reasons. There were five serious adverse events in the LTSE, of which two occurred at each of the 10 mg and 25 mg doses and one occurred at the 50 mg dose. None of the serious adverse events, which were typically related to hospitalizations for pre-existing conditions, was considered likely to be related to OCA therapy, and no serious adverse event was considered to be hepatic in nature.

In the LTSE, patients continued to receive open label OCA, increasing from a dose of 10 mg to as high as 50 mg each day. In patients whose dose was increased, there was a benefit of increasing the dose up to 25 mg from 10 mg (with an incremental 9% fall in ALP), but not in increasing the dose above 25 mg. Over two-thirds of the patients were increased to a dose of OCA of 20 mg or more. Pruritus was the most common adverse event, reported in 68 of the 78 patients (approximately 87%). Other adverse events included fatigue, insomnia and upper respiratory tract infection,

each of which was reported by approximately 13% of the patients in the LTSE.

The chart below demonstrates that patients taking OCA achieved mean reductions in ALP to approximately 1.67 times ULN after having been on therapy for three months and maintained that treatment response throughout a 12-month period and beyond. Furthermore, after 12 months, more than 50% of the patients had met the Phase 3 POISE trial primary endpoint, with a reduction in ALP levels to below 1.67 times ULN, along with at least a 15% reduction in ALP, and a normal bilirubin level. Taken together with the data from our ongoing monotherapy LTSE trial discussed below, we believe that these LTSE phases

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of our Phase 2 trials demonstrate that a large majority of patients taking OCA for at least 12 months, with some currently on therapy for more than 3 years, maintain a durable therapeutic response.

Phase 2 Combination Trial LTSE

* SEM is defined as the standard error of the mean, which is a statistical estimate of the amount that an obtained mean may be expected to differ by chance from the true mean.

*** p<0.0001

Phase 2 Trial: OCA as Monotherapy in PBC Patients

We have completed a 59 patient double-blind, placebo-controlled Phase 2 clinical trial of OCA given as a monotherapy to patients with PBC. The trial evaluated the effects of 10 mg and 50 mg doses of OCA compared to placebo in patients with baseline ALP levels of higher than 1.5 times ULN. Patients either had never taken ursodiol or had not been taking ursodiol for at least 3 months before the start of the trial. The trial was comprised of a 12-week treatment period, with a two-week follow up. At the end of the 12-week treatment period, statistically significant reductions in ALP were seen in the treated patients (38% to 45% mean ALP reductions compared with no change in the placebo-treated patients). Patients in the 10 mg dose group experienced absolute reductions in ALP levels from a mean of approximately 3.9 times ULN to approximately 1.9 times ULN at the end of the study. Even greater reductions in GGT (63% to 75%) were seen in the OCA-treated groups (compared to 3% for placebo-treated groups). There were also significant improvements in ALT levels and bilirubin levels. In addition, IgM also improved. Pruritus was seen more commonly in the patients treated with OCA, with the incidence, severity and discontinuation rate all increasing with dose; otherwise, the other adverse events were not clearly different across the groups.

Ongoing Open Label Long-Term Safety and Efficacy Trial for OCA as a Monotherapy

Following the completion of the double-blind portion of the Phase 2 monotherapy trial described above, some patients were given the option to enroll in an open label long-term safety and efficacy extension study, or monotherapy LTSE. The monotherapy LTSE phase is currently ongoing. Patients continue to receive open label OCA in this phase, and have been increased from a starting dose of 10 mg to as high as 50 mg.

As of January 31, 2013, 20 patients were continuing in the monotherapy LTSE, among whom eight patients had been on OCA therapy for more than three years. Approximately half of the patients are currently taking 20 mg or more of OCA. Consistent with the combination trial LTSE, continued improvements in

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biochemistry have been demonstrated. Pruritus is the most common adverse event and has been reported over the course of the monotherapy LTSE in 25 of the 28 subjects (or 89%) for whom data are available. Other adverse events include headache, arthralgia, constipation, fatigue and nausea, which have been reported in approximately 36%, 32%, 29%, 29% and 25% of the patients, respectively. The chart below demonstrates that patients taking OCA maintained mean reductions in ALP to approximately 1.67 times ULN throughout a 36-month period and beyond. Furthermore, after 12 months, approximately half of the patients had met the Phase 3 POISE trial primary endpoint, with a reduction in ALP levels to below 1.67 times ULN, along with at least a 15% reduction in ALP, and a normal bilirubin level. We believe that the LTSE phase of our Phase 2 trials demonstrate that a large majority of patients taking OCA for at least 12 months, with some currently on therapy for more than 3 years, maintain a durable therapeutic response.

Phase 2 Monotherapy Trial LTSE

Summary of Completed Phase 1 Trials

OCA has been evaluated in two Phase 1 clinical trials to study its safety and pharmacokinetic profile in healthy volunteers. The first was a single ascending dose trial in 24 subjects testing single OCA doses in the range of 50 mg to 500 mg. The second was a multiple ascending dose trial in 50 subjects testing repeated OCA doses in the range of 25 mg to 250 mg for 12 consecutive days. Adverse events seen in the Phase 1 trials were generally mild. Only two adverse events, upper abdominal pain and nasopharyngitis, were observed in one subject each in the single ascending dose trial. In the multiple ascending dose trial, doses from 25 mg to 100 mg were generally well-tolerated. At the highest dose of 250 mg, ALT and AST increases were seen, consistent with our animal toxicology data. This dose is 25-times greater than the 10 mg dose in the POISE trial and ten-times greater than the 25 mg dose being tested in our ongoing Phase 2b trial for NASH, called the FLINT trial. Half of the subjects in the 250 mg dosing group reported mild pruritus and one discontinued due to a rash.

Additional Potential Clinical Indications for OCA

Based on the potential protective effects of OCA in the liver, we are conducting clinical trials in additional chronic liver disease indications with potential greater market opportunities, with the view of expanding OCA s therapeutic applications.

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Potential Use of OCA to Treat Portal Hypertension

A study in an animal model of cirrhosis showed that OCA treatment can acutely reverse portal hypertension through a localized vasodilatory mechanism that is independent of its longer term anti-fibrotic effects. Portal hypertension results from increased pressure in the portal vein, which feeds most of the blood supply to the liver. The condition typically occurs as the liver becomes cirrhotic and more rigid, thereby offering more resistance to blood inflow from the portal vein. Many patients with liver cirrhosis go on to develop portal hypertension, which is a common cause of morbidity and mortality at the end stage of all chronic liver diseases. An early manifestation of portal hypertension is the development of esophageal varices, which are distended and weakened veins in the lower part of the esophagus that can burst and cause catastrophic bleeding. More than 40% of patients with cirrhosis have varices at the time of diagnosis. The standard assessment of portal venous pressure is to measure the hepatic venous pressure gradient, or HVPG, and clinically significant portal hypertension is defined as an HVPG of greater than ten millimeters of mercury, or mm Hg, where one to five mm Hg HVPG is considered normal. Patients with an HVPG of greater than 12 mm Hg are at particularly high risk of variceal bleeding, with each episode carrying an approximately 20% mortality risk. There are no approved therapies for the treatment of portal hypertension, although beta blockers are commonly used to treat patients. However, they are effective in only 25% to 33% of patients and have significant safety issues in patients with portal hypertension. Among other concerns, beta blockers lower systemic blood pressure in these patients who already tend to have low blood pressure, or hypotension, which predisposes them to fainting and inadequate blood perfusion of vital organs.

Phase 2 Trial for Portal Hypertension

It has been shown clinically that reducing pressure in the portal vein, as determined by HVPG measurement, can lower the risk of adverse outcomes such as the incidence of variceal bleeding. We therefore believe that HVPG reduction is an appropriate therapeutic endpoint to demonstrate clinical proof-of-concept in patients with portal hypertension.

We are currently conducting an open label Phase 2a trial of OCA, called the PESTO trial, in patients with alcoholic liver cirrhosis and portal hypertension in order to evaluate the ability of OCA to reduce HVPG in patients with end-stage liver disease. The primary endpoint of the trial is the reduction of HVPG after seven days of treatment by 15% or more, or to less than 12 mm Hg, a level at which the risk of adverse clinical outcomes has been shown to be significantly reduced. We presented results from a 10 mg dose group of the PESTO trial at the 2012 AASLD annual meeting. The results from the first 10 mg dose group showed that OCA was well tolerated in all twelve patients in the trial and five of eight patients who underwent portal circulation pressure assessments met the primary efficacy endpoint. A sixth patient experienced slightly more than a 14% reduction in HVPG. Importantly, patients who responded to OCA therapy with a reduction in HVPG did not experience a concomitant reduction in systemic blood pressure.

The PESTO trial is ongoing with a 25 mg dose of OCA currently being evaluated and another 10 mg dose group being tested at a second center. We anticipate completing the trial in the fourth quarter of 2013. We are utilizing the safety data from the PESTO trial to supplement our safety data set for our planned NDA and MAA filings for PBC to include the evaluation of OCA in patients with end-stage liver disease. If the PESTO trial supports the further development of OCA for the treatment of portal hypertension, we intend to initiate a placebo-controlled, randomized Phase 2 clinical trial in patients with portal hypertension for a longer treatment period. However, we will need to secure funding to continue to advance OCA beyond that point for this indication.

Potential Use of OCA to Treat Nonalcoholic Steatohepatitis (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. Nonalcoholic fatty liver disease, or NAFLD, is believed to be the most common chronic liver disease worldwide and we believe that more than 75 million patients are affected in the United States alone. The disease is associated with the Western diet, which is rich in processed foods with high fat and sugar content. NAFLD can lead to excessive fat accumulation in the liver, insulin resistance and increased risk of developing metabolic syndrome, type 2 diabetes and cardiovascular disease. A subset of approximately 30% of NAFLD patients develop NASH,

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which is a more serious liver disease. In these patients, for reasons that are still not completely understood, the fat build-up in the liver induces chronic inflammation which leads to progressive fibrosis that can lead to cirrhosis and liver failure.

NASH is currently diagnosed by liver biopsy. Studies have shown that at least 15% of NASH patients will develop liver cirrhosis over a ten to 15 year period. In the United States, the most recent epidemiological studies have concluded that more than 12% of the general population has NASH, while approximately 2.7%, or more than eight million patients, have advanced liver fibrosis or cirrhosis due to the disease. In the past decade, the proportion of liver transplants attributed to NASH increased from 1% to 10%, establishing NASH as the third leading and a rapidly increasing indication for liver transplant in the United States. The epidemiological data from other developed countries in Europe and Japan are similar, and NASH has also become a highly prevalent liver disease in developing countries such as India and China.

There are currently no drugs approved for the treatment of NAFLD or NASH. It has been reported that in 2010, there were approximately $615 million in off-label sales of various therapeutics for the treatment of NASH, such as insulin sensitizers (e.g., metformin), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol. Lifestyle changes and exercise to reduce body weight and treatment of concomitant diabetes and dyslipidemia are accepted as the standard of care but have not conclusively been shown to prevent disease progression.

Ongoing Phase 2 Trial for NASH

OCA is currently being tested in a Phase 2b NASH trial, called the FLINT trial, which is testing a 25 mg single daily dose of OCA versus placebo in 280 patients with NASH. We are sponsoring the FLINT trial in collaboration with the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, which oversees a clinical research network of eight leading NASH centers in the United States. The NIDDK submitted an IND to the FDA for OCA for the treatment of NASH in 2010. The primary endpoint in the 72-week double-blind FLINT trial is based on liver biopsy and is defined as an improvement of two or more points in the NAFLD activity score (a system of scoring the histopathological features in the liver) with no worsening of liver fibrosis. The NIDDK is providing the majority of funding for the trial.

In June 2012, the NIDDK s data and safety monitoring board, or DSMB, for the FLINT trial completed an interim analysis and recommended that the trial should continue based on data from 101 patients who had completed at least 24 weeks and up to 15 months of the trial. The interim analysis reviewed the change from baseline in ALT levels as the efficacy criterion variable and all available safety data. Based on the recommendation of the DSMB, the NIDDK steering committee decided to continue the FLINT trial.

In November 2012, the NIDDK completed enrollment of the FLINT trial, achieving the target of 280 patients for this trial. We anticipate that final results will be available in late 2014. If this trial supports the further development of OCA as a treatment for NASH, we anticipate that we will need to secure additional funding to advance OCA for this indication.

In addition, our collaborator DSP has initiated a second Phase 2 NASH trial in Japan. This trial is evaluating the efficacy and safety of a once-daily dose of OCA as compared to placebo, with a targeted enrollment of 200 patients. This trial is anticipated to be completed in the first half of 2016.

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

We have also completed a Phase 2 clinical trial of OCA in 64 type 2 diabetic patients with NAFLD. This double-blind, placebo-controlled trial tested 25 mg and 50 mg doses of OCA over a six-week period and assessed the effects of OCA on insulin sensitivity. The trial demonstrated that OCA therapy significantly improved insulin sensitivity both in the liver and peripheral tissues, thereby meeting the primary endpoint in the trial. Significant improvements in weight loss and reductions in liver enzymes such as GGT and ALT were also noted. The trial also showed that OCA was well-tolerated by the trial patients, with side effects no different than those reported on placebo (apart from mild constipation in the 50 mg group).

Potential Use of OCA to Treat Bile Acid Diarrhea

In July 2012, investigators at the Imperial College of London initiated enrollment of an open label Phase 2a trial, called the OBADIAH trial, to investigate whether OCA can stimulate fibroblast growth factor 19, or FGF19, in patients with PBAD. PBAD, also known as idiopathic bile acid malabsorption, is a common

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chronic diarrheal condition due to excessive bile acid loss. PBAD is estimated to affect approximately one percent of the population and about one-third of patients diagnosed with diarrhea-predominant irritable bowel syndrome, or IBS-D. Prior studies have shown these patients have low levels of FGF19, a protein hormone released by the ileum, under FXR control, which suppresses bile acid production by the liver. The resulting excess bile acids spill into the intestine where they produce diarrhea by stimulating intestinal secretion. FGF19 is synthesized in the small intestine under the direct regulation of FXR and we have shown in all three of our completed Phase 2 trials that OCA markedly stimulates the release of FGF19.

The primary outcome measure of the OBADIAH trial is to assess the change in FGF19 levels and symptom scores over a two-week period in ten patients with PBAD and in two control groups, one enrolling patients with secondary bile acid diarrhea due to Crohn s disease and the other enrolling IBS-D patients who have normal FGF19 levels. The Imperial College of London is acting as the sponsor of the OBADIAH trial. The initial results from this trial in the PBAD group demonstrate that treatment with OCA is associated with a statistically significant improvement in clinical symptoms and levels of FGF19. An abstract based on initial results in the PBAD group from this study was accepted for presentation at the Digestive Diseases Week annual conference in May 2013. We currently anticipate that the enrollment for the OBADIAH trial will be completed in mid-2013 and that final results for all three study groups will be available in the second half of 2013. If this trial supports the further development of OCA as a treatment for PBAD, we anticipate that we will need to secure additional funding to advance OCA for this indication.

Other OCA Clinical Trials

The Sahlgrenska University Hospital in Sweden is sponsoring and has initiated a Phase 2a pharmacodynamic trial of OCA in patients undergoing bariatric surgery or gallstone surgery, or the OCABSGS trial. The primary purpose of the trial is to evaluate the effects of OCA on bile acid, lipid and glucose turnover in 20 morbidly obese patients and 20 gallstone patients who will be administered a 25 mg dose of OCA once daily for three weeks prior to undergoing bariatric and gallstone surgery, respectively. We anticipate that the OCABSGS trial will be completed in 2014.

Other Potential Indications for OCA

We believe that OCA may have potential therapeutic application in other chronic diseases such as PSC, another autoimmune cholestatic liver disease; inflammatory bowel disease, including Crohn s disease and/or ulcerative colitis; biliary atresia, a pediatric disease characterized by deficient bile duct development; and Alagille Syndrome, a very rare genetic disorder that affects the liver and other organs. We anticipate that we will need to secure additional funding for the advancement of OCA for any of these indications.

Potential Future Product Candidates

In addition to OCA, we have 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. We intend to continue advancing these and other product candidates as we build our pipeline, in some cases subject to the procurement of additional funding.

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 five-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 own exclusive worldwide, royalty-free rights to INT-767.

We currently plan to advance INT-767 through the preclinical studies required to support the advancement of this product candidate to an IND, with an intended focus on developing it as a novel treatment for chronic kidney diseases, such as diabetic nephropathy, that involve progressive fibrosis leading to kidney failure. If the preclinical and Phase 1 clinical data support the advancement of INT-767 into Phase 2 clinical trials, we anticipate that we will need to secure additional funding for the further development of this compound.

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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. We own exclusive worldwide, royalty-free rights to INT-777. In order to advance this product candidate into clinical trials, we will need to secure additional funding and may seek a strategic collaborator.

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 and associated metabolic disorders.

Strategic Collaborations and Research Arrangements

Dainippon Sumitomo Pharma

On March 29, 2011, we entered into a license agreement with Dainippon Sumitomo Pharma Co. Ltd., under which we granted DSP 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, DSP is required to use commercially reasonable efforts to develop and commercialize OCA in Japan and China for the treatment of PBC and NASH, and we are obligated under the agreement to use commercially reasonable efforts to develop OCA outside of Japan and China. DSP has agreed during the term of the agreement to not commercialize any compound that is a FXR agonist for use in the treatment of PBC or NASH other than pursuant to the agreement.

We granted DSP 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. DSP may exercise this option with respect to any indication at any time during the two-year period commencing on the date we notify DSP of the commencement of a Phase 3 clinical trial involving OCA for such indication, subject to DSP s payment of an option fee for each additional indication. No option fee is required to be paid by DSP if it exercises its option for any additional indication only in China.

We also granted DSP 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. DSP 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 DSP s payment of an option fee for each country. We may not offer rights to a third party to develop and commercialize OCA in any of these countries for an agreed upon time period, and, if after this date, 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 DSP and DSP 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 negotiations with DSP with respect to the grant to DSP of exclusive rights to develop and commercialize OCA in such countries.

DSP made an up-front payment to us in the amount of $15.0 million upon execution of the agreement. In addition, DSP 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. DSP is also

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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 DSP 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.

DSP 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 DSP 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 DSP 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 DSP 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 DSP s material breach or if DSP were to voluntarily terminate the agreement, DSP s license under the agreement would terminate.

Les Laboratories Servier and Institut de Recherches Servier

On August 1, 2011, we entered into a research, development, license and commercialization agreement with Les Laboratories Servier and Institut De Recherches Servier, or Servier, under which we granted Servier the exclusive license to research, develop and commercialize novel TGR5 agonists (other than INT-767 and INT-777) for use in the treatment of diabetes, obesity, atherosclerosis and reperfusion injury in all countries other than the United States and Japan, and Servier granted us an exclusive royalty-free license to research and develop such compounds for use in the treatment of diabetes, obesity, atherosclerosis and reperfusion injury in the United States and Japan. Under the terms of the agreement, Servier is required to use commercially reasonable efforts to develop compounds outside the United States and Japan and we are required to use commercially reasonable efforts to develop compounds in the United States and Japan.

We are obligated to conduct and are conducting a research program under the agreement to identify and optimize compounds that meet certain specified criteria sufficient for further development by Servier. The initial term of the research program is one year, subject to extension by mutual agreement. We are obligated under the agreement to provide Servier with a specified number of full time equivalent employees for the research program up to a specified maximum per year. In July 2012 and again in February 2013, we entered into amendments to this agreement to extend the term of the research program, which now expires on July 31, 2013, on the same financial terms as the original research program, including the reimbursement by Servier of the full time equivalent costs incurred by us in the conduct of the research program, up to a set maximum amount.

Servier has agreed to pay for the development costs we or Servier incur in conducting certain preclinical trials and clinical trials with respect to any compound that meets specified criteria. We have agreed to reimburse Servier up to a mid-double digit percentage of the total historical development costs incurred by Servier in relation to clinical development activities aimed at achieving regulatory approval in the European Union and the United States if we enter into a partnership agreement, or commence development or commercialization activities on our own, with respect to a compound in the United States. Servier may credit a portion of any such reimbursable development costs against any milestone or royalty payments due and payable by Servier under the agreement until all such reimbursable amounts are repaid. We have not incurred any such development costs since inception, and we do not anticipate

incurring any such development costs during fiscal 2013. In addition, if we enter into a partnership agreement with respect to a compound developed under the agreement solely in Japan, we and Servier have agreed to enter into good faith negotiations regarding the terms and conditions applicable to the reimbursement of development costs. If we do not enter into a partnership agreement with respect to the compound in the United States or Japan within three years from the date regulatory approval is received for a compound in the European Union, Servier will have the first right to negotiate with us regarding the terms and conditions applicable to the grant to Servier of an exclusive license to develop and commercialize the product in the United States and/or Japan.

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We have the right to conduct clinical trials and obtain regulatory approvals involving compounds developed under the agreement at our sole expense in the United States and Japan, and Servier has the right to conduct clinical trials and obtain regulatory approvals involving compounds developed under the agreement at its sole expense in all other countries. We and Servier have agreed during the term of the research program not to research or develop any TGR5 agonist and, during the term of the agreement, not to commercialize any TGR5 agonist covered by the agreement other than pursuant to the agreement. However, this provision does not restrict us from developing INT-767 and INT-777.

Servier has made an up-front payment to us in the amount of €1.0 million upon execution of the agreement and has agreed to reimburse us for a portion of the full time equivalent costs incurred by us in the conduct of the research program, up to a set maximum amount. In addition, Servier may be required to pay us up to an aggregate of approximately €8.5 million for the achievement of development milestones, €10.0 million for the achievement of regulatory submission and approval milestones and €90.0 million for the achievement of sales milestones based on aggregate sales amounts. Servier is also obligated to pay us tiered single digit percentage royalties based on net sales of products developed under the agreement on a country-by-country basis. Servier s obligation to pay royalties for each product expires on a country-by-country basis upon the later of the expiration of the last to expire patent licensed by us that covers the product and ten years from the date of first commercial sale of that product. Royalty rates are subject to reduction under the agreement in specified circumstances, including with respect to any country if sales of generic products reach a certain threshold in that country.

The agreement expires when no payment obligations are or will become due. Servier may terminate the agreement at any time for any reason or if we consummate a change of control transaction. Either we or Servier may terminate the agreement in the event of the uncured material breach or insolvency of the other party. Upon the termination of the agreement by Servier for our material breach or insolvency, Servier may, at its election, have its license from us under the agreement become perpetual and royalty-free following the effective date of termination. Upon termination of the agreement by Servier without cause, we will maintain our rights to the technology licensed to Servier outside of the United States and Japan and Servier will pay us the balance of any unpaid funding under the research program. Upon the termination of the agreement by us for Servier s material breach or insolvency, we may, at our election, have our license from Servier under the agreement become perpetual following the effective date of termination.

National Institute of Diabetes and Digestive and Kidney Diseases

In July 2010, we entered into a cooperative research and development agreement, or CRADA, with the NIDDK, a division within the National Institutes of Health, to conduct our ongoing Phase 2b FLINT trial for the treatment of NASH with OCA. In June 2012, the DSMB for the FLINT trial completed an interim analysis and recommended that the trial should continue based on data from 101 patients who had completed at least 24 weeks and up to 15 months of the trial. The interim analysis reviewed the change from baseline in ALT levels as the efficacy criterion variable and all available safety data. The primary endpoint of the FLINT trial is based on liver biopsy. Based on the recommendation of the DSMB, the NIDDK steering committee decided to continue the FLINT trial. In November 2012, the NIDDK completed enrollment of the FLINT trial, achieving the target of 280 NASH patients for this trial.

The NIDDK is providing the majority of funding for the trial. In accordance with the terms of the CRADA, we have made payments of $3.0 million to date and no further payments are required under the agreement.

Under the terms of the CRADA, any inventions under the CRADA will be owned by the party that produced such inventions. However, any inventions jointly developed by the parties will be jointly owned. We will have the first opportunity to file patent applications in respect of any jointly developed inventions under the CRADA. If we do not

exercise our rights, the NIDDK will be able to file a patent application in respect of such inventions.

The CRADA provides that we have an exclusive option to an exclusive or nonexclusive commercialization license on any inventions made solely by the NIDDK under the CRADA. The U.S. government has also been granted a worldwide, nonexclusive, nontransferable, irrevocable, paid-up license in

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respect of any subject inventions under the CRADA, including inventions made solely by us to the extent that such license is for research or other government purposes.

The CRADA has a term of four years, ending in July 2014. The parties to the CRADA may terminate the CRADA by mutual written consent. Either party may terminate the CRADA at any time by providing 60 days prior written notice to the other party. However, if we unilaterally terminate the CRADA, the NIDDK may be entitled to retain any funds transferred to the NIDDK under the CRADA and, unless the termination was for safety reasons, we may be required to supply sufficient quantities of OCA and placebos to complete the trial. We have agreed that the NIDDK may continue developing OCA if we suspend the development of OCA without transferring our development efforts, assets and obligations to a third party within 90 days of discontinuation. In such circumstances, we would also be required to grant a nonexclusive, irrevocable worldwide, paid up license for any of our inventions relating to OCA, its manufacture and any method of use of OCA for the treatment of NASH, including the right to sublicense.

If the FLINT trial supports the further development of OCA for NASH, we anticipate that we will need to secure additional funding for the further development of OCA in NASH.

University of Perugia and Professor Roberto Pellicciari

On January 1, 2012, we entered into a sponsored research agreement with the University of Perugia and Professor Roberto Pellicciari, whom we refer to as the Research Parties, to research and realize improvements to the process for synthesizing and supplying gram scale reference standard quantities of OCA, INT-767 and INT-777. Professor Pellicciari is one of our founders.

Pursuant to this agreement, we are obligated to pay the University of Perugia an aggregate of €80,000 during the term of the agreement in quarterly installments of €20,000.

Under the terms of the sponsored research agreement, we have been assigned all rights, title and interest in patent rights and technology upon creation related to the research project, effective as of the date of creation. We have the right and final decision-making ability as to the filing, prosecution or maintenance of all patents or patent applications covering any patent rights or technology developed through the agreement. The Research Parties are required to promptly and fully disclose to us in writing any invention conceived and/or reduced to practice in the conduct of the agreement. Under the terms of the agreement, we have a right of first refusal to negotiate terms to expand the agreement prior to the end of its term, or upon renewal, to include certain other research programs.

The sponsored research agreement has a term of one year from the date of execution. Since the expiration of the previous term on December 31, 2012, we have been ascertaining our specific requirements concerning the supply of certain reference standards relating to OCA, INT-767 and INT-777 and we are currently negotiating a revised agreement to provide for their supply. Either we or the Research Parties may terminate the agreement in the event of the uncured material breach of the other party after receipt of notice in writing of such breach from the other party. If the agreement is terminated by the Research Parties for a material breach by us during any quarterly period, the agreement provides that the Research Parties will be entitled to all rights, title and interest in and to the patent rights and technology created and assigned to us during that quarterly period. If the agreement is terminated by us for a material breach by the Research Parties, the agreement provides that all funds paid by us to the Research Parties not expended or irrevocably committed upon the effective date of termination will be refunded to us. Also, Professor Pellicciari will be required to return all materials and tangible documentation containing confidential information. We may also terminate the agreement if Professor Pellicciari is unable or unwilling to continue to conduct research or otherwise perform his obligations under the agreement.

TES Pharma Srl

On August 1, 2011, we entered into a research and development agreement with TES Pharma Srl, or TES, to conduct research and development activities for our TGR5 program. The research program is managed by Professor Roberto Pellicciari, who is an owner of TES.

We are required under the agreement to pay TES an aggregate amount of €250,000 each quarter during the term of the agreement. Payments will be made on a quarterly basis. The agreement provides that any funds paid to TES that have not been expended or irrevocably committed will be refunded to us.

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Under the terms of the agreement, any inventions created in connection with the activities performed under the agreement will be our sole and exclusive property and all original works of authorship made by TES within the scope of the project that are protectable by copyright are works made for hire. TES has agreed to assign to us all of its rights, titles and interests in all inventions and other intellectual property rights under the agreement.

The agreement has a term of one year unless we, in our sole discretion, extend the term of this agreement for one additional year on the same terms and conditions as the current agreement. In July 2012 and February 2013, we entered into amendments to extend the term of this agreement, which now expires on July 31, 2013, in conjunction with the extension of the term of our research program with Servier, on the same financial terms as our original agreement with TES. Either we or TES may terminate the agreement in the event of an uncured material breach after receipt of written notice in of such breach from the other party. If we terminate the agreement for a material breach by TES, any funds paid to TES that have not been expended or irrevocably committed by them will be returned to us. TES is also obligated to deliver to us all remaining compounds and tangible documentation containing confidential information upon our request. If the agreement is terminated by TES for a material breach by us, TES is entitled to the balance of payments owed to them once the appropriate quarterly reports have been submitted to us.

Consulting Agreements with Professor Pellicciari

Servier TGR5 Agonists

On August 1, 2011, we entered into a consulting agreement with Professor Roberto Pellicciari to provide scientific guidance for a research program relating to selective or non-selective TGR5 agonists to be undertaken by TES and to supervise and coordinate this research program. Professor Pellicciari will also act as our designated representative on a joint steering committee formed pursuant to our collaboration agreement with Servier.

The agreement provides that Professor Pellicciari will receive compensation at an annual rate of €150,000 for his services during the term of the agreement in quarterly installments of €37,500. The agreement also provides that Professor Pellicciari will be eligible for a €50,000 performance bonus based on the success of the research collaboration. The performance bonus is a discretionary bonus based upon our assessment of the success of the initial work performed under the collaboration, as extended. No such bonus has been agreed upon by the parties as of December 31, 2012.

Under the terms of the agreement, all inventions created in connection with the activities performed under the agreement are our sole and exclusive property and all original works of authorship made by Professor Pellicciari that are protectable by copyright are works made for hire. Professor Pellicciari has also assigned to us all rights, title and interest in all inventions and any other intellectual property rights created under the agreement from January 1, 2011 through the end of its term. Professor Pellicciari must provide timely written notice of any inventions that he develops during the term of the agreement.

The agreement has a term of one year. However, at our sole discretion, we may extend the term of the agreement by one additional year. In July 2012 and February 2013, we entered into amendments to extend the term of this agreement, which now expires on July 31, 2013, in conjunction with the extension of the term of our research program with Servier, on the same financial terms as our original consulting agreement with Professor Pellicciari. Either we or Professor Pellicciari may terminate the agreement in the event of a material breach by the other party that is not remedied within 30 days after receipt of written notice of such breach from the other party.

OCA, INT-767 and INT-777

On January 1, 2012, we entered into a consulting agreement with Professor Pellicciari to provide scientific guidance for our research program relating to OCA, INT-767 and INT-777 and to supervise and coordinate this research program.

The agreement provides that Professor Pellicciari will receive compensation at an annual rate of €100,000 for his services during the term of the agreement in quarterly installments of €25,000.

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Under the terms of the agreement, all inventions created in connection with the activities performed under the agreement are our sole and exclusive property and all original works of authorship made by Professor Pellicciari that are protectable by copyright are works made for hire. Professor Pellicciari has also assigned to us all rights, title and interest in all inventions and any other intellectual property rights created under the agreement. Professor Pellicciari must provide timely written notice of any inventions that he develops during the term of the agreement.

The agreement has a term of one year. However, at our sole discretion, we may extend the term of the agreement by one additional year. We are currently contemplating the extension of this agreement in conjunction with our negotiations with Professor Pellicciari and the University of Perugia regarding the revised agreement to supply us with reference standards relating to OCA, INT-767 and INT-777. Either we or Professor Pellicciari may terminate the agreement in the event of a material breach by the other party that is not remedied within 30 days after receipt of written notice of such breach from the other party.

WIL Research Laboratories, LLC

On October 2, 2007, we entered into a master laboratory services agreement with WIL Research Laboratories, LLC, or WIL, to perform certain research and laboratory services. The agreement was amended on October 28, 2011.

On November 16, 2011, we finalized work orders with WIL for the FDA-required studies in mice and rats to investigate the presence or absence of carcinogenic potential of OCA. We have agreed to pay WIL an aggregate of $4.0 million for the studies, consisting of a combination of quarterly installment payments of approximately $300,000 and milestone payments totaling approximately $400,000 upon delivery of final result reports. If additional costs are incurred beyond the amounts specified in the work orders, we have agreed to pay such reasonable additional costs upon receipt of proper invoice. We anticipate that the studies will continue through completion, all milestones will be satisfied and that we will pay to WIL an aggregate of $4.0 million under this agreement.

Under the terms of the agreement, we own all work product and data prepared or generated by WIL in the course of its services, assuming our payment of all required amounts specified in the contract. We have no property rights in WIL s intellectual property.

The agreement has a term ending on October 2, 2013, which automatically extends for successive one year periods, unless either party gives written notice to the other party at least 60 days prior to the end of the current term. Either we or WIL may terminate the agreement upon 90 days written notice. However, if a work order pertaining to the ongoing studies is outstanding, WIL may not terminate the agreement with 90 days written notice until the work order has been completed or otherwise terminated.

Commercialization

Given our stage of development, we have not yet fully established a commercial organization or distribution capabilities. In the United States and Europe, due to the rare nature of PBC and the limited options for treatment, patients suffering from PBC and their physicians often have a high degree of organization and are well informed, which may make it easier to identify target populations if and when OCA is approved. The market for the treatment of PBC is a specialty care market driven by key opinion leaders. Most patients with PBC are treated at a limited number of academic centers or otherwise by physicians who specialize in the treatment of liver disease. 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 force that calls on a limited and focused group of physicians.

Our current plan is to commercialize OCA for PBC ourselves in the United States and Europe if it is approved. We have started the initial phase of assessing our commercial strategy. We anticipate that our commercialization efforts will include both our internal commercial organization and contract reimbursement specialists, sales people and medical education specialists, and other outside resources. Outside of the United States and Europe, subject to obtaining necessary marketing approvals, we likely will seek to commercialize OCA through distribution or other collaboration arrangements for PBC. 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 provided us with a growing knowledge of the physicians we plan to target for commercial

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launch of OCA for PBC, subject to marketing approval in the United States and Europe. In March 2011, we exclusively licensed rights to OCA to DSP in Japan and China, along with an option to expand this exclusive license into certain other Asian countries. If we pursue approval for OCA in more prevalent liver diseases such as NASH, we would plan to do so selectively either on our own or by establishing collaborations with one or more pharmaceutical companies.

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 and reimbursement.

Our most advanced product candidate, OCA, is currently being developed as a second line treatment for PBC. Currently, ursodiol is the only therapy that is approved for the treatment of PBC. Although there are currently no other drugs approved for the treatment of PBC, we are aware of other companies, including Eli Lilly, Exelixis, Inc. and Phenex Pharmaceuticals AG that have FXR agonists in Phase 1 or earlier stages of preclinical development that could be used to treat PBC and the other liver diseases we are targeting. In addition, Johnson & Johnson and NovImmune SA are each currently conducting Phase 2a proof-of-concept open label clinical trials of monoclonal antibodies as potential treatments for PBC. Finally, Dr. Falk Pharma GmbH, which markets ursodiol, is conducting a Phase 3 clinical trial of combination ursodiol and budesonide, a steroid, as a treatment for PBC.

For the treatment of portal hypertension, the only therapeutic products available are beta blockers, which clinical studies have shown are effective only in approximately 25% to 33% of patients, while having significant safety issues. We are aware of only one other company, Dr. Falk Pharma GmbH, which has a new product candidate in Phase 2 clinical development for the treatment of portal hypertension.

There are currently no therapeutic products approved for the treatment of NASH or NAFLD. There are several marketed therapeutics that are currently used off label for the treatment of NASH, such as insulin sensitizers (e.g., metformin), antihyperlipidemic agents (e.g., gemfibrozil), pentoxifylline and ursodiol, but none has been clearly shown in clinical trials to alter the course of the disease. We are aware of several companies that have product candidates in Phase 2 clinical development for the treatment of NASH, including Dr. Falk Pharma GmbH, Galmed Medical Research Ltd., Immuron Ltd., Mochida Pharmaceutical Co., Ltd., NasVax Ltd. and Raptor Pharmaceutical Corp., and there are other companies with candidates in earlier stage programs. In addition, it is possible that one or more of the FXR agonist product candidates mentioned above that are being developed by our competitors could be used for the treatment of NASH.

For the treatment of PBAD, bile acid binding resins such as cholestyramine are currently used as the only available targeted therapy. Patients with this disease represent a subset of patients diagnosed with IBS-D, and we are aware of several companies with product candidates in Phase 2 or 3 clinical development for the treatment of IBS-D, including Astellas Pharma US, Inc., AstraZeneca, Salix Pharmaceuticals, Inc. and Tioga Pharmaceuticals, Inc. In addition, there are several marketed products indicated for the treatment of IBS-D, including GlaxoSmithKline s Lotronex and the over-the-counter product Imodium.

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

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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.

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 any 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 1.A, Risk Factors Risks Relating to Our Intellectual Property.

OCA (formerly called INT-747) (first-in-class 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 March 15, 2013, we owned five U.S. patents, four pending U.S. patent applications, and corresponding foreign patents and patent applications. Foreign patents have been granted in Europe, Norway, Spain, Denmark, Germany, Austria, Australia, Japan, Canada, Belgium, Cyprus, Finland, France, Greece, Ireland, Israel, Italy, Luxembourg, Monaco, Netherlands, Portugal, Sweden, Switzerland, Turkey and the United Kingdom. We expect the composition of matter patent, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2022 (worldwide). 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 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 and patent applications in the portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from 2022 to 2028.

INT-767 (dual FXR/TGR5 agonist)

The patent portfolio for INT-767 contains a patent and patent applications directed to compositions of matter and methods of use. As of March 15, 2013, we owned one U.S. patent, three pending U.S. patent applications, and corresponding foreign patent applications have been filed in Australia, Canada, China, Europe, India, Israel, Japan and Hong Kong. We expect the issued composition of matter patent in the U.S., 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 pending foreign patent applications in the portfolio, if issued, and 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 have received assignments of rights to the INT-767 patent portfolio from all inventors, other than one inventor. That inventor is contractually obligated to provide an assignment to us. We believe that we are the owner of the INT-767 patent portfolio by virtue of this contractual obligation and the other patent assignments we have received.

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INT-777 (TGR5 agonist)

The patent portfolio for INT-777 contains a patent and patent applications directed to compositions of matter and methods of use. As of March 15, 2013, we owned one U.S. patent, two pending U.S. patent applications, and corresponding foreign patent applications have been filed in Australia, Brazil, Canada, China, Eurasia, Europe, India, Israel, Japan, Korea, Mexico, Singapore, South Africa and Hong Kong. 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 corresponding foreign patent applications and other patent applications in the portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from 2028 to 2029. Patent term extension may be available in certain foreign countries upon regulatory approval.

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 our preclinical research and clinical trials, including the Phase 3 trials for OCA for the treatment of PBC. We are currently seeking to contract to qualify a back-up API manufacturer. 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 if they are approved. As OCA and any of our other product candidates continue to progress towards potential regulatory approval, 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 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

Governmental authorities in the United States, at the federal, state and local level, and 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.

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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. 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 an applicant 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 process required by the FDA before a drug may be marketed in the United States generally involves the following:

completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLPs, or other applicable regulations;
submission to the FDA of an IND, which must become effective before human clinical trials may begin;
performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the proposed drug for its intended use;
submission to the FDA of an NDA;
satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity; and
FDA review and approval of the NDA.

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 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

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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 institutional review board, or 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.

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.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for a 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. A 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,

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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 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. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for the approval of a drug on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a drug candidate receiving accelerated approval perform post-marketing clinical trials.

In the recently enacted Food and Drug Administration Safety and Innovation Act, or FDASIA, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law requires the FDA to issue related draft guidance within a year after the law s enactment and also promulgate confirming regulatory changes. For example, sponsors may request that their drug be designated as a Breakthrough Therapy. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment

to an IND. FDA is in the process of developing guidance related to this designation, but in the interim has posted on its website criteria that should be followed and has already granted the designation to several new drugs.

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We currently plan to seek accelerated approval of OCA for the treatment of PBC assuming satisfactory achievement of a surrogate endpoint in our Phase 3 POISE trial that we believe is reasonably likely to predict clinical benefit. We also intend to have commenced a clinical outcomes trial to confirm clinical benefit at the time of the NDA submission which we plan to complete on a post-marketing basis if the NDA is approved.

Patent Term Restoration and Marketing 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 a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product s approval date. The patent term restoration 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 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.

Market 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 marketing 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, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, 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. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan Drug Designation

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.

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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.

Post-approval Requirements

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.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

record-keeping requirements;

reporting of adverse experiences with the drug;
providing the FDA with updated safety and efficacy information;
drug sampling and distribution requirements;
notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
complying with FDA promotion and advertising requirements.

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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.

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.

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 either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology or those medicines intended to treat AIDS, cancer, neurodegenerative disorders or diabetes and optional for those medicines which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments report, each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

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 unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

ATU

We may apply to make OCA available for use under a cohort Autorisation Temporaire d Utilisation, or Temporary Authorization for Use, or ATU, in France. Under an ATU, the French Health Products Safety Agency, or Afssaps, allows the use of a drug in France before marketing approval has been obtained in France in order to treat serious or rare diseases for which no other treatment is available in that country. Afssaps will only grant an ATU where the

benefit of the product outweighs the risk. An ATU is granted for one year and may be renewed. If an ATU is granted for OCA, we will be required to gather and analyze data concerning OCA s use and submit a periodic report to Afssaps. We also will be responsible for submitting pharmacovigilance reports, as necessary. An ATU may be modified, suspended, or withdrawn for reasons of public health or if the conditions under which the ATU was granted are no longer met. We believe the granting of an ATU and subsequent use by patients in France prior to marketing approval may enable us to begin recognizing some product sales revenue for OCA prior to its approval in the United States and the remainder of the European Union.

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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 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 third-party payors do not consider our products to be cost-effective 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.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. 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 Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription 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 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.

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 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.

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, enacted in March 2010, is expected to have a significant impact on the health care industry. ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, ACA is

expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions which has not yet occurred. In addition, although the United States Supreme Court recently upheld the constitutionality of most of the ACA, some states have indicated that they intend to not implement certain sections of the ACA, and some members

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of the U.S. Congress are still working to repeal parts of the ACA. These challenges add to the uncertainty of the legislative changes enacted as part of ACA.

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.

Employees

As of March 15, 2013, we had 25 employees, of which 17 are involved in our drug development operations and eight are in general and administrative functions. 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 18 Desbrosses Street, New York, NY 10013, and our telephone number is (646) 747-1000.

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.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2017; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the JOBS Act, and references herein to emerging growth company shall have the meaning associated with it in the JOBS Act.

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Item 1A. Risk Factors

Except for the historical information contained herein or incorporated by reference, this report and the information incorporated by reference 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 report. 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 report and in any documents incorporated in this report by reference.

You should consider carefully the following risk factors, together with all of the other information included or incorporated in this report. 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 Relating 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 not yet submitted any product candidates for approval by regulatory authorities in the United States or elsewhere for our lead indication, primary biliary cirrhosis, or PBC, or any other indication. We have incurred net losses in each year since our inception, including net losses of $15.1 million, $12.7 million and $43.6 million for the years ended December 31, 2010, 2011 and 2012, respectively. We had an accumulated deficit of $118.2 million as of December 31, 2012. As of December 31, 2012, our working capital was $98.8 million and our cash, cash equivalents and investment securities available for sale was $110.2 million.

To date, we have devoted most of our financial resources to our corporate overhead and research and development, including our drug discovery research, preclinical development activities and clinical trials. We 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 to support our product development efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years as we complete our Phase 3 clinical trial of OCA in PBC, which we call the POISE trial, and related activities required for regulatory approval of OCA and continue pursuing additional indications for OCA in clinical trials, and initiate pre-commercialization activities. 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. As a result of the foregoing, we expect to continue to experience net losses and negative cash flows for the foreseeable future. These 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, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. In addition, our expenses could increase if we are required by the U.S. Food and Drug Administration, or 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. 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 have never been profitable. Currently, we have no products approved forcommercial sale, and to date we have

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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. We will require substantial additional future capital in order to complete clinical development and commercialize OCA, and to conduct the research and development and clinical and regulatory activities necessary to bring other product candidates to market. If the FDA or EMA requires that we perform additional preclinical studies or clinical trials, our expenses would further increase beyond what we currently expect and the anticipated timing of any potential NDA or MAA would likely be delayed.

Our existing cash and cash equivalents will not be sufficient to complete advanced clinical development of any of our product candidates other than OCA for PBC. Accordingly, we will continue to require substantial additional capital to continue our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds we will require to complete research and development and commercialize our products under development.

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

the progress, costs, results of and timing of our Phase 3 POISE trial of OCA for the treatment of PBC, and the clinical development of OCA for other potential indications;

the willingness of the FDA and EMA to accept our POISE trial, as well as our other completed and planned clinical and preclinical studies and other work, as the basis for review and approval of OCA for PBC;

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 our product candidates in preclinical development, such as INT-767 and INT-777;

the ability of our product candidates to progress through clinical development successfully;

our need to expand our research and development activities;

the costs associated with securing and establishing commercialization and manufacturing capabilities;

market acceptance of our product candidates;

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 additional management and scientific and medical personnel;

the effect of competing technological and market developments;

our need to implement additional internal systems and infrastructure, including financial and reporting systems; 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.

Some of these factors are outside of our control. Based upon our currently expected level of operating expenditures, we believe that we will be able to fund our operations through mid-2015. This estimate reflects our enrollment of a greater number of patients in our POISE trial than originally planned; additional

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nonclinical studies and clinical trials to support our planned regulatory submissions for OCA in PBC; and an anticipated increase in pre-commercial activities for OCA in PBC. This period could be shortened if there are any significant increases in planned spending on development programs or more rapid progress of development programs than anticipated or if we accelerate pre-commercialization activities. We do not expect our existing capital resources to be sufficient to enable us to complete the commercialization of OCA, if approved, or to initiate all of the clinical trials or additional development work needed for any of our other product candidates. Accordingly, we expect that we will need to raise additional funds in the future.

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 one or more of our research or development programs. 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 up-front payments received under our collaboration and license agreements with Dainippon Sumitomo Pharma Co. Ltd., or DSP, and Les Laboratoires Servier and Institut de Recherches Servier, which are collectively referred to as Servier. Additional payments under each of the DSP and Servier agreements are based on 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 DSP and Servier under their respective collaboration and license agreements are uncertain because DSP or Servier, as the case may be, may choose not to continue research or development of 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. 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 Phase 3 POISE trial, and our other completed and planned 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;

difficulties in identifying and treating patients suffering from our target indications, and PBC in particular, which is considered to be a rare disease;

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the success of our clinical trials through all phases of clinical development, including our POISE trial of OCA for the treatment of PBC;
potential side effects of our product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
our ability to obtain additional funding to develop our product candidates;
our ability to identify and develop additional product candidates;
market acceptance of our product candidates;
our ability to establish 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 sufficient reimbursement for our products;
our ability to adhere to clinical study 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 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 our finance infrastructure and improve our accounting systems and controls;
potential product liability claims;
potential liabilities associated with hazardous materials; and
our ability to obtain and maintain adequate insurance coverage.

In addition, our financial results may vary due to fluctuations in our warrant liability. Because our common stock is publicly traded, these fluctuations are expected to increase or decrease significantly based on changes in the price of our common stock. For example, the fair value of the warrant liability increased from $6.3 million at September 30, 2012 to approximately $30.4 million at December 31, 2012 primarily due to increase in the fair value of our common stock from $11.21 per share as of September 30, 2012, prior to our IPO, to $34.24 per share as of December 31, 2012,. Accordingly, our financial results for any period should not be relied upon as indications of future operating performance.

Our recurring losses from operations may raise substantial doubt regarding our ability to continue as a going concern.

Our recurring losses from operations may raise substantial doubt about our ability to continue as a going concern. If in the future, our independent registered public accounting firm were to include an explanatory paragraph in its report on our consolidated financial statements stating there is substantial doubt about our ability to continue as a going concern, such an opinion could materially limit our ability to raise additional funds through the issuance of new debt or equity securities or otherwise. There is no assurance that sufficient financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

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Risks Relating 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 without regulatory approval we will not be able to market our product candidates.

We are initially developing OCA for the treatment of patients with PBC, portal hypertension, nonalcoholic steatohepatitis, or NASH, and bile acid diarrhea, and are also consulting with investigators to develop protocols for other indications. 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 for the treatment of PBC and other indications 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 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. We have not submitted any marketing applications 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. If we submit an NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA. Regulators of other jurisdictions, such as the EMA, have their own procedures for approval of product candidates. Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications 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. 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. 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. Also, regulatory approval for any of our product candidates may be withdrawn.

We have completed three Phase 2 trials for OCA: two in patients with PBC and one in patients with type 2 diabetes with co-morbid nonalcoholic fatty liver disease. We completed enrollment in our POISE trial in December 2012 and anticipate that results from the 12 month double-blind portion of the POISE trial will be available in the second quarter of 2014. Before we submit an NDA to the FDA or an MAA to the EMA for OCA for the treatment of patients with PBC, we must successfully complete this trial. In addition, we must complete other preclinical and clinical

studies, such as a study to evaluate the potential effects and clinical significance of OCA on the lipid profile of patients with PBC and a Phase 1 clinical trial in healthy volunteers to evaluate the effect of OCA on the heart s electrical cycle, known as the QT interval and two-year, two-species carcinogenicity studies. We cannot predict whether our future trials and studies 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.

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 cannot be certain that OCA or any of our other product candidates willreceive regulatory approval, and without

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We may never reach an agreement with the FDA on a surrogate endpoint for the accelerated approval of OCA for the treatment of PBC. The FDA, EMA and other regulators may require us to complete additional Phase 3 trials prior to the submission of an application for OCA for the treatment of PBC.

Typically, the FDA requires two pivotal clinical trials to approve an NDA. However, for OCA as a treatment for PBC, we currently plan to request accelerated approval from the FDA based on the Phase 3 POISE trial, the primary endpoint of which is a surrogate endpoint that we believe is reasonably likely to predict clinical benefit, therefore meeting the FDA s requirements for consideration under its accelerated approval regulation. However, the FDA has not yet provided any assurance that it will accept our approach, and we do not know if we will receive further written guidance from the FDA prior to submitting an NDA as to the acceptability of the POISE trial surrogate endpoint to support an approval of OCA for the treatment of PBC.

In order to build additional consensus regarding the clinical utility of the surrogate endpoint, we are sponsoring an independent study pooling and analyzing long-term PBC patient data from a number of leading PBC academic centers. Furthermore, an academic consortium in the United Kingdom recently 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, 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. The FDA has 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. We believe that this clinical outcomes trial will need to be substantially underway at the time we submit an NDA. It is possible that our 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 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.

Because the FDA normally requires two pivotal clinical trials to approve an NDA, even if we achieve favorable results in our ongoing POISE trial, the FDA may not accept this 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 OCA for the treatment of PBC. Furthermore, the EMA and regulatory authorities in other countries in which we may seek approval for, and market, OCA, 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 PBC, the labeling for OCA in the United States, Europe or other countries in which we seek approval may include limitations that could impact the commercial success of OCA.

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 completed enrollment of our Phase 3 POISE trial in December 2012 and anticipate that results from the 12 month double-blind portion of the POISE trial will be available in the second quarter of 2014. Although we anticipate that our existing cash, cash equivalents and investment securities available for sale, and interest on our cash balances, will be sufficient to fund our projected operating requirements through the completion of our POISE trial, the results from this trial 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 PBC, in which case we would require additional funding. In addition, we do not know whether any future trials or studies of our other product candidates, including any clinical outcomes trial of OCA, will begin on time or

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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;
- 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;
- 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;
- 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 study 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.

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, a clinical trial may be suspended or terminated at any time by us, our current or future collaborators, the FDA or other regulatory authorities due to a number of factors, including:

- our failure or the failure of our collaborators to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- unforeseen safety issues or any determination that a clinical trial presents unacceptable health risks;
- lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions; and
- 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 DSP and Servier.

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.

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

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Clinical failure can occur at any stage of clinical development and we have never conducted a Phase 3 trial or submitted an NDA or MAA before. The results of earlier clinical trials are not necessarily predictive of future results and any product candidate we, DSP, 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, even after seeing promising results in earlier clinical trials.

Both of our Phase 2 clinical trials of OCA in PBC patients showed statistically significant results against a primary endpoint that is similar to the endpoint of our Phase 3 POISE trial protocol currently underway. However, in our Phase 2 PBC trials, the primary endpoint was a reduction in alkaline phosphatase, or ALP, to a threshold below 1.5 times upper limit normal, or ULN, compared to placebo after 12 weeks of treatment, but the primary endpoint for our POISE trial is both a reduction in ALP to below a threshold of 1.67 times ULN, with a minimum of 15% reduction in ALP from baseline, and a normal bilirubin level, compared to placebo after 12 months of therapy. We cannot assure you that our POISE trial will achieve positive results. Moreover, the fact that a retrospective analysis of the data from our Phase 2 PBC trials appears to demonstrate that the defined endpoint in our POISE trial was achieved based on the Phase 2 data does not mean that this endpoint will be successfully achieved in the POISE trial.

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 have limited experience in designing clinical trials and 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 and our business would be harmed. For example, if the results of our Phase 3 POISE trial of OCA do not achieve the primary efficacy endpoints or demonstrate expected safety, the prospects for approval of OCA would be materially and adversely affected.

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 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.

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require them 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 bile acid CDCA, which has been approved to treat cholesterol gallstone dissolution and a rare lipid storage disease, 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 were pruritus, or itching, headaches, fatigue, nausea, constipation and diarrhea. In our Phase 2 PBC clinical trial of OCA in combination with ursodiol, approximately 8% of the

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patients enrolled in the 10 milligram (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. 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. Although the discontinuation rate due to pruritus in our Phase 3 POISE trial has been lower than that seen in the 10 mg OCA dose group in our Phase 2 combination study, the trial is still ongoing and severe pruritus or other adverse events may occur.

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.

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, DSP, 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.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, 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, we cannot be certain that reimbursement policies will not 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.

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.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. If th

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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.

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. While we cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of OCA or any future product candidates. In addition, although the United States Supreme Court upheld the constitutionality of most of the ACA, some states have indicated that they intend to not implement certain sections of the ACA, and some members of the U.S. Congress are still working to repeal the ACA. We cannot predict whether these challenges will continue or other proposals will be made or adopted, or what impact these efforts may have on us.

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.

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 patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration 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 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 assuming they withstand any challenge. We expect that the other patents and patent applications for the OCA portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2028.

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. 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 other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in

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

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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, we may not be able to commercialize any of our product candidates.

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 our Phase 3 POISE trial of OCA for the treatment of PBC and the other trials and preclinical studies that we believe we will need to conduct prior to seeking regulatory approval. However, we do not have agreements for commercial supplies of OCA or any of our other product candidates and we may not be able to reach agreements with these or other contract manufacturers for sufficient supplies to commercialize OCA if it is approved. 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;
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 or prevent us from commercializing our product candidates successfully. 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.

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

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Even if our product candidates receive regulatory approval, we may still 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, DSP, Servier or our potential future collaborators;

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

seize or detain products.

Risks Relating 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.

The commercial success of OCA or our other product candidates, if approved, will depend upon their acceptance among the medical community, including physicians, health care 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. 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;

Even if approved, our product candidates may not achieve broad marketacceptance among physicians, patients an

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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.

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 initial phases of developing an internal commercial organization. To develop internal sales, distribution and marketing capabilities, we will have 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 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 DSP for the development and commercialization of OCA in Japan and China and other potential 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.

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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 DSP regarding the development and commercialization of OCA for PBC and NASH in Japan and China and provided DSP 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:

DSP 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 DSP 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. In the event of any such decision, our business and prospects may be adversely affected due to our inability to progress such compounds ourselves;
Our agreement with DSP 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 DSP 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 DSP 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;
DSP or Servier may change the focus of their development and commercialization efforts or pursue higher-priority programs;
DSP 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;
DSP 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;
DSP 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
DSP 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 DSP 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. 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

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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, establishing 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. For example, we have entered into collaborations with DSP 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 DSP or for our earlier stage TGR5 program in the United States or Japan and 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, DSP has the exclusive rights to OCA in Japan and China and the option to exclusively 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 DSP 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. 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 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. 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.

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If serious adverse events or other undesirable side effects are identified during the development of OCA for one indication, we may need to abandon our development of OCA for other indications.

Product candidates in clinical stages of development have a high risk of failure. We cannot predict when or if OCA will prove effective or safe in humans or will receive regulatory approval. To date, the most common side effects observed in clinical trials of OCA were pruritus, headaches, fatigue, constipation and diarrhea. New side effects could, however, be identified as we expand our clinical trials for OCA to other indications. 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 and other potential indications. We 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.

Risks Relating 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 chronic liver and other 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 Aptalis Pharma US, Inc., Astellas Pharma US, Inc., AstraZeneca, Dr. Falk Pharma GmbH, Eli Lilly, Exelixis, Inc., Galmed Medical Research Ltd., Immuron Ltd., Johnson & Johnson, Mochida Pharmaceutical Co., Ltd., NasVax Ltd., NovImmune SA., Phenex Pharmaceuticals AG, Raptor Pharmaceutical Corp., Salix Pharmaceuticals, Inc. and Tioga Pharmaceuticals, Inc. In addition, many universities and private and public research institutes may become active in our target disease areas. 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.

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;

We face competition from other biotechnology and pharmaceutical companiesand our operating results will suffer if

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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 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. Our agreements with third-party service providers and CROs are on a study-by-study and project-by-project basis. Typically, we may terminate the agreements with notice and are responsible for the supplier s previously incurred costs. In addition, any CRO 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 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. Although we have not experienced any significant difficulties with our third-party contractors since then, it is possible that we could experience 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. 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, and we may be subject to the imposition of civil or criminal penalties if their conduct of clinical trials violates applicable law.

Our third-party service providers may not be 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

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

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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.

Prior to April 2011, we operated a wholly-owned subsidiary in Italy where our bile acid receptor research was primarily conducted. Subsequently, until March 15, 2013, our Italian subsidiary was in the process of voluntary liquidation under Italian law. Effective March 15, 2013, we have decided to remove our Italian subsidiary from the liquidation process and it will continue to act as our legal representative for our clinical trials in the European Union to satisfy European Union regulatory requirements. In addition, we have entered into an agreement with DSP 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, 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;

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 any 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.

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

As of March 15, 2013, we had 25 employees. As we 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. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. 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;

We will need to expand our operations and increase the size of our company,and we may experience difficulties in

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manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites;
develop a marketing and sales infrastructure; and
continue to improve our operational, financial and management controls, reporting systems and procedures.

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 management, finance, scientific and clinical personnel and consultants 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 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; Barbara Duncan, our chief financial officer and treasurer; Daniel Regan, our chief commercial officer hired in March 2013; Luciano Adorini, our chief scientific officer; and our other key employees and consultants, such as Professor Roberto Pellicciari, our co-founder who provides ongoing consulting services to us. 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. Our failure to retain key personnel or consultants could materially harm our business.

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 build our finance infrastructure and improve our 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 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.

We have begun implementing our system of internal controls over financial reporting and preparing the documentation necessary to perform the evaluation needed to comply with Section 404(a) of the

Failure to build our finance infrastructure and improve our accountingsystems and controls could impair our ability to

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Sarbanes-Oxley Act. We anticipate that we will need to retain additional finance capabilities and build our financial infrastructure as a public company, including complying with the requirements of Section 404 of the Sarbanes-Oxley Act. We plan to continue improving our financial infrastructure with the retention of additional financial and accounting capabilities, the enhancement of internal controls and additional training for our financial and accounting staff.

Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting, starting with the second annual report that we would expect to file with the Securities and Exchange Commission. However, for as long as we remain an emerging growth company as defined in the JOBS Act, we have and intend to continue to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. We may continue to take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2017; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

Until we are able to expand our finance and administrative capabilities and establish necessary financial reporting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures or comply with the Sarbanes-Oxley Act or existing or new reporting requirements. 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.

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 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 code of 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;

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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.

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 lesser 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 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.

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.

If we engage in an acquisition, reorganization or business combination, wewill incur a variety of risks that could adv

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

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other 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. 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.

Risks Relating 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 or may in the future own 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, 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;

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.

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As of March 15, 2013, we were the owner of record of 51 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 of record of 9 pending U.S. and non-U.S. patent applications relating to OCA in these areas.

In addition, as of March 15, 2013, we were the owner of record of 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 and methods of using these compounds in various indications. We were also the owner of record of 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 if the appropriate maintenance fee renewal, annuity, or other government fees are paid. We expect that the other patents and patent applications for the OCA portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2022 to 2028. We expect the issued INT-767 composition of matter patent in the United States, if the appropriate maintenance fee, renewal, annuity, or other governmental fees are paid, to expire in 2029. We expect the other pending patent applications in the INT-767 portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2027. We expect the issued INT-777 composition of matter patent in the United States, if the appropriate maintenance fee, renewal, annuity, or other governmental fees are paid, to expire in 2030. We expect the other pending patent applications in the INT-777 portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2028 to 2029.

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.

We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or feasible. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. 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.

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 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 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 incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual p

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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 a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to 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 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 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 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

We may infringe the intellectual property rights of others, which may prevent or delay our product development effo

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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 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. 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 our trademarks and failure to secure those registrations could adversely affect our business.

If we seek to register any of our trademarks, our trademark applications may not be allowed for registration or our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. 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.

We may be subject to claims that our employees have wrongfully used ordisclosed alleged trade secrets of their for

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In addition, we have not yet proposed 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 must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of 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 FDA.

Risks Relating to Owning Our Common Stock

The trading market in our common stock has been extremely limited and substantially less liquid than the average trading market for a stock quoted on the NASDAQ Global Market.

Since our initial listing on the NASDAQ Global Market on October 11, 2012, the trading market in our common stock has been extremely limited and substantially less liquid than the average trading market for companies quoted on the NASDAQ Global Market. The quotation of our common stock on the NASDAQ Global Market does not assure that a meaningful, consistent and liquid trading market currently exists. We cannot predict whether a more active market for our common stock will develop 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, 2012, approximately 63.0% of our outstanding shares of common stock was held by our officers, directors, beneficial owners of 5% or more of our securities 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. In addition, as of December 31, 2012, 11,594,188 shares of common stock, or 70.2% of our outstanding shares, were restricted from resale under securities laws or as a result of lock-up agreements, further limiting the liquidity of our common stock; however, such lock-up agreements will expire at the close of business on April 8, 2013.

Our share price may be volatile, which could subject us to securities class action litigation and result in substantial losses to our stockholders.

The trading price of our common stock is 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 $42.67 per share. In addition to the factors discussed in this Risk Factors section and elsewhere in this Annual Report on Form 10-K, 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 future 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 future product candidates;
failure to maintain our existing strategic alliances or enter into new alliances;

failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;

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;

Our share price may be volatile, which could subject us to securities classaction litigation and result in substantial lo

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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;
announcement or expectation of additional financing efforts;
significant lawsuits, including patent or stockholder litigation;
sales of our common stock by us, our insiders or our other stockholders;
market conditions for biopharmaceutical stocks in general; and
general economic and market conditions.

Furthermore, the stock markets 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 addition, such fluctuations could subject us to securities class action litigation, 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, 2012, Genextra owned 7,187,217 shares of our common stock and warrants to purchase an additional 865,381 shares of our common stock. The shares of common stock owned by Genextra represented approximately 43.5% of our outstanding shares of common stock as of December 31, 2012. Accordingly, Genextra exerts significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors, 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. In addition, if Genextra obtains a majority of our common stock, Genextra would be able to control all matters submitted to our stockholders for approval,

We have a significant stockholder, which will limit your ability to influence corporate matters and may give rise to co

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as well as our management and affairs. For example, Genextra would be able to control the election of directors, amendments to our organizational documents and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization. In addition, if Genextra obtains a majority of our common stock, we would be deemed a controlled company for purposes of NASDAQ listing requirements. Under NASDAQ rules, a controlled company may elect not to comply with certain NASDAQ corporate governance requirements, including (i) the requirement that a majority of our board of directors consist of independent directors, (ii) the requirement that the compensation of our officers be determined or recommended to the board by a majority of independent directors or a compensation committee that is composed entirely of independent directors, and (iii) the requirement that director nominees be selected or recommended to the board by a majority of independent directors or a nominating committee that is composed of entirely independent directors.

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 seven directors, including two affiliated with Genextra, has the power to set the number of directors on our board from time to time.

Being a public company has increased and will continue to increase our expenses and administrative burden.

As a public company, we are incurring, and will continue to incur, significant legal, insurance, accounting and other expenses. In addition, our administrative staff is required to perform additional tasks and we are required to bear all of the internal and external costs of preparing and distributing periodic public reports in compliance with our obligations under the securities laws.

In addition, laws, regulations and standards applicable to public companies relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act and related regulations implemented by the Securities and Exchange Commission and the NASDAQ Stock Market, are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment will result in increased general and administrative expenses and may divert management s time and attention from product development activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. In connection with our initial public offering, we increased our directors and officers insurance coverage, which increased our insurance cost. In the future, it may be more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

We are an emerging growth company and the reduced disclosure requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we have and intend to continue to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We are an emerging growth company and the reduced disclosurerequirements applicable to emerging growth co

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We cannot predict if investors will find our common stock less attractive because we have and may continue to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2017; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Commencing with our annual report on Form 10-K for the year ending December 31, 2013, we will be required, under Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404 of the Sarbanes-Oxley Act also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. However, for as long as we remain an emerging growth company, as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the independent registered public accounting firm attestation requirement.

Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begin its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the NASDAQ, the Securities and Exchange Commission or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

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 Securities and Exchange Commission. We believe that any disclosure controls and procedures or internal controls and

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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.

A significant portion of our total outstanding shares of common stock is restricted from resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur in the future. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

As of December 31, 2012, we had 16,526,885 shares of common stock outstanding. Of these shares, 4,932,697 shares may be resold in the public market immediately and the remaining 11,594,188 shares are currently restricted under securities laws or as a result of lock-up agreements entered into in connection with our initial public offering but will be able to be resold on April 9, 2013, the first day after the lock-up expires, subject to Rule 144. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

In addition, holders of an aggregate of 12,667,685 shares of our common stock, including shares underlying options and warrants of such holders, will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered 2,051,028 shares of common stock that may be issued under our equity compensation plans and, as such, they can be freely sold in the public market upon issuance and once vested, subject to applicable lock-up agreements. Any sales of securities by these stockholders, option holders and warrant holders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock pursuant to our equity incentive plans and our outstanding warrants could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2012 Equity Incentive Plan, or the 2012 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. As of January 1, 2013, we had outstanding options to purchase 1,526,150 shares and restricted stock units for 176,188 shares of common stock. Furthermore, as of such date, 1,009,765 were reserved for future issuance under the 2012 Plan (including 661,075 shares of common stock added to the 2012 Plan in January 2013 in accordance with its terms). Sales of shares granted under our equity incentive plans or upon exercise of warrants may result in material dilution to our existing stockholders, which could cause our share price to fall.

The number of shares available for future grant under the 2012 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given

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year. Currently, we plan to register the 661,075 additional shares of common stock that were added to the 2012 Plan on January 1, 2013 under this provision, and the increased number of shares available for issuance under the 2012 Plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. 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 stock or change their opinion of our stock, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

NASDAQ may delist our securities from its exchange, which could limit investors ability to make transactions in our securities and subject us to additional trading restrictions.

If we fail to maintain the listing of our common stock on the NASDAQ Global Market, the liquidity for our common stock would be significantly impaired, which may substantially decrease the trading price of our common stock. We cannot assure you that, in the future, our securities will meet the continued listing requirements to be listed on NASDAQ. If NASDAQ delists our common stock from trading on its exchange, we could face significant material adverse consequences, including:

a limited availability of market quotations for our securities;
a determination that our common stock is a penny stock which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
a limited amount of news and analyst coverage for our company; and
a decreased ability to issue additional securities or obtain additional financing in the future.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders. These provisions include:

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.

These provisions may also frustrate or prevent any attempts by our stockholders to replace or remove our current management or members of our board of directors. In addition, we are subject to Section 203 of the

Some provisions of our charter documents and Delaware law may haveanti-takeover effects that could discourage a

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Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

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 Delaware General Corporation Law, 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 Delaware General Corporation Law, our restated certificate of incorporation and restated bylaws provide that we shall indemnify, to the fullest extent authorized by the Delaware General Corporation Law, 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 Delaware General Corporation Law 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.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful stockho

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We do not anticipate paying cash dividends, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We do not anticipate paying cash dividends in the future. As a result, only appreciation of the market price of our common stock, which may never occur, will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

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

As of December 31, 2012, we had federal net operating loss carryforwards, or NOLs, of $70.2 million, which expire from 2024 through 2032. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code. The limitations apply if an ownership change, as defined by Section 382, 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 assessed whether one or more ownership changes as defined under Section 382 have occurred since our inception and have determined that there have been at least two such changes. Accordingly, although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be utilized against future taxes. As a result, we may not be able to take full advantage of these carryforwards for federal and state tax purposes. Future changes in stock ownership may also trigger an ownership change and, consequently, a Section 382 limitation.

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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 3,500 and 12,700 square feet of space, respectively.

The lease for our New York office expires in November 2013. We are currently seeking additional office space for our New York location.

In March 2013, we entered into an amendment to the lease for our San Diego office, which, among other things, added approximately 5,100 square feet of space and extended the term of the existing lease. The lease for our San Diego office, as amended, will expire in December 2015.

Item 3. Legal Proceedings

We are not a party to any legal proceedings and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

Item 4. Mine Safety Disclosures

Not applicable

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PART II

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

Market Information

Our common stock began trading on the NASDAQ Global Market on October 11, 2012 under the symbol ICPT . Prior to that time, there was no public market for our common stock. Shares sold in our initial public offering on October 10, 2012 were priced at $15.00 per share.

On March 15, 2013, the closing price for our common stock as reported on the NASDAQ Global Market was $37.55. The following table sets forth the high and low sales prices per share of our common stock as reported on the NASDAQ Global Market for the period indicated.

Year Ended December 31, 2012	High	Low
Fourth Quarter (beginning October 11, 2012)	$ 35.99	$ 17.96

Stockholders

As of March 15, 2013, there were 92 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers. We believe that, when our record holders and stockholders whose shares are held in nominee or street name by brokers are combined, we have in excess of 300 beneficial holders of our common stock.

Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since October 10, 2012, which is the date our initial public offering, 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. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

Comparison of 3 Month 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.

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 the Exchange Act, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

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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

Set forth below is information regarding securities sold by us during the year ended December 31, 2012 that were not registered under the Securities Act. Also included is the consideration, if any, received by us for the securities and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

Issuances of securities

On August 9, 2012, we issued 15,000,000 shares of Series C convertible preferred stock at a price of $2.00 per share for an aggregate purchase price of $30.0 million. Upon the completion of our initial public offering, the Series C preferred stock was converted into shares of common stock.

Between October and December 2012, we issued an aggregate of 43,402 shares of common stock upon exercise of previously issued and outstanding warrants to purchase common stock, all of which were issued upon the cashless exercise of such warrants.

No underwriters were involved in the foregoing sales of securities. The securities described above were issued and sold in reliance on the exemptions from registration provided by Section 4(2) of the Securities Act and/or Rule 506 of Regulation D promulgated under the Securities Act. Each of the purchasers in these transactions represented to us in connection with its purchase that it was acquiring the securities for investment and not for distribution and that it could bear the risks of the investment. Each purchaser received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

Stock option and other equity awards

On July 31, 2012, we granted stock options to purchase 23,797 shares of common stock with an exercise price of $9.31 per share pursuant to our 2003 Stock Incentive Plan to our non-employee directors as of January 1, 2012 for service during fiscal year 2012. The issuances of such options were exempt either pursuant to Rule 701 under the Securities Act, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2) of the Securities

Act, as a transaction by an issuer not involving a public offering.

In addition, on September 13, 2012, we agreed to grant to our employees and directors (i) options to purchase 207,505 shares of our common stock and (ii) restricted stock units for 173,592 shares of our common stock, in each case, under our 2012 Plan, on the 31st day after the completion of our initial public offering. These securities were issued on November 16 and 18, 2012 and were registered under the Securities Act pursuant to a Registration Statement on Form S-8 filed on November 7, 2012 (File No. 333-184810).

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.

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Use of Proceeds from Registered Securities

On October 10, 2012, we completed our initial public offering of 5,750,000 shares of our common stock at a price of $15.00 per share for aggregate gross proceeds of approximately $86.3 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1, which was declared effective on October 10, 2012 (File No. 333-183706), and a registration statement on Form S-1 filed pursuant to Rule 462(b) of the Securities Act (File No. 333-184370). Merrill Lynch, Pierce, Fenner & Smith Incorporated acted as book-running manager for the offering and as representatives of the underwriters. BMO Capital Markets, Needham & Company, Wedbush PacGrow Life Sciences, and ThinkEquity LLC acted as the co-managers for the offering. The offering commenced on October 10, 2012 and did not terminate until the sale of all of the shares offered.

We received aggregate net proceeds from the offering of approximately $78.7 million, after deducting approximately $6.1 million of underwriting discounts and commissions, and approximately $1.5 million of estimated offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to our directors or officers or their associates or to persons owning 10 percent or more of our common stock or to any of our affiliates.

We have invested the net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments such as commercial paper and corporate debt securities and U.S. government securities. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) under the Securities Act on October 11, 2012. We have broad discretion in the use of the net proceeds from our initial public offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our stock.

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Item 6. Selected Financial Data

The selected financial data set forth below is derived from our audited consolidated financial statements and may not be indicative of future operating results. 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 report. 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,			Period From September 4, 2002 (Inception) Through December 31, 2012
(In thousands, except share and per share data)	2010	2011	2012	(Unaudited)
Statement of Operations Data:				
Licensing revenues	$	$1,805	$2,446	$4,251
Operating expenses:				
Research and development	12,710	11,426	16,183	71,435
General and administrative	3,644	4,209	5,177	29,598
Total operating expenses	16,354	15,635	21,360	101,033
Loss from operations	(16,354)	(13,830)	(18,914)	(96,782)
Total other income (expense), net	1,266	1,093	(24,729)	(21,402)
Net loss	$(15,088)	$(12,737)	$(43,643)	$(118,184)
Dividend on preferred stock, not declared	(2,901)	(3,000)	(2,630)	
Net loss attributable to common stockholders	$(17,989)	$(15,737)	$(46,273)	
Net loss per share, basic and diluted	$(5.40)	$(4.73)	$(7.36)	
Weighted average shares outstanding, basic and diluted	3,329,666	3,329,666	6,283,238	

	December 31,		
	2010	2011	2012
	(In thousands)		
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 15,424	$ 17,707	$ 110,194
Total assets	17,118	19,470	112,179
Accounts payable, accrued expenses, and other liabilities	1,587	1,504	3,746
Warrant liability	6,881	5,836	30,359
Deferred revenue		14,608	12,162
Common and preferred stock	31	31	17
Additional paid-in capital	70,268	72,134	184,100
Accumulated deficit during development stage	(61,803)	(74,540)	(118,183)
Total stockholders equity (deficit)	8,318	(2,560)	65,912

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

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 report, 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 chronic liver diseases utilizing our proprietary bile acid chemistry. 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. OCA is a first-in-class product candidate that selectively binds to and induces activity in the farnesoid X receptor, or FXR, which we believe has broad liver-protective properties. We are developing OCA initially for primary biliary cirrhosis, or 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. We are conducting a Phase 3 clinical trial of OCA in PBC, which we call the POISE trial, that we anticipate will serve as the basis for seeking regulatory approval in the United States and Europe. As of December 19, 2012, we have completed enrollment of the POISE trial with 217 patients, exceeding the originally targeted number of patients by approximately 20%. We currently expect results from the POISE trial to be available in the second quarter of 2014. OCA has received orphan drug designation in the United States and Europe for the treatment of PBC. We own worldwide rights to OCA outside of Japan and China, where we have exclusively licensed the compound to Dainippon Sumitomo Pharma, or DSP, and granted it an option to exclusively license OCA in certain other Asian countries.

On October 16, 2012, we completed our initial public offering in which we sold 5,750,000 shares of common stock at $15.00 per share and received net proceeds of $78.7 million, after underwriting discounts and commissions and offering expenses payable by us. The initial public offering included the exercise in full by the underwriters of their option to purchase an additional 750,000 shares of common stock. Upon the closing of our initial public offering, all 7,403,817 outstanding shares of our convertible preferred stock automatically converted into an aggregate of 7,403,817 shares of common stock. We filed an amended and restated certificate of incorporation on October 16, 2012 to authorize 25,000,000 shares of common stock and 5,000,000 shares of undesignated preferred stock. Our common stock trades on the NASDAQ Global Market, or NASDAQ, under the trading symbol ICPT.

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 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, 2012, 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 totaling $181.5 million (net of issuance costs of $9.9 million), including $29.7 in net proceeds from our Series C financing in August 2012 and $78.7 million in net proceeds from our initial public offering in October 2012, and through the receipt of $16.4 million of up-front payments under our collaborative

agreements.

We have incurred net losses in each year since our inception in 2002. Our net losses were approximately $15.1 million, $12.7 million and $43.6 million for the years ended December 31, 2010, 2011 and 2012, respectively. As of December 31, 2012, we had an accumulated deficit of approximately $118.2 million. Substantially all our net losses resulted from costs incurred in connection with our research and development

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programs and from general and administrative costs associated with our operations, and particularly in 2012, from the mark-to-market of our liability-classified warrants.

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;
seek to obtain regulatory approvals for OCA;
outsource the commercial manufacturing of OCA for any indications for which we receive regulatory approval;
contract with third parties for the sales, marketing and distribution of OCA for any indications for which we receive regulatory approval;
continue our research and development efforts with our preclinical development compounds, INT-767 and INT-777;
maintain, expand and protect our intellectual property portfolio;
add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts; and
operate as a public company.

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 we expect will take a number of years and is subject to significant uncertainty. Accordingly, we anticipate that we will need to raise additional capital prior to the commercialization of OCA or any of our other product 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.

Prior to April 2011, we operated a wholly-owned subsidiary in Italy where our bile acid receptor research was primarily conducted. Subsequently, until March 15, 2013, our Italian subsidiary was in the process of voluntary liquidation under Italian law. Effective March 15, 2013, we have decided to remove our Italian subsidiary from the liquidation process and it will continue to act as our legal representative for our clinical trials in the European Union to satisfy European Union regulatory requirements. Although our Italian subsidiary was undergoing the liquidation process from April 2011 through March 2013, we have continued our early stage TGR5 research program through our collaboration with Les Laboratories Servier and Institut de Recherches Servier, or collectively Servier.

Financial Overview

Revenue

To date, we have not generated any revenue from the sale of products. All our revenue has been derived from our collaborative agreements for the development and commercialization of certain of our product candidates. In March 2011, we entered into an exclusive licensing agreement with DSP for the development of OCA in Japan and China. Under the terms of the agreement, we received an up-front payment of $15.0 million and may be eligible to receive up to approximately $300 million in additional payments for development, regulatory and commercial sales milestones for OCA in Japan and China. In August 2011, we entered into a collaboration agreement with Servier for the discovery, research and development of bile acid-derived agonists, or substances that bind to receptors of cells and

trigger responses by those cells, for a dedicated bile acid receptor called TGR5. Under the terms of the agreement, we received an up-front payment from Servier of $1.4 million. Servier may be required to pay us up to an aggregate amount of approximately

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€108 million (approximately $142.7 million as of December 31, 2012) upon the achievement of specified development, regulatory and commercial sale milestones, as well as royalties on sales, based on the successful outcome of the collaboration. For accounting purposes, the up-front payments from both transactions are recorded as deferred revenue and amortized over time. We recognized $2.4 million in license revenue for the relevant amortization of the two up-front payments and did not receive any milestone payments during 2012 related to these agreements. As the Servier up-front payment has been fully recognized as of the third quarter of 2012, no further revenue will be recognized in respect of such payments. We anticipate that we will recognize revenue of approximately $1.6 million per year through 2020, the expected end of the development period, for the amortization of the up-front payment from DSP.

In the future, we may generate revenue from a combination of license fees and other upfront payments, research and development payments, milestone payments, product sales and royalties in connection with strategic alliances. 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 strategic alliance partners. If our strategic alliance 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.

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:

salaries and related overhead expenses for personnel in research and development functions;
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 acquiring and manufacturing clinical trial materials;
depreciation of leasehold improvements, laboratory equipment and computers;
costs related to compliance with regulatory requirements; and
costs related to stock options or other stock-based compensation granted to personnel in research and development functions.

From inception through December 31, 2012, we have incurred approximately $71.4 million in research and development expenses. 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 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. Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs, in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. We have been developing OCA and other agonists of FXR, as well as TGR5 agonists, and typically use our employee and infrastructure resources across multiple research and development programs. We do not allocate salaries, stock-based compensation, employee benefit or other indirect costs related to our research and development function to specific product candidates. Those expenses are included in Indirect

research and development expense in the table below.

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	Years Ended, December 31,		
	2010	2011	2012
Direct research and development expense by program:			
OCA	$ 8,001	$ 8,056	$ 10,495
INT-777	2,234	195	52
Total direct research and development expense	10,235	8,251	10,547
Personnel costs	2,078	2,750	4,947
Indirect research and development expense	397	425	689
Total research and development expense	$ 12,710	$ 11,426	$ 16,183

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 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 U.S. Food and Drug Administration, or 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.

OCA

The majority of our research and development resources are focused on the Phase 3 POISE trial and our other planned clinical and preclinical studies and other work needed to submit OCA for the treatment of PBC for regulatory approval in the United States and Europe. We have incurred and expect to continue to incur significant expense in connection with these efforts, including:

In January 2012, we initiated enrollment in our POISE trial, a Phase 3 clinical trial in patients with PBC, and we completed patient enrollment for our POISE trial in December 2012. We currently expect results from the trial to be available in the second quarter of 2014. Patients who complete twelve months of treatment will be eligible to continue in an open label safety extension trial for five years.

We are continuing to treat PBC patients from our Phase 2 trial with OCA in a long-term safety extension trial. As of January 31, 2012, there were 20 patients being followed in this trial and we anticipate the trial to continue through 2015.

We are currently dosing both mice and rats to investigate the carcinogenic potential of OCA. We anticipate dosing will be completed in the first quarter of 2014.

We plan to initiate a Phase 2 clinical trial evaluating the potential effects and clinical significance of OCA on the lipid profile of patients with PBC, a Phase 1 clinical trial in healthy volunteers to evaluate the effect of OCA on the heart s electrical cycle, known as the QT interval, and additional Phase 1 clinical trials in 2013.

We have contracted with third-party manufacturers to produce the quantities of OCA needed for regulatory approval as well as the necessary supplies for our other contemplated trials.

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In addition, we are evaluating OCA in other chronic liver and other diseases. In connection with these efforts, we have incurred significant expenses relating to our agreement with the National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, for milestones related to the FLINT trial, a Phase 2b clinical trial in patients with nonalcoholic steatohepatitis, or NASH. These expenses include $1.0 million that was paid in June 2012 and an additional $1.25 million that is was paid in connection with the full enrollment of the FLINT trial, which occurred on November 12, 2012.

INT-767 and INT-777

We are currently conducting research in collaboration with Servier to discover and develop additional novel TGR5 agonists. We intend to continue to develop our two existing compounds not included in this collaboration, our dual FXR/TGR5 agonist INT-767 through preclinical development and, if warranted, Phase 1 clinical trials and INT-777 through potential collaborations with third parties, over the next several years.

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, operational, finance and human resources functions. Other significant general and administrative expenses include allocation of facilities costs, professional fees for directors, accounting and legal services and expenses associated with obtaining and maintaining patents.

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 believe that these increases will likely include increased costs for director and officer liability insurance, costs related to the hiring of additional personnel and increased fees for outside consultants, lawyers and accountants. 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.

Other Income, Net

Other income consists of interest income earned on our cash, cash equivalents and investment securities, offset by interest expense pertaining to equipment currently under a capitalized lease. This capitalized lease matured in 2012 and, as such, we will no longer be subject to the interest expense under this capitalized lease. We expect interest income to increase in future periods as we invest the proceeds from our preferred stock financings and initial public offering.

Revaluation of Warrants

In conjunction with various financing transactions, we issued warrants to purchase shares of our common stock. Certain of the warrants include a provision that provides for a reduction in the warrant exercise price if there are 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 are deemed to be derivative instruments and as such, are recorded as a liability and marked-to-market at each reporting period. Our remaining warrants include a provision that requires the shares underlying the warrants to be registered upon the completion of an initial public offering. As a result, these warrants were reclassified as a liability as of the date of our initial public offering and are also market-to-market at each reporting date since the offering. The fair value estimates of these warrants are determined using a Black-Scholes option-pricing model and are based, in part, on subjective assumptions and could differ materially in the future. Non-cash changes in the

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fair value of the common stock warrant liability from the prior period is recorded as a component of other income and expense. We will continue to adjust the fair value of the common stock warrant liability at the end of each reporting period for changes in fair values until the earlier of the exercise or expiration of the applicable common stock warrants or until such time that the warrants are no longer determined to be derivative instruments. Because our common stock is publicly traded, these fluctuations are expected to increase or decrease significantly based on changes in the price of our common stock. For example, the fair value of the warrant liability increased from $6.3 million at September 30, 2012 to approximately $30.4 million at December 31, 2012 primarily due to increase in the fair value of our common stock from $11.21 per share as of September 30, 2012, prior to our IPO, to $34.24 per share as of December 31, 2012.

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 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 2 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 DSP and Servier. 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, none of which have been received to date. 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.

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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 and restricted stock units, or RSUs, 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 and RSUs at their fair value as of the grant date. We then periodically re-measure the awards 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 includes stock options and RSUs granted to employees and non-employees and has been reported in our statements of operations as follows:

	Years Ended December 31,		
	2010	2011	2012
	(In thousands)		
Research and development	$ 648	$ 472	$ 1,712
General and administrative	1,045	1,394	1,637
Total	$ 1,693	$ 1,866	$ 3,349

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 subjective 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:

Because there was no public market for our common stock prior to October 10, 2012, we lacked company-specific historical and implied volatility information to estimate the volatility of our common stock price. 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. We plan to continue to use the guideline peer group volatility information until the historical volatility of our common stock is relevant to measure expected volatility for future option grants.

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.

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The assumptions used in the Black-Scholes option-pricing model for the years ended December 31, 2010, 2011 and 2012 are set forth below:

	Years Ended December 31,		
	2010	2011	2012
Volatility	112 - 113 %	107 - 113 %	107 - 115 %
Expected term (in years)	5.6 - 5.7	5.0 - 6.0	5.0 - 6.0
Risk-free interest rate	1.6 - 1.7 %	1.1 - 1.4 %	0.7 - 0.8 %
Expected dividend yield	%	%	%
Stock price	$ 8.67	$ 8.67	$ 8.67 - $34.24

We expect the impact of stock 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. Due to the lack of historical forfeiture activity of our plan, we expect to estimate our forfeiture rate based on peer company data with characteristics similar to our company. For 2010, 2011 and 2012, we used a forfeiture rate of five percent. There have been an insignificant number of forfeitures through December 31, 2012.

Due to the absence of an active market for our common stock prior to our initial public offering in October 2012, the fair value of our common stock for purposes of determining the exercise price for stock option grants was determined by our board of directors, with the assistance and upon the recommendation of management, in good faith, based on a number of objective and subjective factors consistent with the methodologies outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid, including:

the prices at which we most recently sold our preferred stock and the rights, preferences and privileges of the preferred stock as compared to those of our common stock, including the liquidation preferences of the preferred stock;

our results of operations, financial position and the status of our research and development efforts, including the status of clinical trials for OCA and our specific regulatory status and interactions with regulatory authorities;

the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, given prevailing market conditions, or a strategic merger or sale of our company, or an M&A transaction;

the material risks related to our business;

achievement of enterprise milestones, including the results of clinical trials and our entry into or termination of collaboration and license agreements;

the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to us;

external market conditions affecting the life sciences and biotechnology industry sectors; and

the valuation prepared by an independent third-party consultant performed as of March 31, 2010 and July 31, 2012.

Each valuation methodology included estimates and assumptions that required our judgment. These estimates included assumptions regarding future performance, including the successful completion of clinical trials and the time to completing an initial public offering or sale. Significant changes to the key assumptions used in the valuations could have resulted in different fair values of common stock at each valuation date.

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Common Stock Warrant Liability

In conjunction with various financing transactions, we issued warrants to purchase shares of our common stock as discussed above under Revaluation of Warrants. The Black-Scholes option-pricing model requires the use of subjective assumptions, including but not limited to stock price volatility, the expected life of the warrants, the risk free interest rate and the fair value of the common stock underlying the warrants. The fair value of the underlying common stock is determined as discussed above under Stock-Based Compensation. Significant changes to the key assumptions used in the valuations could have resulted in different fair values of the warrants at each valuation date. We will continue to adjust the fair values of the warrants at each financial reporting period end for any changes in fair value until the earlier of the exercise or expiration of the applicable common stock warrants or until such time that the warrants are no longer determined to be derivative instruments. Our warrant liability is expected to fluctuate based on the assumptions used in our valuation model.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Subject to certain conditions set forth in the JOBS Act, as an emerging growth company, we have and intend to continue to rely on certain exemptions and reduced reporting requirements provided by the JOBS Act, including without limitation, (i) providing an auditor s attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2017; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

Results of Operations

Comparison of the Years Ended December 31, 2011 and 2012

The following table summarizes our results of operations for the years ended December 31, 2011 and 2012, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar Change	% Change
	2011	2012		
		(In		

		thousands)			
Licensing revenue	$ 1,805	$ 2,446	$ 641	35.5	%
Operating expenses:					
Research and development	11,426	16,183	4,757	41.6	%
General and administrative	4,209	5,177	968	23.0	%
Loss from operations	(13,830)	(18,914)	(5,084)	36.8	%
Warrant revaluation income (expense)	1,045	(24,626)	(25,671)	*	
Other income, net	48	88	40	*	
Foreign currency loss		(192)	(192)	*	
Net loss	$ (12,737)	$ (43,644)	$ (30,907)	*	

* Not meaningful or not calculable.

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Licensing Revenue

For the year ended December 31, 2011, we recorded a total of $1.8 million of licensing revenue, consisting of $1.2 million and $600,000 from the amortization of the up-front payments from the collaboration agreements entered into during 2011 with DSP and Servier, respectively. For the year ended December 31, 2012, we recorded a total of $2.4 million of licensing revenue, consisting of $1.6 million and $824,000 from the amortization of the up-front payments from the collaboration agreements entered into during 2011 with DSP and Servier, respectively. The revenue recorded for the DSP agreement increased in 2012 as the agreement was only in place for nine months of 2011. The revenue related to the up-front payment from Servier was fully recognized in the third quarter of 2012.

Research and Development Expenses

Research and development expenses were $11.4 million and $16.2 million for the years ended December 31, 2011 and 2012, respectively. The net increase in research and development expenses was $4.8 million, or 42%. This increase in research and development expense primarily reflects:

an increase in personnel on our development team to manage the increased activities around our development program for OCA, resulting in increased compensation expense of approximately $2.2 million, of which $1.2 million was due to stock compensation expense, approximately $265,000 was due to associated overhead and approximately $360,000 was due to bonus expense;

increased direct development expense for our Phase 3 POISE trial of approximately $2.1 million;

increased expenses of $1.8 million payable by us to the NIDDK relating to milestones achieved under the NIDDK agreement;

increased costs associated with regulatory consultants of $200,000 related to the OCA development program;

increased direct development expense for the Phase 2 clinical trial of OCA in portal hypertension of approximately $137,000;

increased direct development expense for the initiation of our two-year animal carcinogenicity studies of OCA in two species of approximately $110,000;

reduced direct research and development expense of approximately $1.2 million resulting from the closure of our research facility in June 2011 and research associated with our TGR5 program, which was previously paid by us and is now funded by Servier through our collaboration with it;

reduced direct research and development expense with respect to the completion of our Phase 2 trials for OCA and reduced expenses for the long-term safety extension study of approximately $360,000;

reduced direct research and development expense relating to INT-777 of approximately $145,000 related primarily to decreased stability and optimization work; and

decreased costs associated with market research of OCA in PBC of $100,000.

General and Administrative Expenses

General and administrative expenses were $4.2 million and $5.2 million for the years ended December 31, 2011 and 2012, respectively. The increase in general and administrative expenses of $1.0 million, or 23%, was mainly due to an increase in stock-based compensation costs for options and restricted stock units granted to our employees and directors of $243,000, increased bonus expense of $272,000, and increased accounting fees of $175,000 related to our operating as a public company.

Warrant Revaluation Income (Expense)

Our outstanding warrants are deemed to be derivative instruments that require liability classification and mark-to-market accounting. As such, at the end of each reporting period, the fair values of the warrants were

determined by us using a Black-Scholes option-pricing model, resulting in the recognition of a gain of $1.0 million for the year ended December 31, 2011 and a loss of $24.6 million for the year ended

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December 31, 2012. For the year ended December 31, 2011, the gain was primarily due to the reduction in value of the warrants, as their estimated life declined and changes in volatility of the shares of common stock underlying the warrants. For the year ended December 31, 2012, the fair value of the warrants increased primarily because of the significant increase in the price of the common stock underlying the warrants, which was based on the market price of our common stock as reported on the NASDAQ Global Market following our initial public offering in October 2012. Because our common stock is publicly traded, these fluctuations are expected to increase or decrease significantly based on changes in the price of our common stock.

Other Income, Net

The change in other income, net primarily reflects an increase in net interest income compared to the year ended December 31, 2011. The increase was primarily the result of higher average investment balances during 2012 as compared to 2011 due to our investment of the proceeds from our initial public offering in October 2012.

Comparison of the Years Ended December 31, 2010 and 2011

The following table summarizes our results of operations for the years ended December 31, 2010 and 2011, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar Change	% Change
	2010	2011		
		(In thousands)		
Licensing revenue	$	$ 1,805	$ 1,805	*
Operating expenses:				
Research and development	12,710	11,426	(1,284)	(10.1)%
General and administrative	3,644	4,209	565	15.5 %
Loss from operations	(16,354)	(13,830)	2,524	15.4 %
Other income, net	105	48	(57)	(54.3)%
Warrant revaluation income	672	1,045	373	55.5 %
Qualified therapeutic development project	489		(489)	*
Net loss	$ (15,088)	$ (12,737)	$ 2,351	15.6 %

* Not meaningful or not calculable.

Licensing Revenue

For the year ended December 31, 2011, we recorded a total of $1.8 million of licensing revenue, consisting of $1.2 million and $600,000 from the amortization of the up-front payments from the collaboration agreements entered into during 2011 with DSP and Servier, respectively. We had no revenue in 2010.

Research and Development Expenses

Research and development expenses were $12.7 million and $11.4 million for the years ended December 31, 2010 and 2011, respectively. The net decline in research and development expenses of $1.3 million, or 10.1%, was primarily due to:

reduced direct research and development expense relating to INT-777 of approximately $2.0 million;
reduced direct research and development expense resulting from the closure of our research facility in June 2011 and research associated with our TGR5 program, which was previously paid by us and was funded through our collaboration with Servier beginning in August 2011, of approximately $1.2 million;
reduced direct research and development expense with respect to the completion of our Phase 2 trials for OCA of approximately $600,000;
reduced direct research and development expense related to payments to the NIDDK for the FLINT trial of $250,000;

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increased direct expenditures associated with the preparation for the initiation of the Phase 3 POISE trial of approximately $1.2 million;
increase in personnel in our development team to manage the increased activities around our development program for OCA, resulting in increased compensation expense of approximately $400,000;
increased expenditures for direct research and development expense relating to our Phase 2 clinical trial for portal hypertension of approximately $400,000;
increased costs to manufacture our clinical trial supplies of approximately $500,000; and
increased costs associated with market research of $200,000.

General and Administrative Expenses

General and administrative expenses were $3.6 million and $4.2 million for the years ended December 31, 2010 and 2011, respectively. The increase in general and administrative expenses of $566,000, or 15.5%, was mainly due to an increase in stock-based compensation costs for options granted to our employees and legal costs associated with the DSP and Servier collaboration agreements.

Other Income, Net

Other income, net was $105,000 and $48,000 for the years ended December 31, 2010 and 2011. The decrease of $57,000, or 54%, was driven by lower average cash balances.

Warrant Revaluation Income (Expense)

Some of our outstanding warrants are deemed to be derivative instruments that require liability classification and mark-to-market accounting. At the end of each reporting period, the fair values of these warrants were determined using a Black-Scholes option-pricing model, resulting in the recognition of gains of $700,000 and $1.0 million for the years ended December 31, 2010 and 2011, respectively. These gains were primarily due to the reduction in value of the warrants, as their estimated life declines and changes in volatility of the shares of common stock underlying the warrants.

QTDP Grant

In 2010, we were awarded $489,000 under the federal Qualifying Therapeutic Discovery Grant Program, or QTDP, in support of our development of OCA and INT-777. The QTDP was included in the healthcare reform legislation, and established a one-time pool of $1 billion for grants to small biotechnology companies developing novel therapeutics which show potential to result in new therapies that either treat areas of unmet medical need, or prevent, detect or treat chronic or acute diseases and conditions; reduce long-term health care costs in the United States; or significantly advance the goal of curing cancer within a 30-year period.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred losses and cumulative negative cash flows from operations since our inception in September 2002 and, as of December 31, 2012, we had an accumulated deficit of $118.2 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.

Since our inception through December 31, 2012, we have funded our operations principally with $181.5 million (net of issuance costs of $9.9 million) from the sale of common stock, preferred stock, convertible notes and warrants, including $29.7 in net proceeds from our Series C financing in August 2012 and $78.7 million in net proceeds from our initial public offering in October 2012, and the receipt of $16.4 million in up-front payments under our licensing and collaboration agreements with DSP and Servier. As of December 31, 2012, we had cash, cash equivalents and investment securities of approximately

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$110.2 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.

Cash Flows

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

	Years Ended December 31,		
	2010	2011	2012
	(In thousands)		
Net cash provided by (used in):			
Operating activities	$ (13,658)	$ 2,606	$ (15,749)
Investing activities	58	(66)	(64,857)
Financing activities	24,618	(250)	108,418
Effect of exchange rate changes	(29)	(6)	(7)
Net increase (decrease) in cash and cash equivalents	$ 10,989	$ 2,284	$ 27,805

Operating Activities. Net cash used in operating activities of $13.7 million during the year ended December 31, 2010 was primarily a result of our $15.1 million net loss, offset by the add-back of non-cash expenses of $1.7 million for stock-based compensation and $480,000 for depreciation and warrant liability revaluation income of $672,000.

Net cash provided by operating activities of $2.6 million during the year ended December 31, 2011 was primarily a result of $16.4 million in up-front payments from our licensing and collaboration agreements with DSP and Servier, $14.6 million of which was classified as deferred revenue as described in note 3 to our financial statements included elsewhere in this Annual Report on Form 10-K. The cash payments from the collaboration agreements and the classification of those payments as deferred revenue led to an overall net increase in operating assets of $13.9 million, to which non-cash items of $1.9 million for stock-based compensation, $410,000 for depreciation and $217,000 for a loss on the sale of assets in connection with the potential liquidation of our Italian subsidiary were added. These positive additions to cash flow were offset against our $12.7 million net loss and an additional $1.0 million decrease in assets due to the revaluation of our warrant liabilities.

Net cash used in operating activities of $15.7 million during the year ended December 31, 2012 was primarily a result of our $43.6 million net loss and net changes in our operating assets and liabilities of $592,000, offset by the add-back of non-cash expenses of $24.6 million for warrant liability revaluation, $3.3 million for stock-based compensation, $201,000 for depreciation and $192,000 foreign currency loss.

Investing Activities. For fiscal 2010 and 2011, net cash used in investing activities primarily reflected our use of cash to purchase equipment. Cash provided by short-term investments was partially offset by sales of short-term investments.

Net cash used in investing activities during the year ended December 31, 2012 primarily reflected our net investment of proceeds of the Series C financing and the initial public offering in securities, offset slightly by the redemptions of certificates of deposits.

Financing Activities. Net cash provided by financing activities in the year ended December 31, 2010 consisted primarily of approximately $24.0 million of net proceeds from the sale of Series B preferred stock and warrants to

purchase common stock issued in 2010, offset by capital lease payments. Net cash used in financing activities in the year ended December 31, 2011 consisted primarily of capital lease payments. Net cash provided by financing activities in the year ended December 31, 2012 consisted primarily of approximately $29.7 million of net proceeds from the sale of Series C preferred stock and $78.7 million from the completion of our initial public offering.

On August 9, 2012, we entered into a securities purchase agreement with an affiliated fund of OrbiMed Advisors LLC and Genextra S.p.A., or Genextra, pursuant to which the we agreed to issue up to an aggregate of 25,000,000 shares of Series C preferred stock at a price of $2.00 per share for gross proceeds of up to

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$50.0 million, or the Series C financing. The securities purchase agreement for the Series C financing provided for the issuance of the Series C preferred stock in two tranches, consisting of 15,000,000 and 10,000,000 shares. On August 8, 2012, we amended and restated our certificate of incorporation in its entirety to increase the number of shares of preferred stock we are authorized to issue to 52,777,778 shares and designate 25,000,000 of such shares as Series C preferred stock. On August 9, 2012, we issued the first tranche of Series C preferred stock, which resulted in net proceeds of $29.7 million to us. The closing of the second tranche was only contemplated to occur if we did not complete an initial public offering of our common stock on or prior to August 2013. Upon the completion of our initial public offering, the Series C preferred stock was converted into shares of common stock and the agreement to issue the second tranche of Series C preferred stock was nullified.

In October 2012, we completed our initial public offering pursuant to a registration statement on Form S-1. In the initial public offering, we sold an aggregate of 5,750,000 shares of common stock under the registration statement at a public offering price of $15.00 per share. Net proceeds were approximately $78.7 million, after deducting underwriting discounts and commissions and offering expenses payable by us. Upon the closing of the initial public offering, all outstanding shares of our preferred stock were converted into 7,403,817 shares of 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 candidates. 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. We have incurred and expect to incur additional costs associated with operating as a public company. 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. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Based upon our current operating plan, we believe that our existing cash, cash equivalents, short-term investments and anticipated funding under our DSP and Servier collaborations will enable us to fund our operating expenses and capital expenditure requirements through mid-2015. This estimate reflects our enrollment of a greater number of patients in our POISE trial than originally planned; additional nonclinical studies and clinical trials to support our planned regulatory submissions for OCA in PBC; and an anticipated increase in pre-commercial activities for OCA in PBC. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our product candidates.

Our future capital requirements will depend on many factors, including:

the progress, costs, results and timing of our POISE trial, and the clinical development of OCA for other potential indications;
the willingness of the FDA and the European Medicines Agency, or EMA, to accept our POISE trial, as well as our other completed and planned clinical and preclinical studies and other work, as the basis for review and approval of OCA for PBC;
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 our product candidates in preclinical development;

the ability of our product candidates to progress through clinical development successfully;

our need to expand our research and development activities;

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the costs associated with securing and establishing commercialization and manufacturing capabilities;

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 additional management and scientific and medical personnel;

the effect of competing technological and market developments;

our need to implement additional internal systems and infrastructure, including financial and reporting systems; and

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

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

The following table summarizes our significant contractual obligations and commercial commitments at December 31, 2012 and the effects such obligations are expected to have on our liquidity and cash flows in future periods:

	Total	Less than 1 year	1 3 years	3 5 years	More than 5 years
	(In thousands)				
Operating lease	$ 544	$ 331	$ 213		
Purchase obligations	2,480	1,979	501		
Total	$ 3,024	$ 2,310	$ 714		

We lease general and administrative office space in New York, New York and San Diego, California pursuant to operating leases that expire in 2013 and 2015, respectively. The lease for our New York office expires in November 2013 and the minimum rent we are obligated to pay during 2013 is approximately $108,000. We are currently seeking additional office space for our New York location. In March 2013, we entered into an amendment to the lease for our San Diego office, which, among other things, added approximately 5,100 square feet of space and extended the term of the existing lease. The lease for our San Diego office, as amended, will expire in December 2015. Under the amended lease, our future minimum lease payments for 2013, 2014 and 2015 are approximately $339,000, $411,000 and $467,000, respectively.

Our commitments as of December 31, 2012 under our consulting agreement with Professor Pellicciari for the compounds relating to the Servier agreement and our research and development agreement with TES Pharma Srl are reflected in the table above. In February 2013, our agreements with TES Pharma Srl and our agreement with Professor Pellicciari for the compounds relating to the Servier agreement were extended until July 2013. During the extension

period, we are required to pay TES Pharma Srl and Professor Pellicciari an

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aggregate of €500,000 and €75,000, respectively. All the commitments under our consulting agreement with Professor Pellicciari and our agreement with TES Pharma Srl, in each case, for the compounds related to the Servier agreement were covered by the reimbursement provisions under our agreement with Servier. See Item 1. Business Strategic Collaborations and Research Arrangements for more information relating to these agreements.

In addition, during 2011, we entered into an agreement with WIL Research Laboratories, LLC, or WIL, to perform certain research and laboratory services for animal studies and have agreed to pay WIL a total of $4.0 million in periodic installment payments, of which $1.2 million in payments were made each year in 2011 and 2012. The remaining amounts are included in table above.

We are a party to license 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 have employment agreements with certain employees which require the funding of specific levels of payments, if certain events, such as a change in control or termination without cause, occur. We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

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

Under our agreement with Servier, we are obligated to conduct and are conducting a research program to identify and optimize compounds that meet certain specified criteria sufficient for further development by Servier. We are obligated under the agreement to provide Servier with a specified number of full time equivalent employees for the research program and Servier has agreed to reimburse us on a quarterly basis for the associated costs up to a set maximum amount per year. Servier has agreed to pay for the development costs we or Servier incur in conducting certain preclinical trials and clinical trials with respect to any compound that meets specified criteria. We have agreed to reimburse Servier for a certain percentage of the development costs incurred by Servier if we enter into a partnership agreement, or commence development or commercialization activities on our own, with respect to a compound in the United States. Servier may credit a portion of any such reimbursable development costs against any milestone or royalty payments due and payable by Servier under the agreement until all such reimbursable amounts are repaid. In addition, if we enter into a partnership agreement with respect to a compound developed under the agreement solely in Japan, we and Servier have agreed to enter into good faith negotiations regarding the terms and conditions applicable to the reimbursement of development costs. These amounts are not included in the table above because they are not quantifiable or because they are reimbursable under the agreement.

Net Operating Losses

As of December 31, 2011 and 2012, we had federal net operating loss carryforwards, or NOLs, of $55.0 million and $70.2 million, respectively, which expire from 2024 through 2032. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code. The limitations apply if an ownership change, as defined by Section 382, 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 assessed whether one or more ownership changes as defined under Section 382 have occurred since our inception and have determined that there have been at least two such changes. Accordingly, although we believe that these ownership changes have not resulted in material limitations on our ability to use these NOLs, our ability to

utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be utilized against future taxes. As a result, we may not be able to take full advantage of these carryforwards for federal and state tax purposes. Future changes in stock ownership may also trigger an ownership change and, consequently, a Section 382 limitation.

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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 February 2013, the Financial Accounting Standards Board, or the FASB, issued ASU No. 2013-02, Other Comprehensive Income (Topic 220): Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income, or ASU No. 2013-02. ASU No. 2013-02 supersedes the presentation requirements for reclassifications out of accumulated other comprehensive income in ASUs 2011-05 and 2011-12 and requires an entity to provide additional information about reclassifications out of accumulated other comprehensive income. ASU No. 2013-02 became effective for us beginning January 1, 2013. The adoption of this amendment will not have a material impact on our results of operations or financial position.

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

Our Series A, B and C preferred stock represented participating securities. However, since we have operated at a loss, and losses are not allocated to the preferred stock, the two class method did not affect our calculation of earnings per share.

Dilutive common stock equivalents would include the dilutive effect of convertible securities, common stock options, RSUs for common stock and warrants for common stock. Potentially dilutive common stock equivalents totaled approximately 7,888,566 shares, 8,309,074 shares and 2,864,303 shares for the years ended December 31, 2010, 2011 and 2012, respectively. Upon the closing of our initial public offering, all outstanding shares of our preferred stock were converted into 7,403,817 shares of common stock. 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.

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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, 2012, 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 equivalents and available for sale investments have significant risk of default or illiquidity. While we believe our cash and equivalents and available for sale investments do 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 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 2010, 2011 or 2012.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. 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, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were adequate and effective. In designing and evaluating our disclosure controls and procedures, our management recognized 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 was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management s Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control, that occurred during the last fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2013 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 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2013 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 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2013 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 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2013 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 is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2013 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 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(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.

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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 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: April 1, 2013

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

By:

/s/ Barbara Duncan

Date: April 1, 2013

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 and Chief Executive Officer (Principal Executive Officer)	April 1, 2013
/s/ Barbara Duncan Barbara Duncan	Chief Financial Officer (Principal Financial and Accounting Officer)	April 1, 2013
/s/ Lorenzo Tallarigo, M.D. Lorenzo Tallarigo, M.D.	Chairman of the Board of Directors	April 1, 2013
/s/ Srinivas Akkaraju, M.D., Ph.D. Srinivas Akkaraju, M.D., Ph.D.	Director	April 1, 2013
/s/ Paolo Fundaro Paolo Fundaro	Director	April 1, 2013
/s/ Jonathan Silverstein Jonathan Silverstein	Director	April 1, 2013
/s/ Klaus Veitlinger, M.D., Ph.D. Klaus Veitlinger, M.D.	Director	April 1, 2013
/s/ Nicole Williams Nicole Williams	Director	April 1, 2013

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Index to Consolidated Financial Statements

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders
Intercept Pharmaceuticals, Inc.:

We have audited the accompanying consolidated balance sheets of Intercept Pharmaceuticals, Inc. and subsidiaries (a development stage enterprise) as of December 31, 2011 and 2012, and the related consolidated statements of operations and comprehensive loss, changes in stockholders equity, and cash flows for each of the years ended December 31, 2010, 2011 and 2012 and for the period from September 4, 2002 (inception) to December 31, 2012. 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. The cumulative statements of operations and comprehensive loss, changes in stockholders equity, and cash flows for the period September 4, 2002 (inception) to December 31, 2012 include amounts for the period from September 4, 2002 (inception) to December 31, 2007, which were audited by other auditors whose report has been furnished to us, and our opinion, insofar as it relates to the amounts included for the period September 4, 2002 through December 31, 2007 is based solely on the report of other auditors.

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, based on our audits and the report of other auditors, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Intercept Pharmaceuticals, Inc. and subsidiaries (a development stage enterprise) as of December 31, 2011 and 2012, and the results of their operations and their cash flows for each of the years ended December 31, 2010, 2011 and 2012 and for the period September 4, 2002 (inception) to December 31, 2012, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP
New York, New York
April 1, 2013

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders of
Intercept Pharmaceuticals, Inc.

We have audited the consolidated statements of operations and comprehensive loss, changes in stockholders equity and cash flows of Intercept Pharmaceuticals, Inc. and subsidiary (a development stage company) (the Company) for the period from September 4, 2002 (inception) through December 31, 2007. The consolidated statements of operations and comprehensive loss and cash flows for this period are not presented separately herein. The consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements 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 the financial statements are free of material misstatement. The Company was not required to have, nor were we engaged to perform an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit 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 audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated results of operations and consolidated cash flows of Intercept Pharmaceuticals, Inc. and subsidiary (a development stage company) for the period from September 4, 2002 (inception) through December 31, 2007 (not presented separately herein) in conformity with accounting principles generally accepted in the United States of America.

/s/ EisnerAmper LLP

New York, New York
August 31, 2012

Except for the third paragraph of Note 1 as to which
the date is September 26, 2012

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Consolidated Balance Sheets

	December 31, 2011	2012
Assets		
Current assets:		
Cash and cash equivalents	$17,707,476	$45,511,641
Investment securities, available-for-sale		64,682,270
Prepaid expenses and other current assets	1,196,618	1,584,308
Total current assets	18,904,094	111,778,219
Fixed assets, net	311,366	148,838
Security deposits	254,869	251,540
Total assets	$19,470,329	$112,178,597
Liabilities and Stockholders Equity (Deficit)		
Current liabilities:		
Accounts payable, accrued expenses and other liabilities	$1,504,198	$3,745,773
Short-term portion of warrant liability		7,596,659
Short-term portion of deferred revenue	2,446,107	1,621,622
Short-term portion of capital leases	81,762	
Total current liabilities	4,032,067	12,964,054
Long-term liabilities:		
Long-term portion of deferred revenue	12,162,163	10,540,543
Long-term portion of warrant liability	5,835,877	22,762,135
Total liabilities	22,030,107	46,266,732
Stockholders equity (deficit):		
Series A preferred stock. Authorized, issued, and outstanding 13,888,889 shares as of December 31, 2011; par value $0.001 per share; liquidation preference of $1.80 per share plus accumulated dividends ($5,412,329 at December 31, 2011); none authorized, issued and outstanding as of December 31, 2012	13,889	
Series B preferred stock. Authorized, issued, and outstanding 13,888,889 shares at December 31, 2011; par value $0.001 per share; liquidation preference of $1.80 per share plus accumulated dividends ($2,901,370 at December 31, 2011); none authorized, issued and outstanding as of December 31, 2012	13,889	
Common stock. Authorized 65,000,000 shares and issued and outstanding 3,329,666 shares as of December 31, 2011; 25,000,000 shares authorized and 16,526,885, shares issued and outstanding as of December 31, 2012; par value $0.001 per share	3,330	16,527
Additional paid-in capital	72,133,893	184,100,139

Accumulated other comprehensive loss, net	(184,500)	(21,451)
Accumulated deficit during development stage	(74,540,279)	(118,183,350)
Total stockholders equity (deficit)	(2,559,778)	65,911,865
Total liabilities and stockholders equity (deficit)	$19,470,329	$112,178,597

See accompanying notes to consolidated financial statements.

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Consolidated Statements of Operations and Comprehensive Loss

	Years Ended December 31,			Period From September 4, 2002 (Inception)
	2010	2011	2012	Through December 31, 2012 (Unaudited)
Licensing revenue	$	$1,805,130	$2,446,105	$4,251,235
Costs and expenses:				
Research and development	12,709,590	11,426,155	16,182,564	71,434,691
General and administrative	3,643,623	4,209,429	5,177,129	29,598,082
Total costs and expenses	16,353,213	15,635,584	21,359,693	101,032,773
Other income (expense):				
Revaluation of warrants	672,477	1,044,826	(24,625,598)	(23,075,576)
Foreign currency loss on liquidation			(191,733)	(191,733)
Other income, net	104,554	47,974	87,848	1,376,538
QTDP Grant	488,959			488,959
	1,265,990	1,092,800	(24,729,483)	(21,401,812)
Net loss	(15,087,223)	(12,737,654)	(43,643,071)	(118,183,350)
Dividends on preferred stock, not declared	(2,901,370)	(3,000,000)	(2,630,435)	(10,944,134)
Net loss attributable to common stockholders	$(17,988,593)	$(15,737,654)	$(46,273,506)	$(129,127,484)
Net loss per share, basic and diluted	$(5.40)	$(4.73)	$(7.36)	
Weighted average shares outstanding, basic and diluted	3,329,666	3,329,666	6,283,238	
Other comprehensive gain/(loss):				
Unrealized (loss) on investment securities			(21,451)	(21,451)
Foreign currency translation adjustments	(100,035)	(6,345)	184,500	
Total comprehensive loss	$(15,187,258)	$(12,743,999)	$(43,480,022)	$(118,204,801)

See accompanying notes to consolidated financial statements.

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Consolidated Statements of Changes in Stockholders Equity
For the Period From September 4, 2002 (Inception) Through December 31, 2012

	Series A Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Common Stock		Additional Paid-in Capital	Deficit Accumulated During the Development Stage	Accumulated Other Comprehens Gain (Loss)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
tion		$		$		$	949,035	$949	$26,468	$	$
ptember 10, 2002											
November 1, 2002							60,576	61	1,689		
October 1, 2003							112,498	112	3,138		
ounders											
r 27, 2003							(550,960)	(551)	(15,366)		
nt from October											
n May 5, 2004							392,163	392	2,832,088		
nt November 8,											
							51,922	52	374,948		
nt May 8, 2006							2,087,091	2,087	20,497,913		
romissory											
2006							160,637	161	1,341,088		
egal, and other											
placement									(1,500,138)		
npensation:											
nployees									604,372		
									494,685		
k options							6,129	6	17,699		
rants							51,922	52	374,948		
nsive loss											84,978
period September											
December 31,										(18,656,010)	
mber 31, 2007							3,321,013	$3,321	$25,053,532	$(18,656,010)	$84,978
npensation:											
nployees									682,025		
									127,359		

nt May 23, 2008	13,888,889	$13,889			24,986,111		
egal, and other					(749,075)		
nsive loss							(155,784)
						(13,704,870	
mber 31, 2008	13,888,889	$13,889	3,321,013	$3,321	$50,099,952	$(32,360,880)	$(70,806)
npensation:							
nployees					908,375		
					53,425		
ct of accounting					(2,187,680)		
k options			8,653	9	24,991		
nsive loss							(7,314)
						(14,354,522)	
mber 31, 2009	13,888,889	$13,889	3,329,666	$3,330	$48,899,063	$(46,715,402)	$(78,120)

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Consolidated Statements of Changes in Stockholders Equity
For the Period From September 4, 2002 (Inception) Through December 31, 2012 (continued)

Series A Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Common Stock		Additional Paid-in Capital	Deficit Accumulat During the Developm Stage
Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount		
								1,604,117	
								88,768	
		13,888,889	13,889					19,787,894	
								(111,704)	
13,888,889	$13,889	13,888,889	$13,889			3,329,666	$3,330	$70,268,138	(15,087,2 $(61,802,6
								1,779,785	
								85,970	
13,888,889	$13,889	13,888,889	$13,889			3,329,666	$3,330	$72,133,893	(12,737,6 $(74,540,2
								2,436,430	
								912,559	
				15,000,000	15,000			29,715,000	
(13,888,889)	(13,889)	(13,888,889)	(13,889)	(15,000,000)	(15,000)	7,403,817	7,404	35,374	
						5,750,000	5,750	78,764,246	
						43,402	43	1,018,172	

			(915,535)	
				(43,643,0
	16,526,885	$16,527	$184,100,139	$(118,183

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

Consolidated Statements of Cash Flows

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

Intercept Pharmaceuticals, Inc. (Intercept or the Company), a development stage company, is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat chronic liver diseases utilizing its proprietary bile acid chemistry. The Company s product candidates have the potential to treat orphan and more prevalent liver diseases for which there currently are limited therapeutic solutions.

The Company has its administrative headquarters in New York, New York and an office in San Diego, California. Prior to April 2011, the Company operated a wholly-owned subsidiary in Italy where its bile acid receptor research was primarily conducted. In April 2011, the Company began the process of liquidating this subsidiary and has since disposed of all assets. However, the Company is continuing its early stage TGR5 research through its collaboration with Les Laboratories Servier and Institut de Recherches Servier, or collectively Servier. Effective March 15, 2013, the Company decided to remove the Italian subsidiary from the legal liquidation process to act as the Company s legal representative for its clinical trials in the European Union to satisfy European Union regulatory requirements. Intercept was incorporated in Delaware in September 2002.

On September 13, 2012, the board of directors of the Company approved, and on September 25, 2012 the stockholders of the Company approved, a one-for-5.7778 reverse stock split of the Company s outstanding common stock, which was effected on September 26, 2012. Stockholders entitled to fractional shares as a result of the reverse stock split received a cash payment in lieu of receiving fractional shares. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities. Shares of common stock reserved for issuance upon the conversion of the Company s series A preferred stock, series B preferred stock, and series C preferred stock were proportionately reduced and the respective conversion prices were proportionately increased. All share and per share amounts in the financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

In October 2012, the Company completed the initial public offering (IPO) of its common stock pursuant to a registration statement on Form S-1. In the IPO, the Company sold an aggregate of 5,750,000 shares of common stock under the registration statement at a public offering price of $15.00 per share. Net proceeds were approximately $78.7 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. Upon the closing of the IPO, all outstanding shares of the Company s preferred stock were converted into 7,403,817 shares of common stock. Additionally, upon completion of the IPO, the Company is now authorized to issue 25,000,000 shares of common stock, $0.001 par value per share, and 5,000,000 shares of preferred stock, $0.001 par value per share.

2. Summary of Significant Accounting Policies

A. Basis of Presentation and Use of Estimates

The Company s financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (GAAP). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. The ability of the Company to become profitable depends on several factors, many of which are outside the Company s control. Such factors include the ability to obtain regulatory

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

2. Summary of Significant Accounting Policies (continued)

approval of product candidates and the ability to successfully commercialize any approved product candidate. The Company s lead product candidate, OCA, has completed three Phase 2 clinical trials and is currently being tested in three additional clinical trials. Therefore, the Company s product candidates still require significant research and development efforts. The extent to which the Company will be able to continue its research and development efforts will also partially be determined by factors outside the Company s control, such as the nature and extent of testing that will be required by the U.S. Food and Drug Administration (FDA) and equivalent agencies outside of the United States.

B. Segments

The Company operates in one segment. The Company is a biopharmaceutical company focused on discovering, developing and commercializing treatments for chronic liver diseases utilizing its proprietary bile acid chemistry.

C. Principles of Consolidation

The consolidated financial statements include the accounts of Intercept and its subsidiary, Intercept Italia S.R.L. All intercompany balances and transactions have been eliminated in consolidation.

D. Reclassification

Certain amounts shown in prior years consolidated financial statements have been reclassified to conform to the current year consolidated financial statement presentation.

E. Cash and Cash Equivalents

The Company considers all highly liquid securities with a maturity of three months or less at acquisition to be cash equivalents.

F. Investment Securities

Investment securities are considered to be available-for-sale and are carried at fair value. Unrealized gains and losses, if any, are reported as a separate component of stockholders equity. The cost of investment securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains and losses, if any, are also included in other income, net. The cost of securities sold is based on the specific identification method.

G. Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents, and investment securities. The Company currently invests its excess cash primarily in a money market fund, U.S. Treasury notes, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. The Company has adopted an investment policy that includes guidelines relative to credit quality, diversification and maturities to preserve principal and liquidity. The Company does not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt.

H. Fixed Assets

Fixed assets are recorded at cost, net of depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of three to seven years for equipment and seven years for furniture and fixtures. Leasehold improvements are amortized over the shorter of the asset s useful life or the life of the lease term. Expenditures for maintenance and repairs are charged to expense as incurred.

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INTERCEPT PHARMACEUTICALS, INC.
(A Development Stage Company)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

2. Summary of Significant Accounting Policies (continued)

I. Impairment of Long-Lived Assets

Long-lived assets consist of fixed assets. The Company evaluates long-lived assets for impairment when events and circumstances indicate that the carrying amount of an asset or group of assets may not be fully recoverable.

J. Revenue Recognition

All of the Company s revenue during the periods covered by these financial statements has been derived from its research and development and licensing collaborations. These agreements include non-refundable up-front fees and the potential for research, development, regulatory and commercial milestone fees, as well as royalties on sales of licensed products, if and when such product sales occur. To date, the Company has received only up-front fees from its collaborations.

The Company evaluates all deliverables within an arrangement to determine whether they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed and determinable at the inception of the arrangement is allocated to the separate units of accounting based on relative fair value. The Company may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such units of accounting. For each unit of accounting identified within an arrangement, the Company determines the period over which the performance obligation occurs and recognizes the revenue using a straight-line method.

The Company accounts for the development, regulatory and sales milestones within an arrangement in accordance with the milestone method of revenue recognition. This method allows for the recognition of consideration which is contingent on the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Each future milestone is considered substantive if it (i) relates solely to the past performance of the intellectual property to achieve the milestone; (ii) is reasonable relative to all of the deliverables and payment terms in the arrangement; and (iii) is commensurate with either the Company s performance or the enhanced value of the intellectual property as a result of a specific outcome resulting from the Company s performance.

K. Research and Development

Research and development costs that do not have alternative future use are charged to expense as incurred. This includes the cost of conducting clinical trials, compensation and related overhead for employees and consultants involved in research and development and the cost of materials purchased for research and development.

L. Stock-Based Compensation

In 2003, the Board of Directors and the stockholders of the Company approved the Amended and Restated 2003 Stock Incentive Plan (2003 Plan) which provided for the granting of restricted stock, stock options and other stock-related awards to officers, directors, employees, advisors, and consultants of the Company. Stock options were granted at exercise prices not less than the fair market value of the Company s common stock at the dates of grant. In May 2006, June 2008 and January 2010, the number of common shares available was increased to 519,228, 865,381, and 1,384,610, respectively. Most options are scheduled to vest over a period of up to four years. The 2003 Plan was terminated upon the pricing of the IPO in October 2012, and 555,843 shares available under the 2003 Plan were added to the 2012 Plan. All outstanding options issued under the 2003 Plan as of the date of termination remained outstanding and are subject to their respective terms and the terms of the 2003 Plan.

In September 2012, the Company s board of directors and stockholders approved the 2012 Equity Incentive Plan (2012 Plan), which became effective upon the pricing of the Company s IPO in October 2012.

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2. Summary of Significant Accounting Policies (continued)

The 2012 Plan will expire on September 13, 2022. Under the 2012 Plan, the Company may grant incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and other stock-based awards. As of December 31, 2012, there were 348,690 shares of Company common stock authorized for issuance under the 2012 Plan. On January 1, 2013, 661,075 shares of common stock were added to the 2012 Plan in January 2013 in accordance with its terms.

The Company utilizes the Black-Scholes option-pricing model for determining the estimated fair value of awards. Key inputs and assumptions include the expected term of the option, stock price volatility, risk-free interest rate, dividend yield, stock price and exercise price. Many of the assumptions require significant judgment and any changes could have a material impact in the determination of stock-based compensation expense. The Company estimates forfeitures when recognizing compensation expense and adjusts forfeiture estimates over the vesting period based on actual or anticipated forfeitures.

The Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period of the individual grants, which is generally the vesting period, based on the estimated grant date fair values. Generally, stock options granted to employees fully vest four years from the grant date and have a term of ten years.

M. Warrants to Purchase Common Stock

In conjunction with various financing transactions, the Company issued warrants to purchase the Company s common stock. Certain of the warrants include a provision that provides for a reduction in the warrant exercise price if there are subsequent issuances of additional shares of common stock for consideration per share less than the per share warrant exercise prices and the remaining warrants contain a provision that require the underlying shares to be registered upon an IPO. These warrants are deemed to be derivative instruments and as such, are recorded as a liability and are marked-to-market at each reporting period using the Black-Scholes option pricing model. The Company estimates the fair values of the warrants at each reporting period using a Black-Scholes option-pricing model that uses the inputs detailed in note 8 and the contractual terms of the warrants. Management has concluded, under the Company s facts and circumstances, that the estimated fair values of the warrants using the Black-Scholes option-pricing model approximates, in all material respects, the values determined using a binomial valuation model. The estimates in the Black-Scholes option-pricing model and the binomial valuation model are based, in part, on subjective assumptions, including but not limited to stock price volatility, the expected life of the warrants, the risk free interest rate and the fair value of the common stock underlying the warrants, and could differ materially in the future. Changes in the fair value of the common stock warrant liability from the prior period are recorded as a component of other income and expense.

The Company will continue to adjust the fair value of the common stock warrant liability at the end of each reporting period for changes in fair value from the prior period until the earlier of the exercise or expiration of the applicable

common stock warrants or until such time that the warrants are no longer determined to be derivative instruments.

N. Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax bases of assets and liabilities. A valuation allowance is established against net deferred tax assets if, based on the weight of available evidence, it is more likely than not that some or all of the net deferred tax assets will not be realized.

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be resolved. The effect of a change

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2. Summary of Significant Accounting Policies (continued)

in tax rates or laws on deferred tax assets and deferred tax liabilities is recognized in operations in the period that includes the enactment date of the rate change.

The deferred tax asset or liability represents future tax return consequences of those differences, which will be taxable when the assets and liabilities are recovered or settled. The provision for income taxes may differ from the actual expense that would result from applying the federal statutory rate to income before taxes because certain expenses for financial reporting purposes are not deductible for tax purposes. At December 31, 2011 and 2012, the Company had available net operating loss carryforwards to reduce future taxable income of approximately $55.0 million and $70.2 million, respectively, for tax reporting purposes. These carryforwards expire between 2024 and 2032. The ability of the Company to utilize its net operating losses in future years is subject to limitation in accordance with provisions of Section 382 of the Internal Revenue Code due to previous ownership changes; however, these changes have not resulted in material limitations to the Company s ability to utilize the net operating losses. The Company s combined federal, state and city deferred tax asset of approximately $26.6 million, $32.1 million, and $42.1 million at December 31, 2010, 2011 and 2012, respectively, resulted from the tax effects of net operating losses and differences between the book and tax bases for the share-based compensation and depreciation. The Company does not have any material deferred tax liabilities. Management has determined it is uncertain whether any of the deferred tax assets will be realizable, and has provided an allowance for the full amount of the tax asset. As a result, the Company has not recorded any income tax benefit since its inception.

O. Net Loss per Share

Basic net loss per share is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Net loss attributable to common stockholders is net loss reduced by accrued dividends on preferred shares for the periods the preferred shares were outstanding. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options and warrants are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and, therefore, basic and diluted net loss per share were the same for all periods presented.

P. Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board, or the FASB, issued ASU No. 2013-02, Other Comprehensive Income (Topic 220): Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income, or ASU No. 2013-02. ASU No. 2013-02 supersedes the presentation requirements for reclassifications out of

accumulated other comprehensive income in ASUs 2011-05 and 2011-12 and requires an entity to provide additional information about reclassifications out of accumulated other comprehensive income. ASU No. 2013-02 became effective for us beginning January 1, 2013. The adoption of this amendment will not have a material impact on the Company s results of operations or financial position.

3. Significant Agreements

Dainippon Sumitomo Pharma Co., Ltd. (DSP)

In March 2011, the Company entered into an exclusive license agreement with DSP to research, develop and commercialize obeticholic acid (OCA) as a therapeutic for the treatment of primary biliary cirrhosis (PBC) and nonalcoholic steatohepatitis (NASH) in Japan and China (excluding Taiwan). Under the terms of the license agreement, the Company received an up-front payment from DSP of $15.0 million and may be eligible to receive additional milestone payments up to an aggregate of approximately $30.0 million in development milestones based on the initiation or completion of clinical trials, $70.0 million in regulatory

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3. Significant Agreements (continued)

approval milestones and $200.0 million in sales milestones. The regulatory approval milestones include $15.0 million for receiving marketing approval for OCA for NASH in Japan, $10.0 million for receiving marketing approval for OCA for NASH in China, and up to $5.0 million for receiving marketing approval for OCA for PBC in the United States. The sales milestones are based on aggregate sales amounts of OCA and include $5.0 million for achieving net sales of $50.0 million, $10.0 million for achieving net sales of $100.0 million, $20.0 million for achieving net sales of $200.0 million, $40.0 million for achieving net sales of $400.0 million and $120.0 million for achieving net sales of $1.2 billion. DSP is also required to make royalty payments ranging from the tens to the twenties in percent based on net sales of OCA products in the DSP territory. DSP has the exclusive option to add several other Asian countries to its territory, including Korea and Taiwan, and to pursue OCA for additional indications. DSP will be responsible for the costs of developing and commercializing OCA in its territory.

The Company has evaluated the license agreement with DSP and has determined that it is a revenue arrangement with multiple deliverables, or performance obligations. The Company s substantive performance obligations under this license include an exclusive license to its technology, technical and scientific support to the development plan and participation on a joint steering committee. The Company determined that these performance obligations represent a single unit of accounting, since, initially, the license does not have stand-alone value to DSP without the Company s technical expertise and steering committee participation during the development of OCA. This development period is currently estimated as continuing through June 2020 and, as such, the up-front payment is being recognized ratably over this period. During the year ended December 31, 2011 and 2012, the Company recorded revenue of $1.2 million and $1.6 million, respectively, in License Fees in its Consolidated Statement of Operations for the Company s efforts under the agreement. During 2012, the Company did not achieve any of the milestones relating to the agreement and did not recognize any revenue related to such milestones. The Company has determined that each potential future development, regulatory and sales milestone is substantive.

Les Laboratories Servier and Institut de Recherches Servier (Servier)

In August 2011, the Company entered into a research collaboration agreement with Servier under which the Company granted Servier the exclusive license to research, develop and commercialize TGR5 agonists (other than the Company s preclinical product candidates INT-767 and INT-777) for use in the treatment of diabetes, obesity, atherosclerosis and reperfusion injury in all countries other than the United States and Japan. The agreement expires when no payment obligations are or will become due and may be terminated earlier by the parties in certain circumstances.

Under the terms of the agreement, the Company received an up-front payment from Servier of $1.4 million. The Company is also eligible to receive up to an aggregate of approximately €8.5 million in development milestones based on the initiation of clinical trials by Servier or the selection by Servier of product candidates for development, including a payment of €4.0 million upon the determination by Servier to initiate a Phase 3 clinical trial for the first

product candidate under the agreement. The Company may also receive up to an aggregate of approximately €10.0 million in regulatory submission and approval milestones, including a payment of €5.0 million upon the first product candidate under the agreement achieving regulatory approval in the EU for its initial indication. The agreement also contemplates up to an aggregate of approximately €90.0 million in sales milestones, including a payment of €10.0 million upon the first product candidate under the agreement achieving its first commercial sale, €10.0 million upon achieving net sales of €200.0 million for a product, €20.0 million upon achieving net sales of €400.0 million for a product, €25.0 million for achieving net sales of €500.0 million for a product and €25.0 million for achieving net sales of €600.0 million for a product. Servier is also obligated to pay the Company royalties based on net sales of products developed under the agreement on a country-by-country basis. Servier is also obligated to pay the Company royalties based on net sales of products developed under the agreement on a country-by-country basis.

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3. Significant Agreements (continued)

Intercept and Servier will jointly support the discovery effort, while Servier alone will be responsible for all costs associated with the global development, regulatory approval and commercialization of any compound selected as a lead candidate by the parties. The Company agreed to reimburse Servier up to a mid-double digit percentage of the total historical development costs incurred by Servier in relation to clinical development activities aimed at achieving regulatory approval in the European Union and the United States if the Company enters into a partnership agreement, or commences development or commercialization activities, with respect to any such compound in the United States. Servier may credit a portion of any reimbursable development costs against any milestone or royalty payments due and payable to the Company by Servier under the research collaboration agreement until all such reimbursable amounts are repaid. During the year ended December 31, 2011 and 2012, the Company did not reimburse any development costs to Servier.

The Company has evaluated the research collaboration agreement with Servier and has determined that it is a revenue arrangement with multiple deliverables, or performance obligations. The Company s substantive performance obligations under this research collaboration include an exclusive license to its technology, technical, scientific and intellectual property support to the research plan during the first year of the agreement and participation on an executive committee and a research and development committee. The Company determined that these performance obligations represent a single unit of accounting, since the license does not have stand-alone value to Servier without the Company s technical expertise and committee participation during the initial 12-month period. The research portion of the collaboration may be extended by mutual agreement by the parties for one or more additional years. In July 2012, the term of the research program was extended until January 31, 2013, on the same financial terms as the existing research program, including the reimbursement by Servier of the full time equivalent costs incurred by the Company in the conduct of the research program, up to a set maximum amount. In February 2013, the research program was further extended until July 31, 2013 on the same financial terms as the existing agreement. The up-front payment is being recognized ratably over the estimated 12-month performance period as the research and development and executive committee services are being provided. During the year ended December 31, 2011 and 2012, the Company recorded revenue of $589,000 and $824,000, respectively related to the Company s efforts under the Servier arrangement, which was recorded in License Fees in the Company s Consolidated Statement of Operations. The Company has determined that each potential future development, regulatory and sales milestone is substantive.

The Company is also receiving reimbursement from Servier for research services outlined in the agreements in which the Company engaged Professor Pellicciari and TES as described below. The Company is recognizing this expense reimbursement as a reduction of research and development expenses as the Company is acting as an agent regarding these research activities. All amounts incurred by the Company for research under the Servier agreement during the year ended December 31, 2011 and 2012, including the amounts incurred under the related agreements with Professor Pellicciari and TES, were covered under the Servier agreement. At December 31, 2011 and 2012, the Company has recorded $486,000 and $496,000, respectively in prepaid expenses and other assets for amounts due from Servier for such expense reimbursement.

Sponsored Research Agreement (SRA) with the University of Perugia and Professor Pellicciari

The Company is engaged in a sponsored research agreement with the University of Perugia and Professor Roberto Pellicciari, a founder of the Company, to design, synthesize, optimize, scale-up, and develop pharmacologically active ligands for bile acid receptors. Under the SRA, the Company is assigned ownership of any patent and intellectual property rights arising from the research project. The Company paid the University of Perugia €100,000 quarterly commencing July 1, 2006 through 2010 and €100,000 for the fiscal year 2011. In 2012, the Company amended and restated the SRA to extend the term to the end of 2012 and paid the University of Perugia €80,000 for fiscal 2012. Since the expiration of the previous term on December 31, 2012, the Company has been ascertaining its specific requirements concerning the supply of certain reference standards relating to OCA, INT-767 and INT-777 and is currently negotiating a revised

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3. Significant Agreements (continued)

agreement to provide for their supply. The Company has recognized expense for the years ended December 31, 2010, 2011 and 2012 of $550,000, $138,000 and $104,000, respectively.

Consulting Agreements with Professor Pellicciari

The Company entered into an amended and restated consulting and intellectual property agreement with Professor Pellicciari on November 1, 2008, which was amended on October 27, 2010. Pursuant to this agreement, as amended, the Company was required to pay Professor Pellicciari €8,000 per month through December 31, 2010 for consulting services. The agreement also required the Company to make a lump sum payment of €172,500 and monthly payments of €12,000 through December 31, 2010 for the assignment of certain intellectual property rights. The Company entered into amended and restated consulting and intellectual property agreements with Professor Pellicciari on January 1, 2011 and January 1, 2012, pursuant to which the Company agreed to pay Professor Pellicciari an aggregate of €100,000 per year for services provided through December 31, 2012 for consulting services and intellectual property rights in relation to OCA, INT-767 and INT-777 product candidates. The Company is currently contemplating the extension of this agreement in conjunction with its negotiations with Professor Pellicciari and the University of Perugia regarding the revised agreement to supply the Company with reference standards relating to OCA, INT-767 and INT-777.

On August 1, 2011, the Company signed a separate agreement with Professor Pellicciari for consulting services and intellectual property rights related to his services on the TGR5 program and the Servier license, pursuant to which the Company agreed to pay him an aggregate of €150,000 for his services through July 31, 2012. This agreement also provides that Professor Pellicciari will be eligible for a performance bonus of €50,000 based on the results of the research collaboration. The performance bonus is a discretionary bonus based upon the Company s assessment of the success of the initial work performed under the collaboration, as extended. No such bonus has been agreed upon by the parties as of December 31, 2012. In July 2012 and February 2013, by mutual agreement of the parties, the term of this agreement was extended until January 31, 2013 and July 31, 2013, respectively, in conjunction with the extension of the term of the research program with Servier, on the same financial terms as the original consulting agreement with Professor Pellicciari.

The Company has recognized expense related to these agreements for the years ended December 31, 2010, 2011 and 2012 $318,000, $266,000 and $325,000, respectively.

TES Pharma SRL (TES)

In August 2011, the Company contracted with TES to provide research and development services for the Company s TGR5 program through July 31, 2012 to enable the Company to uphold its obligations for providing such services under the Servier agreement described above. Professor Pellicciari is an owner of TES. The Company is required

under the agreement to pay TES an aggregate amount of €250,000 each quarter during the term of the agreement. The agreement provides that any funds paid to TES that have not been expended or irrevocably committed at the expiration of the agreement will be refunded to the Company.

The agreement has a term of one year unless the Company, in its sole discretion, extends the term of this agreement for one additional year on the same terms and conditions as the current agreement. In July 2012 and February 2013, by mutual agreement of the parties, the term of this agreement was extended until January 31, 2013 and July 31, 2013, respectively, in conjunction with the extension of the term of the research program with Servier, on the same financial terms as the original agreement with TES.

The Company has incurred charges related to this agreement for the year ended December 31, 2011 and 2012 of $596,000 and $1.3 million respectively.

National Institute of Diabetes and Digestive and Kidney Disease Institute (NIDDK)

In 2010, the Company contracted with the NIDDK of the National Institute of Health to research the effects of OCA for the treatment of patients with nonalcoholic steatohepatitis in a Phase 2b clinical trial called the FLINT trial. Under the contract with the NIDDK, the Company made a milestone payment of $1.0 million

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3. Significant Agreements (continued)

in June 2012 following notification in June 2012 that the FLINT trial will continue based upon the results of a blinded interim analysis. The Company has recognized expense related to this contract for the years ended December 31, 2010, 2011 and 2012 of $500,000, $250,000 and $2.3 million, respectively and does not have any additional contractual payments remaining.

WIL Research Laboratories, LLC (WIL)

On October 2, 2007, the Company entered into a master laboratory services agreement with WIL Research Laboratories, LLC to perform certain research and laboratory services. The agreement was amended in October 2011. The agreement has a term ending on October 2, 2013, which automatically extends for successive one year periods, unless either party gives written notice to the other party at least 60 days prior to the end of the current term. Either the Company or WIL may terminate the agreement upon 90 days written notice. However, if a work order pertaining to the ongoing studies is outstanding, WIL may not terminate the agreement with 90 days written notice until the work order has been completed or otherwise terminated.

On November 16, 2011, the Company finalized two work orders with WIL for FDA-required studies in mice and rats to investigate the presence or absence of carcinogenic potential of OCA. The Company has agreed to pay an aggregate of $4.0 million for the studies, consisting of a combination of quarterly installment payments of approximately $300,000 and milestone payments totaling approximately $400,000 upon delivery of final result reports. If additional costs are incurred beyond the amounts specified in the work orders, the Company has agreed to pay such reasonable additional costs upon receipt of proper invoice. The Company anticipates that all the studies will continue through completion, all milestones will be satisfied and that it will pay to WIL an aggregate of $4.0 million under this agreement. The Company has recognized expense related to these contracts and other work orders for the years ended December 31, 2010, 2011 and 2012 of $1.6 million, $1.5 million and $1.6 million respectively.

4. Investments

The following table summarizes the Company s cash, cash equivalents and investments as of December 31, 2012 and December 31, 2011:

	As of December 31, 2012			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			

Cash and cash equivalents:				
Cash and money market funds	$45,512	$	$	$45,512
Investment Securities:				
Commercial paper	12,971	10	(15)	12,966
Corporate debt securities	41,866	7	(23)	41,850
U.S. government and agency securities	9,861	4		9,865
Total investments	64,698	21	(38)	64,681
Total cash, cash equivalents and investments	$110,210	$ 21	$ (38)	$110,193

	As of December 31, 2011			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
Cash and cash equivalents:				
Cash and money market funds	$17,707	$	$	$17,707

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4. Investments (continued)

The following table shows the gross unrealized losses and fair value of the Company s available-for-sale investments aggregated by investment category and length of time that individual securities have been in the position:

	As of December 31, 2012 Less than 12 months (In thousands)	
	Fair Value	Gross Unrealized Holding Losses
Commercial paper	$ 10,461	$ (15)
Corporate debt securities	29,834	(23)
Total available-for-sale securities	$ 40,295	$ (38)

5. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31,	
	2011	2012
	(In thousands)	
Prepaid expenses	$ 359	$ 970
Contract receivable	486	496
Certificates of deposit	201	77
Refundable tax credits	151	42
Prepaid expenses and other current assets	$ 1,197	$ 1,585

6. Fixed Assets, Net

Fixed assets, net consisted of the following:

	Useful Lives (Years)	December 31,	
		2011	2012
		(In thousands)	
Laboratory equipment	5	$ 1,046	$

Office equipment	3	318	357
Leasehold improvements	Over life of lease	178	178
Furniture and fixtures under capitalized lease		157	157
Furniture and fixtures	7	120	121
Subtotal fixed assets		1,819	813
Less: accumulated depreciation and amortization		(1,508)	(664)
Fixed assets, net		$ 311	$ 149

Depreciation and amortization expense for the years ended December 31, 2011 and 2012 was $411,000 and $201,000, respectively. During 2011, the Company closed its facility in Italy and in August 2011, in connection with entering into the TES agreement (note 3), transferred its rights in its certain fixed assets located at the Italian facility to TES. As a result, the Company recognized a $217,000 loss on the disposal of fixed assets.

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7. Accounts Payable, Accrued Expenses and Other Liabilities

Accrued expenses and other liabilities consisted of the following:

	December 31,	
	2011	2012
	(In thousands)	
Accounts payable	$ 604	$ 1,180
Accrued employee compensation	728	1,335
Accrued contracted services & other	172	1,231
Accounts payable, accrued expenses and other liabilities	$ 1,504	$ 3,746

8. Warrants to Purchase Common Stock

The Company s activity related to warrants to purchase shares of common stock of the Company is noted in the table below.

	Warrants to Purchase Common Stock	Weighted Average Exercise Price	Expiration
Warrants issued in 2003	2,163	$ 2.89	10/24/2013
Warrants issued in 2003	2,163	8.67	10/27/2013
Warrants issued in 2004	117,642	2.89	10/27/2013
Warrants issued in 2004	19,609	2.89	5/4/2014
Warrants issued in 2004	117,640	8.67	10/27/2013
Warrants issued in 2005	138,461	7.22	Expired
Warrants issued in 2006	86,538	9.82	Expired
Warrants issued in 2006	20,481	9.82	Expired
Warrants exercised in 2007	(51,922)	7.22	
Warrants issued in 2008	108,169	10.40	5/23/2013
Warrants issued in 2010	865,381	10.40	1/25/2015
Warrants expired in 2010	(86,539)	7.22	
Warrants issued and outstanding as of December 31, 2010	1,339,786	9.42	
Warrants expired in 2011	(107,019)	9.82	
Warrants issued and outstanding as of December 31, 2011	1,232,767	9.38	
Warrants exercised in 2012	(70,802)	8.59	

Warrants issued and outstanding as of December 31, 2012	1,161,965	$ 9.43

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8. Warrants to Purchase Common Stock (continued)

As discussed in note 2, all of the warrants have been deemed to be derivative instruments that require liability classification and mark-to-market accounting. The warrants that contain an exercise price adjustment are deemed derivatives pursuant to an accounting standard that became effective on January 1, 2009. The warrants that require the underlying shares to be registered upon an IPO met the criteria to be a derivative upon the closing of the IPO in October 2012. The fair values of the warrants are reflected in the accompanying balance sheets and were determined using the Black-Scholes option-pricing model using the following weighted average assumptions:

	December 31,	
	2011	2012
Stock price	$8.67	$34.24
Expected dividend yield	%	%
Expected term (in years)	2.78	1.72
Risk free interest rate	0.33 %	0.22 %
Expected volatility	102.76%	84.01%

The expected term is based on the remaining term of each warrant. The risk free interest rate is based on the rate for U.S. Treasury securities for the expected term of each warrant valued. The expected volatility was estimated based on historical volatility information of peer companies that are publicly available.

9. Fair Value Measurements

The carrying amounts of the Company s receivables and payables approximate their fair value due to their short maturities.

Accounting principles provide guidance for using fair value to measure assets and liabilities. The guidance includes a three level hierarchy of valuation techniques used to measure fair value, defined as follows:

Unadjusted Quoted Prices The fair value of an asset or liability is based on unadjusted quoted prices in active markets for identical assets or liabilities (Level 1).

Pricing Models with Significant Observable Inputs The fair value of an asset or liability is based on information derived from either an active market quoted price, which may require further adjustment based on the attributes of the financial asset or liability being measured, or an inactive market transaction (Level 2).

Pricing Models with Significant Unobservable Inputs The fair value of an asset or liability is primarily based on internally derived assumptions surrounding the timing and amount of expected cash flows for the financial instrument. Therefore, these assumptions are unobservable in either an active or inactive market (Level 3).

The Company considers an active market as one in which transactions for the asset or liability occurs with sufficient

frequency and volume to provide pricing information on an ongoing basis. Conversely, the Company views an inactive market as one in which there are few transactions for the asset or liability, the prices are not current, or price quotations vary substantially either over time or among market makers. Where appropriate, non-performance risk, or that of a counterparty, is considered in determining the fair values of liabilities and assets, respectively.

The Company s cash deposits and money market funds are classified within Level 1 of the fair value hierarchy because they are valued using bank balances or quoted market prices. Investments are classified as Level 2 instruments based on market pricing and other observable inputs. None of the Company s investments

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9. Fair Value Measurements (continued)

are classified within Level 3 of the fair value hierarchy. The Company s warrant liability has been valued pursuant to the discussion in note 8 above and thus is included in Level 3.

Financial assets and liabilities, carried at fair value are classified in the tables below in one of the three categories described above:

	Total	Fair Value Measurements Using Quoted Prices in Active Markets for Identical Assets or Liabilities (Level 1) (In thousands)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Description				
December 31, 2010				
Assets:				
Money market funds	$	$	$	$
Liabilities:				
Warrants to purchase common stock	$ (6,881)	$	$	$ (6,881)
Total liabilities	$ (6,881)	$	$	$ (6,881)
December 31, 2011				
Assets:				
Money market funds	$ 1,375	$ 1,375	$	$
Liabilities:				
Warrants to purchase common stock	$ (5,836)	$	$	$ (5,836)
Total liabilities	$ (5,836)	$	$	$ (5,836)
December 31, 2012				
Assets:				
Money market funds	$ 24,862	$ 24,862	$	$
Available for sale securities:				
Commercial paper	$ 12,966	$	$ 12,966	$
Corporate debt securities	41,850		41,850	

U.S. government and agency securities	9,865		9,865	
Total assets:	$ 89,543	$ 24,862	$ 64,681	$
Liabilities:				
Warrants to purchase common stock	$ (30,359)	$	$	$ (30,359)
Total liabilities	$ (30,359)	$	$	$ (30,359)

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9. Fair Value Measurements (continued)

The estimated fair value of marketable debt securities (commercial paper, corporate debt securities and U.S. government and agency securities) as of December 31, 2012, by contractual maturity, are as follows:

	Fair Value (In thousands)
Due in one year or less	$ 32,079
Due after one year through 2 years	32,602
Total investments in debt securities	$ 64,681

Actual maturities may differ from contractual maturities because issuers may have the right to call or prepay obligations without call or prepayment penalties.

10. Stockholders Equity and Preferred Stock

Common Stock

In September 2002, the Company issued 949,035 shares of common stock at a price of $0.03 per share to the founders of the Company (Founders shares).

In November 2002, the Company issued 60,576 shares of common stock at a price of $0.03 per share to the principal investigators and other researchers of the Company pursuant to an authorization by the Board of Directors to issue and sell these shares by subscription to the named parties in conjunction with the signing of certain research agreements.

In October 2003, the Company issued 112,498 shares of common stock at a price of $0.03 per share to the two principal investigators pursuant to an authorization by the Board of Directors to issue and sell these shares by subscription.

In October 2003, the Company repurchased and canceled 550,960 Founders shares from certain founders of the Company at a price of $0.03 per share.

From October 2003 through May 2004, pursuant to a private placement agreement dated October 2003, the Company issued an aggregate of 392,163 shares of common stock at a price of $7.22 per share, receiving net proceeds of $2.4 million after $474,000 in related offering costs. In addition, Class A warrants to purchase 137,251 shares of common stock and Class B warrants to purchase 117,640 shares of common stock were issued to the placement agent and its assigns as additional placement agent commission under the terms of the placement agent agreement.

In November 2005, the Company issued 51,922 shares of common stock, warrants with a two-year term to purchase 51,922 shares of common stock at an exercise price of $7.22 per share and warrants with a five-year term to purchase 86,538 shares of common stock at an exercise price of $7.22 per share, all pursuant to a private subscription agreement with two outside investors, receiving net proceeds of $375,000.

In May 2006, pursuant to a private placement agreement, the Company issued 2,087,091 shares of common stock at a price of $9.82, receiving net proceeds of $19.5 million, after $1.0 million in related offering costs. Also in May 2006, the Company s 6% convertible promissory notes that were issued in February 2005 with a face amount of $1.3 million, along with $91,000 of accrued interest, were converted into 160,637 shares of common stock at a price of $8.35 per share pursuant to the mandatory conversion terms of the notes.

Dividends

The holders of common stock are entitled to receive dividends from time to time as declared by the Board of Directors. No cash dividend may be declared or paid to common stockholders until paid on each series of outstanding preferred stock in accordance with their respective terms.

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10. Stockholders Equity and Preferred Stock (continued)

Voting

The holders of shares of common stock are entitled to one vote for each share held with respect to all matters voted on by the stockholders of the Company.

Preferred Stock

In May 2008, to effectuate the sale of Series A preferred stock, the Company amended and restated its Certificate of Incorporation in its entirety to increase the number of shares of preferred stock it was authorized to issue to 13,888,889 shares and to designate such shares as Series A preferred stock. In May 2008, 13,888,889 shares of Series A preferred stock were sold to Genextra for net proceeds of $24.3 million, after $749,000 in related offering costs. In connection with this financing, the Company issued warrants with a five-year term to purchase 108,169 shares of common stock at $10.40 per share to the placement agent.

In January 2010, the Company further amended and restated its Certificate of Incorporation in its entirety to increase the number of shares of preferred stock it was authorized to issue to 27,777,778 shares and designated 13,888,889 of such shares as Series B preferred stock. In January 2010, 13,888,889 shares of Series B preferred stock and a warrant with a five-year term to purchase 865,381 shares of common stock at $10.40 per share were sold to Genextra for $24.9 million, after $112,000 in related offering costs.

In August 2012, the Company further amended and restated its Certificate of Incorporation in its entirety to increase the number of shares of preferred stock it was authorized to issue to 52,777,778 shares and designated 25,000,000 of such shares as Series C preferred stock. In August 2012, 15,000,000 shares of Series C preferred stock were sold to Genextra and OrbiMed Advisors LLC for $29.7 million, after $300,000 in related offering costs. Upon the completion of the IPO, all outstanding shares of the Company s preferred stock were converted into 7,403,817 shares of common stock and all accrued dividends on the preferred stock were eliminated.

11. 2003 Stock Incentive Plan and 2012 Stock Plan

Upon the pricing of the IPO in October 2012, the 2012 Plan became effective. At the same time, the 2003 Plan was terminated and 555,843 shares available under the 2003 Plan were added to the 2012 Plan. See note 2L.

The estimated fair value of the options that have been granted under the 2003 and 2012 Plans is determined utilizing the Black-Scholes option-pricing model at the date of grant. The fair value of the restricted stock units that have been granted under the 2012 Plan is determined utilizing the closing stock price on the date of grant. There were 60,411 shares available for grant remaining under the 2003 Plan at December 31, 2011 and 348,690 shares available for grant

remaining under the 2012 Plan at December 31, 2012.

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11. 2003 Stock Incentive Plan and 2012 Stock Plan (continued)

Stock-based compensation expense for the years ended December 31, 2010, 2011 and 2012 includes compensation expense for employee, director and consultant stock option grants and restricted stock grants as follows:

	Years Ended December 31,		
	2010	2011	2012
	(In thousands)		
Stock options expense:			
Employees and directors	$ 1,604	$ 1,780	$ 2,162
Consultants	89	86	822
	1,693	1,866	2,984
Restricted stock expense:			
Employees and directors			307
Consultants			58
			365
Total	$ 1,693	$ 1,866	$ 3,349

Stock Options

The Company estimated the fair value of stock options granted in the periods presented using a Black-Scholes option-pricing model utilizing the following assumptions:

	Years Ended December 31,					
	2011			2012		
Volatility	107	113	%	107	115	%
Expected term (in years)	5.0	6.0		5.0	6.0	
Risk-free interest rate	1.1	1.4	%	0.7	0.8	%
Expected dividend yield			%			%
Stock price	$ 8.67			$ 8.67	$34.24	

The common stock price for options granted prior to the IPO was determined based on a valuation of the Company s common stock. For options granted after the IPO, the stock price is the closing price on the date of grant. The risk free interest rate was based on the rate for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected life at the grant date. The expected life for options was based on the simplified method in accordance with SEC Staff Accounting Bulletin Nos. 107 and 110 as the Company does not have sufficient historical exercise data due to the limited period of time the Company s shares have been publicly traded. The expected volatility was estimated based on historical volatility information of peer companies that are publicly available.

For the years ended December 31, 2010, 2011 and 2012, the Company granted options to employees and directors totaling 428,354, 214,962 and 213,991, respectively, with an aggregate fair market value of $3.1 million, $1.5 million and $3.6 million, respectively. For the years ended December 31, 2010, 2011 and 2012, the Company granted options to consultants in the amount of 27,695, 6,056 and 16,441, respectively with an aggregate fair market value of $200,000, $42,000, and $293,000, respectively.

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11. 2003 Stock Incentive Plan and 2012 Stock Plan (continued)

The Company s combined outstanding employee and non-employee option activity for the period from December 31, 2009 through December 31, 2012 is summarized as follows:

	Number of Shares	Weighted Average Exercise Price	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2009	674,537	$ 9.24	$ 380
Granted	456,049	$ 8.67	
Exercised			
Cancelled/forfeited	(2,596)	$ 9.82	
Outstanding at December 31, 2010	1,127,990	$ 9.01	380
Granted	221,018	$ 8.67	
Exercised			
Cancelled/forfeited	(39,644)	$ 8.72	(30)
Outstanding at December 31, 2011	1,309,364	$ 8.98	350
Granted	230,432	$ 20.24	
Exercised			
Cancelled/forfeited	(13,646)	$ 9.26	(63)
Outstanding at December 31, 2012	1,526,150	$ 10.67	$ 35,968

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the underlying options and the deemed fair value of the Company s common stock for those shares that had exercise prices lower than the deemed fair value of the Company s common stock.

The following table summarizes additional information about stock options outstanding:

December 31, 2010						
Options Outstanding				Options Exercisable		
Exercise Price	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)
$2.89	65,766	3.8	$ 380	65,766	3.8	$ 380
$8.67	456,049	9.6		114,003	9.6	

$9.82	454,739	7.3		317,327	6.9	
$10.11	7,787	6.2		7,787	6.2	
$10.41	143,649	7.1		102,144	7.1	
	1,127,990	8.0	$ 380	607,027		$ 380
Options exercisable and expected to become exercisable	1,127,990	8.0	$ 380			

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11. 2003 Stock Incentive Plan and 2012 Stock Plan (continued)

December 31, 2011

Options Outstanding				Options Exercisable		
Exercise Price	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)
$2.89	60,574	2.9	$ 350	60,574	2.9	$ 350
$8.67	671,442	9.0		286,733	8.8	
$9.82	425,912	6.2		375,069	6.1	
$10.11	7,787	5.2		7,787	5.2	
$10.41	143,649	6.1		134,905	6.1	
	1,309,364	7.5	$ 350	865,068		$ 350
Options exercisable and expected to become exercisable	1,309,364	7.5	$ 350			

December 31, 2012

Options Outstanding				Options Exercisable		
Exercise Price	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)	Number of Shares	Weighted-Average Remaining Life	Aggregate Intrinsic Value (In thousands)
$2.89	60,574	1.9	$ 1,899	60,574	1.9	$ 1,899
$8.67	668,374	8.0	17,093	456,467	7.9	11,673
$9.30	15,812	9.6	394	6,909	9.6	172
$9.82	423,316	5.2	10,336	413,802	5.2	10,104
$10.11	7,787	4.2	188	7,787	4.2	188
$10.41	143,649	5.1	3,425	143,649	5.1	3,425
$21.50	206,638	9.9	2,633	6,766	9.9	86
	1,526,150	6.9	35,968	1,095,954		$ 27,547
Options exercisable and expected to become exercisable	1,526,150	6.9	$ 35,968			

As of December 31, 2012, $4.3 million of total unrecognized compensation cost related to unvested stock option grants is expected to be recognized over a weighted-average period of 2.15 years.

Restricted Stock Units

The following table summarizes the aggregate restricted stock activity for the year ended December 31, 2012:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested Shares at December 31, 2011		$
Granted	176,188	$ 17.82
Exercised		
Cancelled/forfeited		$
Non-vested Shares at December 31, 2012	176,188	$ 17.82

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11. 2003 Stock Incentive Plan and 2012 Stock Plan (continued)

As of December 31, 2012, there was $3.6 million of unrecognized compensation expense related to unvested restricted stock, which is expected to be recognized over a weighted average of 3.75 years.

The following table summarizes additional information about restricted stock units outstanding:

	Number of Shares	Issue Price	Intrinsic Value (In thousands)
Employees and directors	158,016	$ 21.50	$ 5,410
Consultants	18,172	$ 21.50	622
Outstanding at December 31, 2012	176,188		$ 6,032

12. QTDP

In 2010, the Company recognized other income related to the Qualifying Therapeutic Discovery Project (QTDP). The QTDP program was created by the United States Congress as part of the Patient Protection and Affordable Care Act and provided for reimbursement of certain costs paid or incurred during 2009 and 2010 directly related to the conduct of a QTDP. During the year ended December 31, 2010, the Company was awarded $489,000 related to this program, which is included in other income in the accompanying statement of operations.

13. Commitment and Contingencies

Facility Leases

The Company leases general and administrative office space in New York, New York and San Diego, California pursuant to non-cancellable operating leases that expire in November 2013 and in December 2014, respectively. In March 2013, the Company entered into an amendment to the lease for its San Diego office, which, among other things, added approximately 5,100 square feet of space and extended the term of the existing lease. The lease for the San Diego office, as amended, will expire in December 2015. In addition, the Company leased office and research space in Perugia, Italy pursuant to a euro denominated operating lease that expired in July 2012. The terms of the leases provide for rental payments on a graduated scale, and the Company recognizes rent expense on a straight-line basis over the non-cancellable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability included in accrued expenses. The Company is required to pay its share of operating expenses, such as property taxes and building costs, and these amounts are not included in rent expense or minimum operating lease payments below. Rent expense under operating leases for facilities for the years ended December 31, 2010, 2011 and 2012, was approximately $299,000, $291,000 and $332,000, respectively. As of

December 31, 2012, minimum operating lease payments under non-cancelable leases (as amended) are as follows:

Year Ending December 31,	Amount (In thousands)
2013	$ 331
2014	213
Total future minimum operating lease payments	$ 544

Contingencies

The Company may become subject to claims and assessments from time to time in the ordinary course of business. Such matters are subject to uncertainties and outcomes are not predictable with assurance. The Company accrues liabilities for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. As of December 31, 2010, 2011 and 2012, the Company does not believe that any such matters, individually or in the aggregate, will have a material adverse effect on the Company s business, financial condition, results of operations or cash flows.

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14. Related Party Transactions

During 2008, the Company retained the services of Jim Mervis, who at the time served as chairman of the board of directors, to assist with business development, resulting in general and administrative expense of $173,000 in 2008, which is included in the Company s cumulative results for the period from September 4, 2002 (inception) through December 31, 2012.

15. Net Loss Per Share

The following table presents the historical computation of basic and diluted net loss per share:

	Years Ended December 31,		
	2010	2011	2012
	(In thousands, except share and per share amounts)		
Historical net loss per share			
Numerator:			
Net loss attributable to common stockholders	$(17,989)	$(15,738)	$(46,274)
Denominator:			
Weighted average shares outstanding, basic and diluted	3,329,666		