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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2013

OR

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

For the transition period from to

Commission File Number 001-34620

IRONWOOD PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**04-3404176**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)
301 Binney Street Cambridge, Massachusetts	**02142**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(617) 621-7722**

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

Title of each class	**Name of each exchange on which registered**
Class A common stock, $0.001 par value	The NASDAQ Stock Market LLC (NASDAQ Global Select Market)

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

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

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

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

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the Registrant was required to submit and post such files). Yes ☒ No ☐

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

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

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

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

Aggregate market value of voting stock held by non-affiliates of the Registrant as of June 30, 2013: $1,108,219,339

As of January 28, 2014, there were 103,113,155 shares of Class A common stock outstanding and 18,360,454 shares of Class B common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2014 Annual Meeting of Stockholders are incorporated by reference into Part III of this report.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contains forward-looking statements. All statements contained in this Annual Report on Form 10-K other than statements of historical fact are forward-looking statements. Forward-looking statements include statements regarding our future financial position, business strategy, budgets, projected costs, plans and objectives of management for future operations. The words "may," "continue," "estimate," "intend," "plan," "will," "believe," "project," "expect," "seek," "anticipate" and similar expressions may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, among other things, statements about:

- the market potential for LINZESS® (linaclotide) in the United States, or the U.S., and CONSTELLA® (linaclotide) in the European Union, or the E.U.;
- the timing, investment and associated activities involved in commercializing LINZESS by us and Forest Laboratories, Inc. in the U.S., including an expanded direct-to-consumer education program;
- the timing and execution of the launches and commercialization of CONSTELLA in the E.U.;
- the timing, investment and associated activities involved in developing and commercializing linaclotide by us and our partners worldwide;
- the ability of our partners and third-party manufacturers to manufacture and distribute sufficient amounts of linaclotide on a commercial scale;
- our expectations regarding U.S. and foreign regulatory requirements, including our post-approval, nonclinical and clinical post-marketing plan with the Food and Drug Administration, or the FDA, to understand linaclotide's efficacy and safety in pediatric patients;
- our partners' ability to obtain foreign regulatory approval of linaclotide and the ability of all of our product candidates to meet existing or future regulatory standards;
- the safety profile and related adverse events of linaclotide and our product candidates;
- the therapeutic benefits and effectiveness of linaclotide and our product candidates;
- our ability to obtain and maintain intellectual property protection for linaclotide and our product candidates;
- the ability of our partners to perform their obligations under our collaboration and license agreements with them;
- our plans with respect to the development, manufacture or sale of our product candidates, as well as the in-licensing or acquisition of externally discovered programs;
- our expectations as to future financial performance, expense levels, capital raising and liquidity sources;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with our products and product candidates;
- the status of government regulation in the life sciences industry, particularly with respect to healthcare reform;
- trends and challenges in our potential markets;
- our ability to attract and motivate key personnel; and
- other factors discussed elsewhere in this Annual Report on Form 10-K.

Any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. These forward-looking statements may be affected by inaccurate assumptions or by known or unknown risks and uncertainties, including the risks, uncertainties and assumptions identified under the heading "Risk Factors" in this Annual Report on Form 10-K. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not occur as contemplated, and actual results could differ materially from those anticipated or implied by the forward-looking statements.

You should not unduly rely on these forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K. Unless required by law, we undertake no obligation to publicly update or revise any forward- looking statements to reflect new information or future events or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the United States Securities and Exchange Commission, or the SEC, after the date of this Annual Report on Form 10-K.

NOTE REGARDING TRADEMARKS

TABLE OF CONTENTS

PART I

Item 1. *Business*

Our Company

We are an entrepreneurial pharmaceutical company focused on creating medicines that make a difference for patients, building value to earn the continued support of our fellow shareholders, and empowering our team to passionately pursue excellence. If we do these things well, we hope to earn the right to continue doing them and, one step at a time, build an enduring pharmaceutical company that helps patients lead better lives.

Our core strategy is to establish a leading gastrointestinal, or GI, therapeutics company, leveraging our development and commercial capabilities in addressing GI disorders as well as our pharmacologic expertise in guanylate cyclase, or GC, pathways. This expertise is based on our work advancing our lead product, linaclotide, which is the first, and to date, only product approved by the U.S. Food and Drug Administration, or FDA, in a new class of GI medicines called guanylate cyclase type-C, or GC-C, agonists. Linaclotide is available to adult men and women suffering from irritable bowel syndrome with constipation, or IBS-C, or chronic idiopathic constipation, or CIC, in the United States under the trademarked name LINZESS, and to adult men and women suffering from IBS-C in the European Union, or the E.U., under the trademarked name CONSTELLA. Linaclotide is also being developed in other parts of the world by certain of our partners. We are exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. In addition to linaclotide-based opportunities, we are advancing multiple GI development programs as well as further leveraging our GC expertise to advance a second GC program targeting soluble guanylate cyclase, or sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

For the foreseeable future, we intend to play an active role in the commercialization of our products in the U.S., and to establish a strong global brand by out-licensing commercialization rights in other territories to high-performing partners. We believe in the long-term value of our drug candidates, so we seek collaborations that provide meaningful economics and incentives for us and any potential partner. Furthermore, we seek partners who share our values, culture, processes and vision for our products, which we believe will enable us to work with those partners successfully for the entire potential patent life of our drugs.

Linaclotide

Linaclotide provides patients and healthcare practitioners with a treatment option for IBS-C and CIC, GI disorders that affect millions of sufferers worldwide, according to our analysis of studies performed by N.J. Talley (published in 1995 in the *American Journal of Epidemiology*), P.D.R. Higgins (published in 2004 in the *American Journal of Gastroenterology*) and A.P.S. Hungin (published in 2003 in *Alimentary Pharmacology and Therapeutics*) as well as 2007 U.S. census data.

Ironwood has been pursuing the development of linaclotide since its discovery by our scientists in 2003. In August 2012, the FDA approved LINZESS as a once-daily treatment for adult men and women suffering from IBS-C or CIC. LINZESS is being commercialized in the U.S. by us and our collaboration partner, Forest Laboratories, Inc., or Forest. We and Forest began commercializing LINZESS in the U.S. in December 2012.

In November 2012, the European Commission granted marketing authorization to CONSTELLA for the symptomatic treatment of moderate to severe IBS-C in adults. Our European partner, Almirall S.A., or Almirall, has exclusive marketing rights for CONSTELLA in Europe (including the

Commonwealth of Independent States and Turkey). Currently, CONSTELLA is commercially available in certain European countries, including the United Kingdom and Germany.

In December 2013, the Health Canada granted approval of CONSTELLA as a once-daily, first-in-class treatment for adult women and men suffering from IBS-C or CIC. Forest has exclusive rights to develop and commercialize linaclotide in Canada.

Beyond our efforts in the U.S., Europe and Canada, we and our partners continue to advance linaclotide in other parts of the world. Astellas Pharma Inc., or Astellas, our partner in Japan, recently completed a double-blind, placebo-controlled, dose-ranging Phase II clinical trial of linaclotide in adult patients with IBS-C. In February 2014, Ironwood received preliminary top level data for the Phase II trial from Astellas indicating that, while all linaclotide dose groups showed numerically higher responder rates in the primary endpoint than placebo, the responder rates were not statistically significant compared to placebo in this study. Linaclotide was well tolerated in all dose groups in this study. Data analysis is still ongoing at Astellas to determine next steps. In the third quarter of 2013, we and AstraZeneca AB, or AstraZeneca, our partner in China, Hong Kong and Macau, initiated a double-blind, placebo-controlled Phase III clinical trial of linaclotide in adult patients with IBS-C. We continue to assess alternatives to bring linaclotide to IBS-C and CIC sufferers in the parts of the world outside of our partnered territories.

We are also exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions.

Upon FDA-approval of LINZESS in the U.S., we received five years of exclusivity under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. In addition, LINZESS is covered by a U.S. composition of matter patent that expires in 2024, subject to possible patent term extension to 2026. Linaclotide is also covered by E.U. and Japanese composition of matter patents, both of which expire in 2024, subject to possible patent term extension.

Linaclotide Partners

We have pursued a partnering strategy for commercializing linaclotide that has enabled us to retain significant oversight over linaclotide's development and commercialization worldwide, share the costs with collaborators whose capabilities complement ours, and retain a significant portion of linaclotide's future long-term value. As of December 31, 2013, licensing fees, milestones, royalties and related equity investments from our linaclotide partners totaled approximately $359.0 million. In addition, we and Forest jointly fund the development and commercialization of LINZESS in the U.S., sharing equally in any net profits or losses, and we and AstraZeneca jointly fund the development and commercialization of linaclotide in China, with AstraZeneca receiving 55% of the net profits or net losses until a specified commercial milestone is achieved, at which point the net profits or losses are shared equally. Such reimbursements for our development and commercialization costs received from Forest or AstraZeneca are excluded from the amount above.

In September 2007, we entered into a collaboration agreement with Forest to develop and commercialize linaclotide in North America. Under the terms of the collaboration agreement, we and Forest are jointly and equally funding the development and commercialization of LINZESS in the U.S., with equal share of any profits or losses. Additionally, we granted Forest exclusive rights to develop and commercialize linaclotide in Canada and Mexico in which we receive royalties in the mid-teens percent on net sales in those countries. In September 2012, Forest sublicensed its commercialization rights in Mexico to Almirall. If linaclotide is successfully commercialized in the U.S., total licensing, milestone payments and related equity investments to us under the Forest collaboration agreement could total up to $330 million, including the $205 million that Forest has already paid to us in license fees and

development-related milestones and the $25 million of our capital stock that Forest has already purchased.

In April 2009, we entered into a license agreement with Almirall to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States and Turkey). In June 2013, we and Almirall amended our license agreement to, among other things, expand the milestone payments payable to us to now include both launch-related and certain sales-related milestones and to adjust the royalty structure. As a result, if linaclotide is successfully commercialized in the Almirall territory, total licensing, milestone payments and related equity investments to us could now total up to $118 million, including the $57 million, net of foreign withholding taxes, that Almirall has already paid to us in development-related milestones, the $15 million of our capital stock that Almirall has already purchased, and the $1.9 million in milestone payments from Almirall related to the commercial launches in the United Kingdom and Germany. Almirall will pay us gross royalties based on sales volume in the Almirall territory, beginning in the low-twenties percent and escalating to the mid-forties percent through April 2017, and thereafter beginning in the mid-twenties percent and escalating to the mid-forties percent at lower sales thresholds than in the period through April 2017. In each case, these royalty payments are reduced by the transfer price paid for the active pharmaceutical ingredient, or API, included in the product actually sold in the Almirall territory and other contractual deductions.

In November 2009, we entered into a license agreement with Astellas to develop and commercialize linaclotide in Japan, South Korea, Taiwan, Thailand, the Philippines and Indonesia. As a result of an amendment to the license agreement executed in March 2013, we regained rights to linaclotide in South Korea, Taiwan, Thailand, the Philippines and Indonesia. If linaclotide is successfully developed and commercialized in the Astellas territory, total licensing and milestone payments to us could total up to $75 million, including the $30 million that has already been paid to us. If Astellas receives approval to market and sell linaclotide, Astellas will pay us gross royalties which escalate based on sales volume in the Astellas territory, beginning in the low-twenties percent, less the transfer price paid for the API included in the product actually sold in the Astellas territory and other contractual deductions.

In October 2012, we entered into a collaboration with AstraZeneca to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau. Under the terms of the agreement, we and AstraZeneca are jointly funding the development and commercialization of linaclotide in China, Hong Kong and Macau, with AstraZeneca receiving 55% of the net profits or incurring 55% of the net losses until a certain specified commercial milestone is achieved, at which time profits or losses will be shared equally thereafter. If linaclotide is successfully developed and commercialized in China, total licensing and milestone payments to us under the collaboration agreement could total up to $150 million, including the $25 million that AstraZeneca has already paid to us. As part of the collaboration, Ironwood's sales force is promoting AstraZeneca's NEXIUM® (esomeprazole magnesium), one of AstraZeneca's products, in the U.S. This co-promotion arrangement is expected to end in May 2014.

We have retained all rights to linaclotide outside of the territories discussed above and continue to evaluate partnership opportunities in those unpartnered regions.

Pipeline

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. Through the discovery, development and commercialization of linaclotide, we have gained strong development and commercialization capabilities in GI disorders as well as pharmacologic expertise in GC pathways. Our internal research and development efforts are focused on leveraging this expertise to establish a leading GI therapeutics company. As such, we are advancing multiple GI development programs with

opportunities to generate proof of concept data. We are also leveraging our GC expertise to advance a second GC program targeting sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

We are also actively engaged in evaluating and licensing rights to externally discovered drug candidates at all stages of development that fit within our core strategy. In evaluating potential assets, we apply the same investment criteria whether the assets are internally or externally discovered.

In order to successfully grow our business, we will need to overcome the enormous challenges inherent in the pharmaceutical product development model. Developing a novel therapeutic agent can take a decade or more and cost hundreds of millions of dollars, and most drug candidates fail to reach the market profitably. We recognize that most companies undertaking this endeavor fail, yet despite the significant risks and our own experiences with multiple failed drug candidates, we are enthusiastic and passionate about our mission to create medicines that make a difference for patients. To achieve our mission, we continue to build a team, a culture and processes centered on creating and marketing important new drugs. If we are successful getting medicines to patients and generating substantial returns for our stockholders, we will continue to reinvest a portion of our future cash flows into our research and development efforts in order to accelerate and enhance our ability to bring new products to market.

We were incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc.

Owner-related Business Principles

We encourage all current and potential stockholders to read the owner-related business principles below that guide our overall strategy and decision making.

1. Ironwood's stockholders own the business; all of our employees work for them.

Each of our employees also has equity in the business, aligning their interests with their fellow stockholders. As employees and co-owners of Ironwood, our management and employee team seek to effectively allocate scarce stockholder capital to maximize the average annual growth of per share value.

Through our policies and communication, we seek to attract like-minded owner-oriented stockholders. We strive to effectively communicate our views of the business opportunities and risks over time so that entering and exiting stockholders are doing so at a price that approximately reflects our intrinsic value.

2. We believe we can best maximize long-term stockholder value by building a great pharmaceutical franchise.

We believe that Ironwood has the potential to deliver outstanding long-term returns to stockholders who are sober to the risks inherent in the pharmaceutical product lifecycle and to the potential dramatic highs and lows along the way, and who focus on superior long-term, per share cash flows.

Since the pharmaceutical product lifecycle is lengthy and unpredictable, we believe it is critical to have a long-term strategic horizon. We work hard to embed our long-term focus into our policies and practices, which may give us a competitive advantage in attracting like-minded stockholders and the highest caliber employees. Our current and future employees may perceive both financial and qualitative advantages in having their inventions or hard work result in marketed drugs that they and

their fellow stockholders continue to own. Some of our key policies and practices that are aligned with this imperative include:

a. Our dual class equity voting structure (which provides for super-voting rights of our pre-IPO stockholders only in the event of a change of control vote) is designed to concentrate change of control decisions in the hands of long-term focused owners who have a history of experience with us.

b. Compensation is weighted to equity over salary for all of our employees, and many employees have a significant portion of their incentive compensation in milestone-based equity grants that reward achievement of major value-creating events a number of years out from the time of grant.

c. We have adopted a change of control severance plan for all of our employees that is intended to encourage them to bring forward their best ideas by providing them with the comfort that if a change of control occurs and their employment is terminated, they will still have an opportunity to share in the economic value that they have helped create for stockholders.

d. All of the members of our board of directors are substantial investors in the company. Furthermore, each director is required to hold all shares of stock acquired as payment for his or her service as a director throughout his or her term on the board.

e. Our partnerships with Forest, Almirall, Astellas and AstraZeneca all include standstill agreements, which serve to protect us from an unwelcome acquisition attempt by one of our partners. In addition, we have change of control provisions in our partnership agreements in order to protect the economic value of linaclotide should the acquirer of one of our partners be unable or unwilling to devote the time and resources required to maximize linaclotide's benefit to patients in their respective territory.

3. We are and will remain careful stewards of our stockholders' capital.

We work intensely to allocate capital carefully and prudently, continually reinforcing a lean, cost-conscious culture.

While we are mindful of the declining productivity and inherent challenges of pharmaceutical research and development, we intend to invest in discovery and development research for many years to come. Our singular passion is to create, develop and commercialize novel drug candidates, seeking to integrate the most successful drugmaking and marketing practices of the past and the best of today's cutting-edge technologies and basic research, development and commercialization advances.

While we hope to improve the productivity and efficiency of our drug creation efforts over time, our discovery process revolves around small, highly interactive, cross-functional teams. We believe that this is one area where our relatively small size is a competitive advantage, so for the foreseeable future, we do not expect our drug discovery team to grow beyond 100-150 scientists. We will continue to prioritize constrained resources and maintain organizational discipline. Once internally- or externally-derived candidates advance into development, compounds follow careful stage-gated plans, with further advancement depending on clear data points. Since most pharmaceutical research and development projects fail, it is critical that our teams are rigorous in making early go/no go decisions, following the data, terminating unsuccessful programs, and allocating scarce dollars and talent to the most promising efforts, thus enhancing the likelihood of late phase development success.

Our global operations and commercial teams take a similar approach to capital allocation and decision-making. By establishing redundancy at each critical node of the linaclotide global supply chain, our global operations team is mitigating against a fundamental risk inherent with pharmaceuticals—unanticipated shortages of commercial product. Likewise, we have established a commercial

organization dedicated to bringing innovative, highly-valued healthcare solutions to all of our customers. Our commercial organization works closely and methodically with our global commercialization partners, striving to maximize linaclotide's commercial potential through focused efforts aimed at educating patients, payers and healthcare providers.

4. Our financial goal is to maximize long-term per share cash flows.

Our goal is to maximize long-term cash flows per share, and we will prioritize this even if it leads to uneven short-term financial results. If and when we become profitable, we expect and accept uneven earnings growth. Our underlying product development model is risky and unpredictable, and we have no intention to advance marginal development candidates or consummate suboptimal in-license transactions in an attempt to fill anticipated gaps in revenue growth. Successful drugs can be enormously beneficial to patients and highly profitable and rewarding to stockholders, and we believe strongly in our ability to occasionally (but not in regular or predictable fashion) create and commercialize great medicines that make a meaningful difference in patients' lives.

If and when we reach profitability, we do not intend to issue quarterly or annual earnings guidance, however we plan to continue to be transparent about the key elements of our performance, including near-term operating plans and longer-term strategic goals.

Our Strategy

Our mission is to create medicines that make a difference for patients, build value to earn the continued support of our fellow shareholders, and empower our team to passionately pursue excellence. Our core strategy to achieve this mission is to establish a leading GI therapeutics company leveraging our development and commercial capabilities in addressing GI disorders as well as our pharmacologic expertise in GC pathways. Key elements of our strategy include:

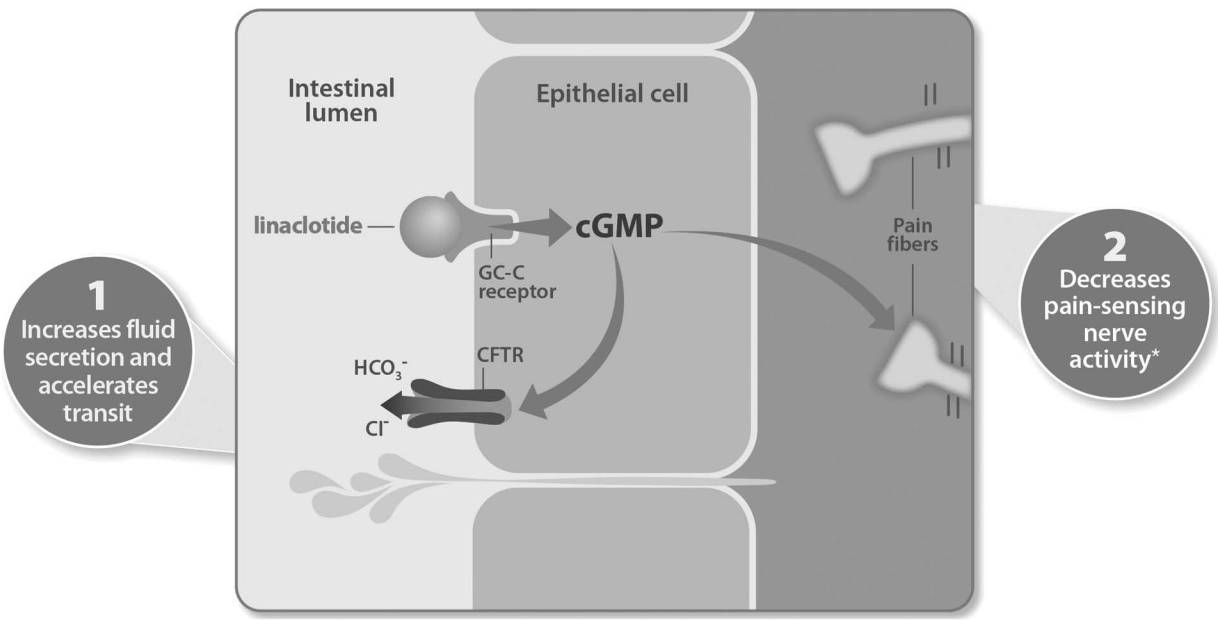
- attracting and incentivizing a team with a singular passion for creating, developing and commercializing medicines that can make a significant difference in patients' lives;
- solidifying and expanding our position as the leader in the field of GC-C agonists;
- successfully and profitably commercializing LINZESS in collaboration with Forest in the U.S.;
- leveraging our commercial capabilities across marketing, reimbursement, patient engagement and sales;
- supporting our global partners to commercialize linaclotide outside of the U.S.;
- harvesting the maximum value of linaclotide outside of our currently partnered territories;
- exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions;
- investing in our pipeline of novel GI product candidates and advancing a second GC program targeting sGC;
- evaluating candidates outside of the company for in-licensing or acquisition opportunities;
- maximizing the commercial potential of our drugs and playing an active role in their commercialization or find partners who share our vision, values, culture and processes; and
- executing our strategy with our stockholders' long-term interests in mind by seeking to maximize long-term per share cash flows.

Linaclotide

In August 2012, LINZESS became the first and only guanylate GC-C agonist approved by the FDA for the treatment of both IBS-C and CIC in adults. Linaclotide is a promising treatment for patients suffering from both abdominal pain associated with IBS-C and constipation symptoms associated with both IBS-C and CIC. In four Phase III clinical trials of more than 2,800 adult patients, linaclotide was demonstrated to reduce abdominal pain and constipation associated with IBS-C, as well as constipation, infrequent bowel movements, incomplete evacuation and hard stools associated with CIC. Improvements were reported in the first week of treatment and maintained throughout the 12-week treatment period. Additionally, patients reported symptoms returned within one week after discontinued use of linaclotide. LINZESS is marketed by us and Forest.

In November 2012, CONSTELLA became the first and only medicine approved by the European Commission for the symptomatic treatment of moderate to severe IBS-C in adults in the E.U. CONSTELLA is a once-daily capsule that improves abdominal pain/discomfort, bloating and constipation associated with IBS-C. CONSTELLA is described as a GC-C agonist with visceral analgesic and secretory activities in the product label for European use and CONSTELLA is marketed in certain European countries, including the United Kingdom and Germany, by our European partner, Almirall.

Linaclotide is a 14 amino acid peptide agonist of GC-C, a receptor found on the luminal surface of the intestinal epithelium. As the figure below shows, activation of GC-C results in an increase of intracellular and extracellular cyclic guanosine monophosphate, or cGMP, which, based on nonclinical studies, is believed to act in two ways. First, elevation in intracellular cGMP stimulates secretion of chloride and bicarbonate into the intestinal lumen, mainly through activation of the cystic fibrosis transmembrane conductance regulator, or CFTR, ion channel, resulting in increased intestinal fluid and accelerated transit. Second, elevation in extracellular cGMP was shown to decrease the activity of pain-sensing nerves. The clinical relevance of the effects on pain-sensing nerves seen in nonclinical studies has not been established.



* Clinical relevance of the effect on pain fibers in nonclinical studies has not been established.

Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC)

IBS-C and CIC are chronic, functional GI disorders that afflict millions of sufferers worldwide. IBS-C and CIC are characterized by frequent and bothersome symptoms that dramatically affect patients' daily lives. Symptoms of IBS-C include abdominal pain, discomfort or bloating and constipation symptoms (*e.g.* incomplete evacuation, infrequent bowel movements, hard/lumpy stools), while CIC is primarily characterized by constipation symptoms. Previously available treatment options primarily improved constipation, leading healthcare providers to diagnose and manage IBS-C and CIC based on stool frequency. However, patients view these conditions as multi-symptom disorders, and while laxatives can be effective at relieving constipation symptoms, they do not necessarily improve abdominal pain, discomfort or bloating, and can often exacerbate these symptoms. This disconnect between patients and physicians, amplified by patients' embarrassment to discuss all of their GI symptoms, often delays diagnosis and may compromise treatment, possibly causing additional suffering and disruption to patients' daily activities.

Based on the Talley and Higgins studies, and 2007 U.S. census data, we estimate that in 2007, approximately 35 million to 46 million people in the U.S. suffered from symptoms of IBS-C or CIC, of whom between 9 million to 15.5 million patients sought medical care. As a result of the less than optimal treatment options previously available, patients seeking care experienced a very low level of satisfaction. Due to patients' lack of satisfaction with existing treatment options, about 70% of patients stop prescription therapy within one month, according to IMS Health. It is estimated that patients seek medical care from five or more different healthcare providers over the course of their illness with limited or no success, as shown in a 2009 study by D.A. Drossman in the *Journal of Clinical Gastroenterology*. Many of the remaining patients are too embarrassed to discuss the full range of their symptoms, or for other reasons do not see the need to seek medical care and continue to suffer in silence while unsuccessfully self-treating with fiber, OTC laxatives and other remedies which improve constipation, but often exacerbate pain and bloating.

We believe that the prevalence rates of IBS-C in Europe, China and Japan are similar to the prevalence rates in the U.S.

Competition

By the time patients seek care from a physician, they have typically tried a number of available remedies and remain unsatisfied. Most IBS-C and CIC patients initially attempt self-treatment with over the counter medications such as laxatives, stool softeners or fiber supplementation, as well as attempts to modify their diet. While some of these therapies offer limited success in transit-related symptoms, they offer little to no effect on other bothersome symptoms from which patients are suffering. Prior to approval of LINZESS, physicians had very limited treatment options beyond what is readily available to the patient alone. Physicians typically relied on fiber and laxatives, which can exacerbate bloating and abdominal pain, the same symptoms from which many patients are seeking relief and which are the most troubling to treat. In an attempt to help alleviate the more severe abdominal symptoms associated with IBS-C and CIC, healthcare providers have occasionally prescribed medications that have not been approved by the FDA for these indications, such as anti-depressant or antispasmodic agents.

Polyethylene glycol, or PEG (such as MiraLAX), and lactulose account for the majority of prescription laxative treatments. Both agents demonstrate an increase in stool frequency and consistency but do not improve bloating or abdominal discomfort. Clinical trials and product labels document several adverse effects with PEG and lactulose, including exacerbation of bloating, cramping and, according to L.E. Brandt in a study published in 2005 in the *American Journal of Gastroenterology*, up to a 40% incidence of diarrhea. Overall, up to 75% of patients taking prescription laxatives report not being completely satisfied with the predictability of when they will experience a bowel movement on treatment, and 50% were not completely satisfied with relief of the multiple symptoms associated with constipation, according to the J.F. Johanson study published in 2007 in *Alimentary Pharmacology & Therapeutics*.

In 2002, the FDA approved Zelnorm® (tegaserod), the first new drug for the treatment of IBS-C, and in 2004, Zelnorm was approved for the treatment of CIC. Zelnorm is a serotonin 5-HT4 receptor agonist, with a mechanism of action completely separate and distinct from the mechanism of action underlying linaclotide's activity. As a newly available treatment option to potentially address some of the symptoms beyond the scope of laxatives and fiber, Zelnorm achieved great success in raising patient and physician awareness of IBS-C and CIC. During the five years that Zelnorm was promoted, total prescriptions in the category grew three fold, and in 2006, there were more than 16 million total prescriptions written for treating patients with IBS-C and CIC, according to IMS Health. In 2006, Zelnorm total sales were approximately $561 million. In 2007, Zelnorm was withdrawn from the market by its manufacturer due to an analysis that found a higher chance of heart attack, stroke and chest pain in patients treated with Zelnorm as compared to placebo. Despite modest effectiveness relieving abdominal pain (1% to 10% of patients responding to treatment as compared to placebo) and bloating (4% to 11% of patients responding to treatment as compared to placebo) as described on the Zelnorm product label, Zelnorm succeeded in establishing a symptom-based approach highlighting the need to recognize and treat, on a chronic basis, both the abdominal and constipation symptoms afflicting these patients.

Until the launch of LINZESS, the only available prescription therapy for IBS-C and CIC in the U.S. was Amitiza® (lubiprostone), which was approved for the treatment of CIC in 2006, for the treatment of IBS-C in 2008, and for the treatment of opioid-induced constipation in 2013.

Resolor (prucalopride) is available solely in Europe for the treatment of CIC. Resolor was approved in 2009 by the EMA and is indicated for the symptomatic treatment of CIC in women for whom laxatives have failed to provide adequate relief. Resolor, which is marketed by Shire-Movetis, is a serotonin 5-HT4 receptor agonist like Zelnorm. Resolor was launched in other European nations in 2012 and recently completed Phase III trials as a potential treatment for CIC in males. Shire has acquired rights to develop and commercialize prucalopride in the U.S. Resolor is not currently approved for use in the U.S. The U.S. patent covering the composition of matter expires in 2015.

Manufacturing and Supply

We currently manage our global supply and distribution of linaclotide through a combination of contract manufacturers and collaboration partners. It is our objective to produce safe and effective medicine on a worldwide basis, with redundancy built into critical steps of the process. We believe that we have sufficient in-house expertise to manage our manufacturing and supply chain network to meet worldwide demand.

Linaclotide production consists of three phases—manufacture of the active pharmaceutical ingredient, or API (sometimes referred to as drug substance), manufacture of drug product and manufacture of finished goods. We have entered into agreements with multiple third party manufacturers for the production of linaclotide API, as it is an objective of our strategy to establish redundancy at critical steps in the supply chain. We continue to pursue additional commercial supply agreements with additional manufacturers for linaclotide API for U.S. and worldwide use. We believe our commercial suppliers will have the capabilities to produce linaclotide API in accordance with current good manufacturing practices, or GMP, on a sufficient scale to meet our development and commercial needs.

Each of Forest, Almirall and Astellas is responsible for drug product manufacturing of linaclotide and finished goods (including bottling and packaging) for its respective territory, and distributing the finished goods to wholesalers. We are responsible for drug product manufacturing and finished goods for China, Hong Kong and Macau as part of our collaboration with AstraZeneca. We also have an agreement with an additional independent third party to provide an additional source of drug product manufacturing of linaclotide for our partnered territories. We are working with our partners to ensure

we will have sufficient redundancy in this component of the linaclotide supply chain, which includes obtaining the necessary regulatory approval for such drug product manufacturer to be included in the marketing authorization in the relevant country.

Prior to linaclotide, there was no precedent for long-term room temperature shelf storage formulation for an orally dosed peptide to be produced in millions of capsules per year. Our efforts to date have led to a formulation that is both cost effective and able to meet the stability requirements for commercial pharmaceutical products. Our work in this area has created an opportunity to seek additional intellectual property protection around the linaclotide program. In conjunction with Forest, we have filed patent applications worldwide to protect the current commercial formulation of linaclotide as well as related formulations. If these patents are issued, they would expire in 2029 or later in the U.S. and foreign jurisdictions and would be eligible for potential patent term adjustments or patent term extensions in countries where such extensions may be available.

Sales and Marketing

For the foreseeable future, we intend to develop and commercialize our drugs in the U.S. alone or with partners, and expect to rely on partners to commercialize our drugs in territories outside the U.S. In executing our strategy, our goal is to retain significant worldwide oversight over the development process and commercialization of our products, by playing an active role in their commercialization or finding partners who share our vision, values, culture and processes.

We have built our commercial capabilities, including marketing, reimbursement, patient engagement and sales, around linaclotide, with the intent to leverage these capabilities for future products. To date, we have established a high-quality commercial organization dedicated to bringing innovative, highly-valued healthcare solutions to our customers, including patients, payers, and healthcare providers.

We are coordinating efforts with all of our partners to ensure that we launch an integrated, global linaclotide brand. By leveraging the knowledge-base and expertise of our experienced commercial team and the insights of each of our linaclotide commercialization partners, we continually improve our collective marketing strategies.

Maximizing the Value of Linaclotide in the U.S.

Our objective is to establish LINZESS as the prescription product of choice for both IBS-C and CIC. We, together with our U.S. commercialization partner Forest, are building awareness that patients suffer from multiple, highly bothersome symptoms of IBS-C or CIC.

Forest has demonstrated the ability to successfully launch innovative products, penetrate primary care markets and drive the growth of multiple brands in highly competitive markets. Forest brings large and experienced sales, national accounts, trade relations, operations and management teams providing ready access to primary care offices and key managed care accounts. Complementing Forest's expertise, we have built strong commercial capabilities across marketing, reimbursement, patient engagement and sales. We have strong alignment with Forest and a shared vision for LINZESS. The combined Ironwood and Forest marketing team possesses a deep understanding of gastroenterology and primary care customers, and we continue to utilize this knowledge to develop a compelling medical message and promotional campaign in the hope of delivering an effective treatment for patients suffering with the defining symptoms of IBS-C or CIC.

In order to continue to maximize the value of LINZESS in the U.S., we and Forest are focusing our commercialization efforts in the following areas:

- Physician education: Our physician education plan encompasses efforts to reach out to the highest prescribing primary care physicians and gastroenterologists in the U.S., with the goal of

helping them identify appropriate patients, educating them on the clinical profile of LINZESS, and enabling them to assess the clinical benefits of LINZESS.

- Patient education: Our patient education plan encompasses efforts to reach out to IBS-C and CIC patients through direct-to-consumer education, including both traditional and digital channels, to enable them to more effectively communicate symptoms and treatment history to their physicians. Based on our research to date, these patients are high information seekers, pursuing multiple information channels in order to learn about the disease state and potential therapies in order to have productive conversations with their doctors.
- Payer value proposition: Based on the existing burden of illness associated with IBS-C and CIC, and the efficacy and safety profile of LINZESS that was demonstrated through its clinical development program, we and Forest are providing a strong value proposition to governmental authorities, private health insurers and other third-party payers. We understand that sufficient access and reasonable reimbursement are essential in order to optimize the commercial potential of LINZESS.

Maximizing the Value of Linaclotide Outside the U.S.

We have out-licensed commercialization rights for Canada and Mexico to Forest, Europe to Almirall and Japan to Astellas. In September 2012, Forest sublicensed the commercialization rights in Mexico to Almirall. We have also partnered with AstraZeneca to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau.

Almirall provides access to the highest potential European markets with an established direct presence in each of the United Kingdom, Italy, France, Germany and Spain, and also has a presence in Austria, Belgium, the Nordics, Poland, Portugal and Switzerland. Almirall is coordinating sales and marketing efforts from its central office in an effort to ensure consistency of the overall brand strategy and objectively assess performance. We believe Almirall's knowledge of the local markets is helping to facilitate regulatory access, reimbursement and market penetration through a customized approach to implementing promotional and selling campaigns in the E.U.

Astellas is one of Japan's largest pharmaceutical companies and has top commercial capabilities in both primary care and specialty categories throughout Asia. Their demonstrated ability to market innovative medicines and their growing GI franchise in Japan make them an ideal partner for Ironwood.

AstraZeneca is a world leader in GI disease medicine and operates in over 100 countries with a growing presence in emerging markets, including China where they have significant commercial and research and development capabilities. We believe that we and AstraZeneca are strongly aligned with our vision for linaclotide in this region.

We have retained all rights to linaclotide outside of the territories discussed above and we continue to evaluate partnership opportunities in those unpartnered regions.

Pipeline Strategy

Patients shape our business, so we seek to incorporate their influence into our drug-making process, from discovery through commercialization, in an effort to better understand and address their needs. We invest significant effort defining and refining our research and development process and teaching internally our approach to drug-making. We favor programs with early decision points, well validated targets, predictive nonclinical models, initial chemical leads and clear paths to approval, all in the context of a target product profile that can address significant unmet or underserved clinical needs. We emphasize data-driven decision making, strive to advance or terminate projects early based on clearly defined go/no go criteria, prioritize programs at all stages and fluidly allocate our capital to the

most promising programs. We continue to work diligently to ensure this disciplined approach is ingrained in our culture and processes and expect that our research productivity will continue to improve as our team gains more experience and capabilities. Moreover, we hope that as our passion and style of drug-making becomes better validated and more widely known, we will be able to attract additional like-minded researchers to join our cause.

To date, almost all of our product candidates have been discovered internally. We believe our discovery team has created a number of promising candidates over the past few years and has developed an extensive intellectual property estate in each of these areas.

In addition we have in-licensed, and are actively seeking to identify additional, attractive external opportunities. We utilize the same critical filters for investment when evaluating external programs as we do with our own, internally-discovered candidates.

Pipeline

We have ongoing efforts to identify product candidates that leverage our development and commercial expertise in an effort to establish a leading GI therapeutics company. Millions of patients suffer from highly symptomatic disorders of the upper or lower GI tract and many of these patients are actively seeking care and new treatment options. Linaclotide is our only product candidate that has demonstrated clinical proof of concept. Through the discovery, development and commercialization of linaclotide, however, we have gained strong development and commercial capabilities in addressing GI disorders as well as pharmacologic expertise in GC pathways. In addition to working to maximize the utility of linaclotide, we are advancing multiple GI development programs as well as further leveraging our GC expertise to advance a second GC program targeting sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

Patents and Proprietary Rights

We actively seek to protect the proprietary technology that we consider important to our business, including pursuing patents that cover our products and compositions, their methods of use and the processes for their manufacture, as well as any other relevant 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 success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technology, inventions and improvements we consider important to our business; defend our patents; preserve the confidentiality of our trade secrets; and operate without infringing the patents and proprietary rights of third parties.

Linaclotide Patent Portfolio

Our linaclotide patent portfolio is currently composed of eight issued U.S. patents, three granted European patents (each of which has been validated in 31 European countries), a granted Japanese patent, 22 issued patents in other foreign jurisdictions, and numerous pending provisional, U.S. non-provisional, foreign and PCT patent applications. We own all of the issued patents and own or jointly own all of the pending applications.

The issued U.S. patents, which will expire between 2024 and 2028, contain claims directed to the linaclotide molecule, pharmaceutical compositions thereof, methods of using linaclotide to treat GI disorders and processes for making the molecule. The granted European patents, which will expire in 2024, contain claims directed to the linaclotide molecule, pharmaceutical compositions thereof and uses of linaclotide to prepare medicaments for treating GI disorders.

We have received a notice of allowance from the United States Patent and Trademark Office, or the USPTO, for one of our jointly owned patent applications covering methods of using our current commercial formulation of linaclotide. Based on this notice of allowance, we expect this patent will be issued in 2014 and expire in 2031. We have other pending patent applications covering the current commercial formulation of linaclotide that, if issued, will expire in August 2029 or later, based upon potential patent term adjustments.

We have pending provisional applications directed to linaclotide products under development that will extend patent protection, if issued, until 2034 or later. We also have pending provisional, U.S. non-provisional, foreign and PCT applications directed to linaclotide and related molecules, pharmaceutical formulations thereof, methods of using linaclotide to treat various diseases and disorders and processes for making the molecule. These additional patent applications, if issued, will expire between 2024 and 2034.

The patent term of a patent that covers an FDA-approved drug is also eligible for patent term extension, which permits patent term restoration as compensation for some of the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of a single patent applicable to an approved drug for up to five years beyond the expiration of the patent but the extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. We have applied to extend the patent term of U.S. Patent 7,304,036, which covers linaclotide and methods of use thereof. If granted, the patent term of this patent will be extended to August 30, 2026, 14 years from the date of linaclotide's approval by the FDA.

Pipeline Patent Portfolio

Our pipeline patent portfolio relating to our GI and sGC research and development programs outside of linaclotide is currently composed of one issued U.S. patent; three issued patents in foreign jurisdictions; and numerous pending provisional, U.S. non-provisional, foreign and PCT patent applications. We own all of the issued patents and pending applications. The issued U.S. patent expires in 2031. The foreign issued patents expire in 2027 and 2030. The pending patent applications, if issued, will expire between 2027 and 2034.

Additional Intellectual Property

In addition to the patents and patent applications related to linaclotide and our GI and sGC pipeline, we currently have two issued U.S. patents; two patents granted in foreign jurisdictions; and a number of pending provisional, U.S. non-provisional, foreign and PCT applications directed to other GC-C agonist molecules and uses thereof. We also have other issued patents and pending patent applications relating to our other research and development programs, and we are the licensee of a number of issued patents and pending patent applications.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. We also expect to apply for patent term extensions for some of our patents once issued, depending upon the length of clinical trials and other factors involved in the submission of a new drug application, or NDA.

Government Regulation

In the U.S., pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, FDA post marketing requirements and assessments, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. The FDA has very broad enforcement authority and failure to abide by applicable regulatory requirements can result in administrative or judicial sanctions being imposed on us, including warning letters, refusals of government contracts, clinical holds, civil penalties, injunctions, restitution, disgorgement of profits, recall or seizure of products, total or partial suspension of production or distribution, withdrawal of approval, refusal to approve pending applications, and civil or criminal prosecution.

FDA Approval Process

We believe that our product candidates will be regulated by the FDA as drugs. No manufacturer may market a new drug until it has submitted an NDA to the FDA, and the FDA has approved it. The steps required before the FDA may approve an NDA generally include:

- nonclinical laboratory tests and animal tests conducted in compliance with FDA's good laboratory practice requirements;
- development, manufacture and testing of active pharmaceutical product and dosage forms suitable for human use in compliance with current GMP;
- the submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for its specific intended use(s);
- the submission to the FDA of an NDA;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current GMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Nonclinical tests include laboratory evaluation of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including good laboratory practices. We must submit the results of the nonclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol to the FDA as part of an IND, which must become effective before we may commence human clinical trials. The IND will automatically become effective 30 days after its receipt by the FDA, unless the FDA raises concerns or questions before that time about the conduct of the proposed trial. In such a case, we must work with the FDA to resolve any outstanding concerns before the clinical trial can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that will cause us or FDA to suspend or terminate such trials. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board for approval. An institutional review board may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the institutional review board's requirements or if the trial

has been associated with unexpected serious harm to subjects. An institutional review board may also impose other conditions on the trial.

Clinical trials involve the administration of the product candidate to humans under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are typically conducted in three sequential phases, though the phases may overlap or be combined. In Phase I, the initial introduction of the drug into healthy human subjects, the drug is usually tested for safety (adverse effects), dosage tolerance and pharmacologic action, as well as to understand how the drug is taken up by and distributed within the body. Phase II usually involves studies in a limited patient population (individuals with the disease under study) to:

- evaluate preliminarily the efficacy of the drug for specific, targeted conditions;
- determine dosage tolerance and appropriate dosage as well as other important information about how to design larger Phase III trials; and
- identify possible adverse effects and safety risks.

Phase III trials generally further evaluate clinical efficacy and test for safety within an expanded patient population. The conduct of clinical trials is subject to extensive regulation, including compliance with good clinical practice regulations and guidance.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. We may also suspend clinical trials at any time on various grounds.

The results of the nonclinical and clinical studies, together with other detailed information, including the manufacture and composition of the product candidate, are submitted to the FDA in the form of an NDA requesting approval to market the drug. FDA approval of the NDA is required before marketing of the product may begin in the U.S. If the NDA contains all pertinent information and data, the FDA will "file" the application and begin review. The review process, however, may be extended by FDA requests for additional information, nonclinical or clinical studies, clarification regarding information already provided in the submission, or submission of a risk evaluation and mitigation strategy. The FDA may refer an application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will typically inspect the facilities at which the product candidate is manufactured and will not approve the product candidate unless GMP compliance is satisfactory. FDA also typically inspects facilities responsible for performing animal testing, as well as clinical investigators who participate in clinical trials. The FDA may refuse to approve an NDA if applicable regulatory criteria are not satisfied, or may require additional testing or information. The FDA may also limit the indications for use and/or require post-marketing testing and surveillance to monitor the safety or efficacy of a product. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The testing and approval process requires substantial time, effort and financial resources, and our product candidates may not be approved on a timely basis, if at all. The time and expense required to perform the clinical testing necessary to obtain FDA approval for regulated products can frequently exceed the time and expense of the research and development initially required to create the product. The results of nonclinical studies and initial clinical trials of our product candidates are not necessarily predictive of the results from large-scale clinical trials, and clinical trials may be subject to additional costs, delays or modifications due to a number of factors, including difficulty in obtaining enough patients, investigators or product candidate supply. Failure by us or our collaborators, licensors or

licensees, including Forest, Almirall, Astellas and AstraZeneca, to obtain, or any delay in obtaining, regulatory approvals or in complying with requirements could adversely affect commercialization and our ability to receive product or royalty revenues.

Hatch-Waxman Act

The Hatch-Waxman Act established abbreviated approval procedures for generic drugs. Approval to market and distribute these drugs is obtained by submitting an Abbreviated New Drug Application, or ANDA, with the FDA. The application for a generic drug is "abbreviated" because it need not include nonclinical or clinical data to demonstrate safety and effectiveness and may instead rely on the FDA's previous finding that the brand drug, or reference drug, is safe and effective. In order to obtain approval of an ANDA, an applicant must, among other things, establish that its product is bioequivalent to an existing approved drug and that it has the same active ingredient(s), strength, dosage form, and the same route of administration. A generic drug is considered bioequivalent to its reference drug if testing demonstrates that the rate and extent of absorption of the generic drug is not significantly different from the rate and extent of absorption of the reference drug when administered under similar experimental conditions.

The Hatch-Waxman Act also provides incentives by awarding, in certain circumstances, certain legal protections from generic competition. This protection comes in the form of a non-patent exclusivity period, during which the FDA may not accept, or approve, an application for a generic drug, whether the application for such drug is submitted through an ANDA or a through another form of application, known as a 505(b)(2) application.

The Hatch-Waxman Act grants five years of exclusivity when a company develops and gains NDA approval of a new chemical entity that has not been previously approved by the FDA. This exclusivity provides that the FDA may not accept an ANDA or 505(b)(2) application for five years after the date of approval of previously approved drug, or four years in the case of an ANDA or 505(b)(2) application that challenges a patent claiming the reference drug (see discussion below regarding Paragraph IV Certifications). The Hatch-Waxman Act also provides three years of exclusivity for approved applications for drugs that are not new chemical entities, if the application contains the results of new clinical investigations (other than bioavailability studies) that were essential to approval of the application. Examples of such applications include applications for new indications, dosage forms (including new drug delivery systems), strengths, or conditions of use for an already approved product. This three-year exclusivity period only protects against FDA approval of ANDAs and 505(b)(2) applications for generic drugs that include the innovation that required new clinical investigations that were essential to approval; it does not prohibit the FDA from accepting or approving ANDAs or 505(b)(2) NDAs for generic drugs that do not include such an innovation.

Paragraph IV Certifications. Under the Hatch-Waxman Act, NDA applicants and NDA holders must provide information about certain patents claiming their drugs for listing in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," also known as the "Orange Book." When an ANDA or 505(b)(2) application is submitted, it must contain one of several possible certifications regarding each of the patents listed in the Orange Book for the reference drug. A certification that a listed patent is invalid or will not be infringed by the sale of the proposed product is called a "Paragraph IV" certification.

Within 20 days of the acceptance by the FDA of an ANDA or 505(b)(2) application containing a Paragraph IV certification, the applicant must notify the NDA holder and patent owner that the application has been submitted, and provide the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. The NDA holder or patent holder may then initiate a patent infringement suit in response to the Paragraph IV notice. If this is done within 45 days of receiving notice of the Paragraph IV certification, a 30-month stay of the FDA's ability to approve the ANDA or

505(b)(2) application is triggered. The FDA may approve the proposed product before the expiration of the 30-month stay only if a court finds the patent invalid or not infringed, or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

Patent Term Restoration. Under the Hatch-Waxman Act, a portion of the patent term lost during product development and FDA review of an NDA or 505(b)(2) application is restored if approval of the application is the first permitted commercial marketing of a drug containing the active ingredient. The patent term restoration period is generally one-half the time between the effective date of the IND and the date of submission of the NDA, plus the time between the date of submission of the NDA and the date of FDA approval of the product. The maximum period of patent term extension is five years, and the patent cannot be extended to more than 14 years from the date of FDA approval of the product. Only one patent claiming each approved product is eligible for restoration and the patent holder must apply for restoration within 60 days of approval. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for patent term restoration.

Other Regulatory Requirements

After approval, drug products are subject to extensive continuing regulation by the FDA, which include company obligations to manufacture products in accordance with GMP, maintain and provide to the FDA updated safety and efficacy information, report adverse experiences with the product, keep certain records and submit periodic reports, obtain FDA approval of certain manufacturing or labeling changes, and comply with FDA promotion and advertising requirements and restrictions. Failure to meet these obligations can result in various adverse consequences, both voluntary and FDA-imposed, including product recalls, withdrawal of approval, restrictions on marketing, and the imposition of civil fines and criminal penalties against the NDA holder. In addition, later discovery of previously unknown safety or efficacy issues may result in restrictions on the product, manufacturer or NDA holder.

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

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, prohibitions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), and principles governing industry- sponsored scientific and educational activities. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors or patients, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar in type and quality to the clinical data supporting the original application for the original indication, and the FDA uses similar procedures and actions in reviewing such NDA supplements as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase IV testing, risk minimization action plans, and surveillance to monitor the effects of an approved product or to place conditions on an approval that restrict the distribution or use of the product.

Outside the U.S., our and our collaborators' abilities to market a product are contingent upon receiving marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from jurisdiction to jurisdiction. At present, foreign marketing authorizations are applied for at a national level, although within the E.U. registration procedures are available to companies wishing to market a product in more than one E.U. member state.

Employees

As of December 31, 2013, we had 534 employees. Approximately 65 were scientists engaged in discovery research, 138 were in our drug development organization, 209 were in our sales and commercial team, and 122 were in general and administrative functions. None of our employees are represented by a labor union, and we consider our employee relations to be good. On January 8, 2014, we announced a headcount reduction of approximately 10% to align our workforce with our strategy to grow a leading GI therapeutics company, and that we expected to complete the reduction in workforce during the first quarter of 2014.

Executive Officers of the Registrant

The following table sets forth the name, age and position of each of our executive officers as of January 28, 2014:

Name	Age	Position
Peter M. Hecht, Ph.D. . . .	50	Chief Executive Officer, Director
Michael J. Higgins	51	Senior Vice President, Chief Operating Officer and Chief Financial Officer
Mark G. Currie, Ph.D. . . .	59	Senior Vice President, Chief Scientific Officer and President of R&D
Thomas A. McCourt	56	Senior Vice President, Marketing and Sales and Chief Commercial Officer

Peter M. Hecht has served as our chief executive officer and a director since our founding in 1998. Prior to founding Ironwood, Dr. Hecht was a research fellow at Whitehead Institute for Biomedical Research. Dr. Hecht earned a B.S. in mathematics and an M.S. in biology from Stanford University, and holds a Ph.D. in molecular biology from the University of California at Berkeley.

Michael J. Higgins serves as our senior vice president, chief operating officer and chief financial officer, and has led our finance, operations and strategy efforts since joining us in 2003. Prior to 2003, Mr. Higgins held a variety of senior business positions at Genzyme Corporation, including vice president of corporate finance. Mr. Higgins earned a B.S. from Cornell University and an M.B.A. from the Amos Tuck School of Business Administration at Dartmouth College.

Mark G. Currie serves as our senior vice president, chief scientific officer and president of research and development, and has led our research and development efforts since joining us in 2002. Prior to joining Ironwood, Dr. Currie directed cardiovascular and central nervous system disease research as vice president of discovery research at Sepracor Inc. Previously, Dr. Currie initiated, built and led discovery pharmacology and also served as director of arthritis and inflammation at Monsanto Company. Dr. Currie earned a B.S. in biology from the University of South Alabama and holds a Ph.D. in cell biology from the Bowman-Gray School of Medicine of Wake Forest University.

Thomas A. McCourt has served as our senior vice president of marketing and sales and chief commercial officer since joining Ironwood in 2009. Prior to joining Ironwood, Mr. McCourt led the U.S. brand team for denosumab at Amgen Inc. from April 2008 to August 2009. Prior to that, Mr. McCourt was with Novartis AG from 2001 to 2008, where he directed the launch and growth of Zelnorm for the treatment of patients with IBS-C and CIC and held a number of senior commercial roles, including vice president of strategic marketing and operations. Mr. McCourt was also part of the founding team at Astra Merck Inc., leading the development of the medical affairs and science liaison group and then serving as brand manager for Prilosec™ and NEXIUM®. Mr. McCourt has a degree in pharmacy from the University of Wisconsin.

Available Information

You may obtain free copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, and amendments to those reports, as soon as reasonably practicable after they are electronically filed or furnished to the SEC, on the Investors section of our website at www.ironwoodpharma.com or by contacting our Investor Relations department at (617) 374-5082. The contents of our website are not incorporated by reference into this report and you should not consider information provided on our website to be part of this report.

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

In addition to the other information in this Annual Report on Form 10-K, any of the factors described below could significantly and negatively affect our business, financial condition, results of operations or prospects. The trading price of our Class A common stock may decline due to these risks.

Risks Related to Our Business and Industry

We are highly dependent on the commercial success of LINZESS in the U.S. for the foreseeable future; we may be unable to attain profitability and positive cash flow from operations.

In August 2012, the FDA approved LINZESS as a once-daily treatment for adult men and women suffering from IBS-C or CIC. We and our partner, Forest, began selling LINZESS in the U.S. during December 2012. The commercial success of LINZESS will depend on a number of factors, including:

- the effectiveness of LINZESS as a treatment for adult patients with IBS-C or CIC;
- the size of the treatable patient population;
- the effectiveness of the sales, managed markets and marketing efforts by us and Forest;
- the adoption of LINZESS by physicians, which depends on whether physicians view it as a safe and effective treatment for adult patients with IBS-C and CIC;
- our success in educating and activating adult IBS-C and CIC patients, including through direct-to-consumer education, to enable them to more effectively communicate their symptoms and treatment history to their physicians;
- our ability to both secure and maintain adequate reimbursement for, and optimize patient access to, LINZESS by providing third party payers with a strong value proposition based on the existing burden of illness associated with IBS-C and CIC and the benefits of LINZESS;
- the effectiveness of our partners' distribution networks;
- the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these areas, associated with LINZESS; and

- the development or commercialization of competing products or therapies for the treatment of IBS-C or CIC, or their associated symptoms.

Our revenues from the commercialization of LINZESS are subject to these factors, and therefore may be unpredictable from quarter-to-quarter. Ultimately, we may never generate sufficient revenues from LINZESS to reach or maintain profitability or sustain our anticipated levels of operations.

Linaclotide may cause undesirable side effects or have other properties that could limit its commercial potential.

The most commonly reported adverse reactions in the placebo-controlled trials that supported the approval of linaclotide in the U.S. and Europe were diarrhea, abdominal pain, flatulence and abdominal distension, with diarrhea being the most common. Severe diarrhea was reported in 2% of the linaclotide-treated patients, and its incidence was similar between the IBS-C and CIC populations in these trials. If we or others identify previously unknown side effects, if known side effects are more frequent or severe than in the past, if we or others detect unexpected safety signals for linaclotide or any products perceived to be similar to linaclotide, or if any of the foregoing are perceived to have occurred, then in any of these circumstances:

- sales of linaclotide may be impaired;
- regulatory approvals for linaclotide may be restricted or withdrawn;
- we may decide to, or be required to, send product warning letters or field alerts to physicians, pharmacists and hospitals;
- reformulation of the product, additional nonclinical or clinical studies, changes in labeling or changes to or reapprovals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of LINZESS within its indicated populations, as well as be precluded from studying linaclotide in additional indications and populations, new formulations and in combination with other products;
- our reputation in the marketplace may suffer; and
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above occurrences would harm or prevent sales of linaclotide, increase our expenses and impair our ability to successfully commercialize linaclotide.

Furthermore, as we explore development opportunities to enhance the clinical profile of LINZESS, any clinical trials conducted may expand the patients treated with linaclotide within or outside of its current indications or patient populations, which could result in the identification of previously unknown side effects, increased frequency or severity of known side effects, or detection of unexpected safety signals. In addition, now that LINZESS and CONSTELLA are commercially available, they are used in wider populations and in less rigorously controlled environments than in clinical studies. As a result, regulatory authorities, healthcare practitioners, third party payers or patients may perceive or conclude that the use of linaclotide is associated with serious adverse effects, undermining our commercialization efforts.

In addition, the FDA-approved label for LINZESS contains a boxed warning about its use in pediatric patients—LINZESS is contraindicated in patients up to 6 years of age and physicians are cautioned to avoid use in patients 6 through 17 years of age. This warning resulted from nonclinical data from studies in young juvenile mice approximately equivalent to human pediatric patients less than 2 years of age. We and Forest have established a nonclinical and clinical post-marketing plan with the FDA to understand the safety and efficacy of LINZESS in pediatric patients, which is discussed below.

We rely entirely on contract manufacturers and our collaboration partners to manufacture and distribute linaclotide. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties, or are otherwise unable to manufacture and distribute sufficient quantities to meet demand, our commercialization efforts may be materially harmed.

We have no internal manufacturing or distribution capabilities. Instead, we rely on a combination of contract manufacturers and our partners to manufacture linaclotide API and final linaclotide drug product, and to distribute that drug product to third party purchasers. We have commercial supply agreements with independent third parties to manufacture the linaclotide API used to support all of our partnered and unpartnered territories. Each of Forest, Almirall and Astellas is responsible for drug product and finished goods manufacturing (including bottling and packaging) for its respective territory, and distributing the finished goods to wholesalers. Among our drug product manufacturers, only Forest and Almirall have manufactured linaclotide on a commercial scale. We have an agreement with an independent third party to serve as an additional source of drug product manufacturing of linaclotide for our partnered territories. We are working with our partners to ensure we will have sufficient redundancy in this component of the linaclotide supply chain, which includes obtaining the necessary regulatory approval for such drug product manufacturer to be included in the marketing authorization in the relevant country. Under our collaboration with AstraZeneca, we are accountable for drug product and finished goods manufacturing for China, Hong Kong and Macau.

Each of our linaclotide API and drug product manufacturers must comply with current good manufacturing practices, or GMP, and other stringent regulatory requirements enforced by the FDA and foreign regulatory authorities in other jurisdictions. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our quality assurance release of linaclotide API. Manufacturers of linaclotide may be unable to comply with these GMP requirements and with other regulatory requirements. We have little control over our manufacturers' or collaboration partners' compliance with these regulations and standards.

Our manufacturers may experience problems with their respective manufacturing and distribution operations and processes, including for example, quality issues, including product specification and stability failures, quality procedural deviations, improper equipment installation or operation, utility failures, contamination and natural disasters. In addition, our API manufacturers acquire the raw materials necessary to make linaclotide API from a limited number of sources. Any delay or disruption in the availability of these raw materials or a change in raw material suppliers could result in production disruptions, delays or higher costs with consequent adverse effects on us.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in commercial production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations and the challenges associated with complex supply chain management. Even if our manufacturers do not experience problems and commercial manufacturing is achieved, their maximum manufacturing capacities may be insufficient to meet commercial demand. Finding alternative manufacturers or adding additional manufacturers could take a significant amount of time and involve significant expense. New manufacturers would need to develop and implement the necessary production techniques and processes, which along with their facilities, would need to be inspected and approved by the regulatory authorities in each applicable territory.

If our API or drug product manufacturers fail to adhere to applicable GMP or other regulatory requirements, experience delays or disruptions in the availability of raw materials or experience manufacturing or distribution problems, we will suffer significant consequences, including product

seizures or recalls, loss of product approval, fines and sanctions, reputational damage, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs. If we experience any of these results, or if our manufacturers' maximum capacities are insufficient to meet demand, we may not be able to successfully commercialize linaclotide.

We must work effectively and collaboratively with Forest to market and sell LINZESS in the U.S. in order for it to achieve its maximum commercial potential.

We are working closely with Forest to implement our joint commercialization plan for LINZESS. The commercialization plan includes an agreed upon marketing campaign that targets the physicians who see patients who could benefit from LINZESS treatment. Our marketing campaign also targets the adult men and women who suffer from IBS-C or CIC, and such efforts are expected to include an expanded direct-to-consumer education program beginning in late March 2014. Our commercialization plan also includes an integrated call plan for our sales forces to optimize the education of specific gastroenterologists and primary care physicians on whom our and Forest's sales representatives call, and the frequency with which the representatives meet with them.

In order to optimize the commercial potential of LINZESS, we and Forest must execute upon this commercialization plan effectively and efficiently. In addition, we and Forest must continually assess and modify our commercialization plan in a coordinated and integrated fashion in order to adapt to the promotional response. Further, we and Forest must continue to focus and refine our marketing campaign to ensure a clear and understandable physician-patient dialogue around IBS-C, CIC and the potential for LINZESS as an appropriate therapy. In addition, we and Forest must provide our sales forces with the highest quality support, guidance and oversight in order for them to continue to effectively promote LINZESS to gastroenterologists and primary care physicians. If we and Forest fail to perform these commercial functions in the highest quality manner, LINZESS will not achieve its maximum commercial potential. Our efforts to further target and engage adult patients with IBS-C or CIC through expanded direct-to-consumer education may not effectively increase appropriate patient awareness or patient/physician dialogue, and may not increase the revenues that we generate from LINZESS.

We are subject to uncertainty relating to pricing and reimbursement policies which, if not favorable for linaclotide, could hinder or prevent linaclotide's commercial success.

Our and Forest's ability to commercialize LINZESS in the U.S. successfully depends in part on the coverage and reimbursement levels set by governmental authorities, private health insurers and other third-party payers. In determining whether to approve reimbursement for LINZESS and at what level, we expect that third-party payers will consider factors that include the efficacy, cost effectiveness and safety of LINZESS, as well as the availability of alternative treatments. Further, in order to maintain acceptable reimbursement levels and access for patients at copay levels that are reasonable and customary, we may face increasing pressure to offer discounts or rebates from list prices or discounts to a greater number of third-party payers or other unfavorable pricing modifications. Obtaining and maintaining favorable reimbursement can be a time consuming and expensive process, and there is no guarantee that we or Forest will be able to negotiate pricing terms with all third-party payers at levels that are profitable to us, or at all. Certain third-party payers also require prior authorization for, or even refuse to provide, reimbursement for LINZESS, and others may do so in the future. Our business would be materially adversely affected if we and Forest are not able to receive approval for reimbursement of LINZESS from third-party payers on a broad, timely or satisfactory basis; if reimbursement is subject to overly restrictive prior authorization requirements; or if reimbursement is not maintained at a satisfactory level or becomes subject to prior authorization. In addition, our business could be adversely affected if private insurers, including managed care organizations, the

Medicare or Medicaid programs or other reimbursing bodies or payers limit or reduce the indications for or conditions under which LINZESS may be reimbursed.

We expect to experience pricing pressures in connection with the sale of linaclotide and our future products due to the healthcare reforms discussed below, as well as the trend toward programs aimed at reducing health care costs, the increasing influence of health maintenance organizations, the ongoing debates on reducing government spending and additional legislative proposals. These healthcare reform efforts or any future legislation or regulatory actions aimed at controlling and reducing healthcare costs, including through measures designed to limit reimbursement, restrict access or impose unfavorable pricing modifications on pharmaceutical products, could impact our and our partners' ability to obtain or maintain reimbursement for linaclotide at a satisfactory level, or at all, which could materially harm our business and financial results.

In some foreign countries, particularly Canada and the countries of Europe, the pricing and payment of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we and our partners may be required to conduct a clinical trial that compares the cost-effectiveness of our products, including linaclotide, to other available therapies. In addition, in countries in which linaclotide is the only approved therapy for a particular indication, such as CONSTELLA as the only product approved for the symptomatic treatment of moderate to severe IBS-C in adults in Europe, there may be disagreement as to what the most comparable product is, or if there even is one. Further, several European countries have implemented government measures to either freeze or reduce pricing of pharmaceutical products. Many third-party payers and governmental authorities also consider the price for which the same product is being sold in other countries to determine their own pricing and reimbursement strategy, so if linaclotide is priced low or gets limited reimbursement in a particular country, this could result in similarly low pricing and reimbursement in other countries. If reimbursement for our products is unavailable in any country in which reimbursement is sought, limited in scope or amount, or if pricing is set at or reduced to unsatisfactory levels, our ability to successfully commercialize linaclotide in such country would be impacted negatively. Furthermore, if these measures prevent us or any of our partners from selling linaclotide on a profitable basis in a particular country, they could prevent the commercial launch or continued sale of linaclotide in that country.

If the pricing and reimbursement of CONSTELLA in the E.U. is low, our royalty revenues based on sales of linaclotide will be adversely affected.

In November 2012, the European Commission granted marketing authorization to CONSTELLA for the symptomatic treatment of moderate to severe IBS-C in adults. This approval followed the positive recommendation received from the European Committee for Medicinal Products for Human Use in September 2012. Currently, CONSTELLA is commercially available in certain European countries, including the United Kingdom and Germany.

The pricing and reimbursement strategy is a key component of Almirall's commercialization plan for CONSTELLA in Europe. Reimbursement sources are different in each country, and each country may include a combination of distinct potential payers, including private insurance and governmental payers. Countries in Europe may restrict the range of medicinal products for which their national health insurance systems provide reimbursement and control the prices of medicinal products for human use. Our revenues may suffer if Almirall is unable to successfully and timely conclude reimbursement, price approval or funding processes and market CONSTELLA in key member states of the E.U., or if coverage and reimbursement for CONSTELLA is limited or reduced. If Almirall is not able to obtain coverage, pricing or reimbursement on acceptable terms or at all, or if such terms change in any countries in its territory, Almirall may not be able to, or may decide not to, sell

CONSTELLA in such countries. Further, Almirall could sell CONSTELLA at a low price. Since we receive royalties on net sales of CONSTELLA in the E.U., which is correlated directly to the price at which Almirall sells CONSTELLA in the E.U., our royalty revenues globally could be limited should Almirall sell CONSTELLA at a low price or elect not to launch in a certain country within the E.U.

Because we work with partners to develop, manufacture and commercialize linaclotide, we are dependent upon third parties, and our relationships with those third parties, in our efforts to commercialize LINZESS and to obtain regulatory approval for, and to commercialize, linaclotide in our other partnered territories.

Forest played a significant role in the conduct of the clinical trials for linaclotide and in the subsequent collection and analysis of data, and Forest holds the NDA for LINZESS. In addition, we are commercializing LINZESS in the U.S. with Forest. Forest is responsible for the further development, regulatory approval and commercialization of linaclotide in Canada and Mexico, which, for Mexico, it has sublicensed its commercialization rights to Almirall. Almirall also holds the marketing authorization for CONSTELLA in the E.U. and is responsible for obtaining regulatory approval of linaclotide in the other countries in its territory. Astellas, our partner in Japan, is responsible for completing the clinical programs and obtaining regulatory approval of linaclotide in its territory. Further, we are jointly overseeing the development, and will jointly oversee the commercialization, of linaclotide in China, Hong Kong and Macau through our collaboration with AstraZeneca, with AstraZeneca having primary responsibility for the local operational execution. Upon any approval, each of Almirall, Astellas and AstraZeneca is responsible for commercializing linaclotide in its respective territory, and each has agreed to use commercially reasonable efforts to do so. Each of our partners is responsible for reporting adverse event information from its territory to us. Finally, each of our partners, other than AstraZeneca, is responsible for drug product manufacturing of linaclotide and making it into finished goods (including bottling and packaging) for its respective territory. The integration of our efforts with our partners' efforts is subject to the uncertainty of the markets for pharmaceutical products in each partner's respective territories, and accordingly, these relationships must evolve to meet any new challenges that arise in those regions.

These integrated functions may not be carried out effectively and efficiently if we fail to communicate and coordinate with our partners, and vice versa. Our partnering strategy imposes obligations, risks and operational requirements on us as the central node in our global network of partners. If we do not effectively communicate with each partner and ensure that the entire network is making integrated and cohesive decisions focused on the global brand for linaclotide, linaclotide will not achieve its maximum commercial potential. As the holder of the global safety database for linaclotide, we are responsible for coordinating the safety surveillance and adverse event reporting efforts worldwide. If we are unsuccessful in doing so due to poor process, execution, oversight, communication, adjudication or otherwise, then our and our partner's ability to obtain and maintain regulatory approval of linaclotide will be at risk.

We have limited ability to control the amount or timing of resources that our partners devote to linaclotide. If any of our partners fails to devote sufficient time and resources to linaclotide, or if its performance is substandard, it will delay the potential submission or approval of regulatory applications for linaclotide, as well as the manufacturing and commercialization of linaclotide in the particular territory. A material breach by any of our partners of our collaboration or license agreement with such partner, or a significant disagreement between us and a partner, could also delay the regulatory approval and commercialization of linaclotide, potentially lead to costly litigation, and could have a material adverse impact on our financial condition. Moreover, although we have non-compete restrictions in place with each of our partners, they may have relationships with other commercial entities, some of which may compete with us. If any of our partners assists our competitors, it could harm our competitive position.

If any of our partners undergoes a change in control or in management, this may adversely affect our collaborative relationship or the success of the commercialization of LINZESS in the U.S. or the continued launches and commercialization of CONSTELLA in the E.U., or the ability to achieve regulatory approval and commercialize linaclotide in our other partnered territories.

We work jointly and collaboratively with Forest, Almirall, Astellas and AstraZeneca on many aspects of the development, manufacturing and commercialization of linaclotide. In doing so, we have established relationships with several key members of the management teams of Forest, Almirall, Astellas and AstraZeneca in functional areas such as development, quality, regulatory, drug safety and pharmacovigilance, operations, marketing, sales, field operations and medical science. The success of our collaborations is highly dependent on the resources, efforts and skills of our partners and their key employees. As we and our partners commercialize LINZESS in the U.S., continue to launch and commercialize CONSTELLA in the E.U. and transition linaclotide from development to commercialization in other parts of the world, the drug's success becomes more dependent on us maintaining highly collaborative and well aligned partnerships. Effective October 1, 2013, Brenton L. Saunders became Forest's Chief Executive Officer and President, succeeding Howard Solomon in such role. In connection with this transition, or if our partners otherwise undergo a change of management or in control, we will need to reestablish many relationships and confirm alignment of our development and commercialization strategy for linaclotide. Given the inherent uncertainty and disruption that arises in a change of control or in management, we cannot be sure that we would be able to successfully execute these courses of action. Finally, any change of control or in management may result in a reprioritization of linaclotide within a partner's portfolio, or such partner may fail to maintain the financial or other resources necessary to continue supporting its portion of the development, manufacturing or commercialization of linaclotide.

If any of our partners undergoes a change of control and the acquirer either is unable to perform such partner's obligations under its collaboration or license agreement with us or has a product that competes with linaclotide that such acquirer does not divest, we have the right to terminate the collaboration or license agreement and reacquire that partner's rights with respect to linaclotide. If we elect to exercise these rights in such circumstances, we will need to either establish the capability to develop, manufacture and commercialize linaclotide in that partnered territory on our own or we will need to establish a relationship with a new partner. We have assembled a team of specialists in manufacturing, quality, sales, marketing, payer, pricing and field operations, and specialized medical scientists, who represent the functional areas necessary for a successful commercial launch of a high potential, GI therapy and who support the commercialization of LINZESS in the U.S. If Forest was subject to a change of control that allowed us to further commercialize LINZESS in the U.S. on our own, and we chose to do so, we would need to enhance each of these functional aspects to replace the capabilities that Forest was previously providing to the collaboration. Any such transition might result in a period of reduced efficiency or performance by our operations and commercialization teams, which could adversely affect our ability to commercialize LINZESS.

Although many members of our global operations, commercial and medical affairs teams have strategic oversight of, and a certain level of involvement in, their functional areas globally, we do not have corresponding operational capabilities in these areas outside of the U.S. If Forest, Almirall, Astellas or AstraZeneca was subject to a change of control that allowed us to continue linaclotide's development or commercialization anywhere outside of the U.S. on our own, and we chose to do so rather than establishing a relationship with a new partner, we would need to build operational capabilities in the relevant territory. In any of these situations, the timeline and likelihood of achieving regulatory approval and, ultimately, the commercialization of linaclotide could be negatively impacted.

Even though LINZESS has been approved by the FDA for the treatment of adults with IBS-C or CIC, it faces future post-approval development and regulatory requirements, which will present additional challenges.

In August 2012, the FDA approved LINZESS as a once-daily treatment for adult men and women suffering from IBS-C or CIC. LINZESS is subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market information.

LINZESS is contraindicated in pediatric patients up to 6 years of age based on nonclinical data from studies in neonatal mice approximately equivalent to human pediatric patients less than 2 years of age. Physicians are also instructed to avoid the use of LINZESS in pediatric patients 6 through 17 years of age based on this nonclinical data and the lack of clinical safety and efficacy data in pediatric patients. We and Forest have established a nonclinical and clinical post-marketing plan with the FDA to understand the safety and efficacy of LINZESS in pediatric patients. The first step in this plan was to undertake additional nonclinical studies to further understand the results of the earlier neonatal mouse study and to understand the tolerability of LINZESS in older juvenile mice. We have conducted these nonclinical studies. While we and Forest are working with the FDA on a plan for clinical pediatric studies, our ability to initiate such studies depends in part on the view of the FDA on whether our recent nonclinical studies support studying the safety and efficacy of LINZESS in pediatrics. Further, our ability to ever expand the indication for LINZESS to pediatrics will depend on, among other things, our successful completion of clinical studies.

We and Forest have also committed to certain nonclinical and clinical studies aimed at understanding: (a) whether orally administered linaclotide can be detected in breast milk, (b) the potential for antibodies to be developed to linaclotide, and if so, (c) whether antibodies specific for linaclotide could have any therapeutic or safety implications. We expect to complete these studies over the next three to five years.

These post-approval requirements impose burdens and costs on us. Failure to complete the required studies and meet our other post-approval commitments would lead to negative regulatory action at the FDA, which could include withdrawal of regulatory approval of LINZESS for the treatment of adults with IBS-C or CIC.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with a facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including requiring implementation of a risk evaluation and mitigation strategy program, withdrawal of the product from the market or suspension of manufacturing. If we, our partners or the manufacturing facilities for linaclotide fail to comply with applicable regulatory requirements, a regulatory agency may:

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

Even though LINZESS has been approved for marketing in the U.S. and CONSTELLA has been approved for marketing in the E.U. and Canada, we or our collaborators may never receive approval to commercialize linaclotide in other parts of the world.

In order to market any products outside of the U.S., we or our partners must comply with numerous and varying regulatory requirements of other jurisdictions regarding safety and efficacy. Approval procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than, those in the U.S., the E.U. and Canada. Potential risks include that the regulatory authorities:

- may not deem linaclotide safe and effective;
- may not find the data from nonclinical studies and clinical trials sufficient to support approval;
- may not approve of manufacturing processes and facilities;
- may not approve linaclotide for any or all indications or patient populations for which approval is sought;
- may require significant warnings or restrictions on use to the product label for linaclotide; or
- may change their approval policies or adopt new regulations.

Regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. If linaclotide is not approved for all indications or patient populations or with the label requested, this would limit the uses of linaclotide and have an adverse effect on its commercial potential or require costly post-marketing studies.

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

The use of our product candidates in clinical trials and the sale of marketed products expose us to product liability claims. If we do not successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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

We currently have product liability insurance coverage for the commercial sale of linaclotide and for the clinical trials of our product candidates which is subject to industry-standard terms, conditions and exclusions. Our insurance coverage may not be sufficient to reimburse us for expenses or losses associated with claims. 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. On occasion, large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

We may face competition in the IBS-C and CIC marketplace, and new products may emerge that provide different or better alternatives for treatment of GI conditions.

Linaclotide competes globally with certain prescription therapies and over the counter products for the treatment of IBS-C and CIC, or their associated symptoms. The availability of prescription competitors and over the counter products for GI conditions could limit the demand, and the price we are able to charge, for linaclotide unless we are able to differentiate linaclotide on the basis of its actual or perceived benefits. New developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render linaclotide obsolete or noncompetitive.

We believe other companies are developing products which could compete with linaclotide, should they be approved by the FDA or foreign regulatory authorities. Currently, there are compounds in late stage development and other potential competitors are in earlier stages of development for the treatment of patients with either IBS-C or CIC. If our potential competitors are successful in completing drug development for their drug candidates and obtain approval from the FDA or foreign regulatory authorities, they could limit the demand for linaclotide.

In addition, certain of our competitors have substantially greater financial, technical and human resources than us. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields.

We will incur significant liability if it is determined that we are promoting any "off-label" use of LINZESS.

Physicians are permitted to prescribe drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Such "off-label" uses are common across medical specialties. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies are not permitted to promote drugs for off-label uses. Accordingly, we may not promote LINZESS in the U.S. for use in any indications other than IBS-C or CIC or in any patient populations other than adult men and women. The FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained. A company that is found to have improperly promoted off-label uses will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchange concerning their products. We intend to engage in medical education activities and communicate with healthcare providers in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program designed to ensure that all such activities are performed in a legal and compliant manner, LINZESS is our first commercial product, so our implementation of our compliance program in connection with commercialization activities is still relatively new.

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

As a manufacturer of pharmaceuticals, even though we do not (and do not expect in the future to) control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We are subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations include:

- federal healthcare program anti-kickback laws, which prohibit, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;
- the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts;
- the federal Foreign Corrupt Practices Act which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity; and
- the federal Physician Payments Sunshine Act, which was passed as part of the Patient Protection and Affordable Care Act of 2010, and similar state laws in certain states, that require pharmaceutical and medical device companies to monitor and report payments, gifts, the provision of samples and other remuneration made to physicians and other health care professional and health care organizations.

If our operations are found to be in violation of any of the laws described above or any other laws, rules or regulations that apply to us, we will be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results.

In preparation for the commercial launch of LINZESS, we assembled an experienced compliance team who compiled a program based on industry best practices that is designed to ensure that our

commercialization of LINZESS complies with all applicable laws, regulations and industry standards. We also hire, manage and incentivize our employees around a culture of compliance, trust, respect and ownership. Because our program is relatively new and the requirements in this area are constantly evolving, we cannot be certain that our program will eliminate all areas of potential exposure. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business, as well as damage our business or reputation. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security, fraud and reporting laws may prove costly.

Healthcare reform and other governmental and private payer initiatives may have an adverse effect upon, and could prevent, our product's or product candidates' commercial success.

The U.S. government and individual states are aggressively pursuing healthcare reform, as evidenced by the passing of the Patient Protection and Affordable Care Act, as modified by the Health Care and Education Reconciliation Act of 2010. These healthcare reform laws contain several cost containment measures that could adversely affect our future revenue, including, for example, increased drug rebates under Medicaid for brand name prescription drugs, extension of Medicaid rebates to Medicaid managed care plans, and extension of so-called 340B discounted pricing on pharmaceuticals sold to certain healthcare providers. Additional provisions of the healthcare reform laws that may negatively affect our future revenue and prospects for profitability include the assessment of an annual fee based on our proportionate share of sales of brand name prescription drugs to certain government programs, including Medicare and Medicaid, as well as mandatory discounts on pharmaceuticals sold to certain Medicare Part D beneficiaries. Other aspects of healthcare reform, such as expanded government enforcement authority and heightened standards that could increase compliance-related costs, could also affect our business.

In addition to governmental efforts in the U.S., foreign jurisdictions as well as private health insurers and managed care plans are likely to continue challenging manufacturers' ability to obtain reimbursement, as well as the level of reimbursement, for pharmaceuticals and other healthcare related products and services. These cost-control initiatives could significantly decrease the available coverage and the price we might establish for linaclotide and our other potential products, which would have an adverse effect on our financial results.

The Food and Drug Administration Amendments Act of 2007 also provides the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. We and Forest have established a nonclinical and clinical post-marketing plan with the FDA to understand the safety and efficacy of LINZESS in pediatrics. The FDA's exercise of this authority has resulted (and is expected to continue to result) in increased development-related costs following the commercial launch of LINZESS for the treatment of adult men and women suffering from IBS-C or CIC, and could result in potential restrictions on the sale and/or distribution of LINZESS, even in its approved indications and patient populations.

In pursuing our growth strategy, we will incur a variety of costs and may devote resources to potential opportunities that are never completed or for which we never receive the benefit. Our failure to successfully discover, acquire, develop and market additional product candidates or approved products would impair our ability to grow.

As part of our growth strategy, we intend to explore further linaclotide development opportunities, and to develop and market additional products and product candidates. We are exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated

populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. These development efforts may fail or may not increase the revenues that we generate from LINZESS. Furthermore, they may result in adverse events, or perceived adverse events, in certain patient populations that are then attributed to the currently approved patient population, which may result in adverse regulatory action at the FDA or in other countries or harm linaclotide's reputation in the marketplace, each of which could materially harm our revenues from linaclotide.

We are pursuing various other programs through our pipeline. We may spend several years and make significant investments in completing our development of any particular current or future internal product candidate, and failure can occur at any stage. The product candidates to which we allocate our resources may not be successful. Our business depends entirely on the successful development and commercialization of our product and product candidates.

In addition, because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising pharmaceutical product candidates and products.

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

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

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

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

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

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

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

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, an institutional review board overseeing the clinical trial at a clinical trial site (with respect to that site), the FDA, or other regulatory authorities due to a number of factors, including:

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

Additionally, changes in regulatory requirements and guidance may occur, and we may need to amend clinical trial protocols to reflect these changes. Each protocol amendment would require institutional review board review and approval, which may adversely impact the costs, timing or successful completion of the associated clinical trials. If we experience delays in completion, or if we terminate any of our clinical trials, the commercial prospects for our product candidate may be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval.

We may not be able to manage our business effectively if we lose any of our current management team or if we are unable to attract and motivate key personnel.

We may not be able to attract or motivate qualified management and scientific, clinical, operations and commercial personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the greater-Boston area. If we are not able to attract and motivate necessary personnel to accomplish our business objectives, we will experience constraints that will significantly impede the achievement of our objectives.

We are highly dependent on the drug discovery, development, regulatory, commercial and financial expertise of our management, particularly Peter M. Hecht, Ph.D., our chief executive officer; Mark G.

Currie, Ph.D., our senior vice president, chief scientific officer and president of research and development; Michael J. Higgins, our senior vice president, chief operating officer and chief financial officer; and Thomas A. McCourt, our senior vice president, marketing and sales and chief commercial officer. If we lose any members of our management team in the future, we may not be able to find suitable replacements, and our business may be harmed as a result. In addition to the competition for personnel, the Boston area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment efforts.

We also have scientific and clinical advisors who assist us in formulating our product development, clinical strategies and our global supply chain plans, as well as sales and marketing advisors who have assisted us in our commercialization strategy and brand plan for linaclotide. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development and commercialization of products that may compete with ours.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, as well as personally identifiable information of linaclotide patients, clinical trial participants and employees. We also have outsourced elements of our information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our partners, vendors and other third party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including criminal groups. Any such breach could compromise our, and their, networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business.

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

Our activities involve the controlled storage, use and disposal of hazardous materials. We are subject to federal, state, city and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures we use for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. We do not currently maintain hazardous materials insurance coverage.

Risks Related to Intellectual Property

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

Our success depends on our ability to obtain and maintain patent protection for our product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others.

The strength of patents in the pharmaceutical industry involves complex legal and scientific questions and can be uncertain. Patent applications in the U.S. and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we were the first to conceive inventions covered by our patents and pending patent applications or that we were the first to file patent applications for such inventions. In addition, we cannot be certain that our patent applications will be granted, that any issued patents will adequately protect our intellectual property or that such patents will not be challenged, narrowed, invalidated or circumvented.

Our U.S. Patent 7,704,947, which covers a group of peptides including LINZESS and related molecules, underwent an inter partes reexamination instigated by a third party request at the USPTO. The USPTO has confirmed that all claims are patentable and this decision is no longer appealable, affirming the strength of our intellectual property and our belief that the reexamination was without merit. This patent is one of several issued patents and pending applications in the U.S. related to LINZESS, including a LINZESS composition of matter and methods of use patent (U.S. Patent 7,304,036) as well as additional patents and applications covering processes for making LINZESS, formulations, and dosing regimens. Although none of our other issued patents currently is subject to a patent reexamination, we cannot guarantee that they will not be subject to reexamination or review by the USPTO in the future. If any or all of our LINZESS-related patents were invalidated, we would still have at least five years of marketing exclusivity under the Hatch-Waxman Act from FDA approval of LINZESS. We believe that each of the patents in our linaclotide patent portfolio was rightfully issued and the portfolio gives us sufficient freedom to operate; however, if any of our present or future patents is invalidated, this could have an adverse effect on our business and financial results, particularly for the period beyond five years following marketing approval.

In March 2013, an opposition to one of our granted patents covering linaclotide was filed in Europe. We believe that this patent was appropriately granted and will be upheld by the European Patent Office but we cannot be certain of this until the opposition period is complete. While the opposition is ongoing, we will incur additional expense and be required to focus additional efforts on the proceedings. However, even if this patent were found to be invalid, we have other composition of matter- and use-related linaclotide patents that are granted and in force, and we believe these patents provide strong and sufficient patent protection in Europe.

Furthermore, the America Invents Act, which was signed into law in 2011, has made several major changes in the U.S. patent statutes. These changes will permit third parties to challenge our patents more easily and will create uncertainty with respect to the interpretation and practice of U.S. patent law for the foreseeable future.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. It is possible, however, that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have

adequate remedies, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

In addition, the laws of certain foreign countries do not protect proprietary rights to the same extent or in the same manner as the U.S., and, therefore, we may encounter problems in protecting and defending our intellectual property in certain foreign jurisdictions.

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

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

We may be exposed to, or threatened with, litigation by third parties alleging that linaclotide or our product candidates infringe their intellectual property rights. If linaclotide or one of our product candidates is found to infringe the intellectual property rights of a third party, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to commercialize linaclotide or the applicable product candidate unless we obtain a license to the intellectual property rights. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the counter-party could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, pending a trial on the merits, which may not occur for several years.

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

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

We may become involved in lawsuits to protect or enforce our patents, which could be expensive and time consuming, and unfavorable outcomes in such litigation could have a material adverse effect on our business.

Competitors may infringe our patents or may assert our patents are invalid. To counter ongoing or potential infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Litigation with generic manufacturers has become increasingly common in the biotechnology and pharmaceutical industries. In addition, in an infringement or invalidity proceeding, a court or patent administrative body may determine that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference or derivation proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents and patent applications or those of our collaborators. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. In addition, we may not be able to prevent, alone or with our collaborators, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, as well as the potential for public announcements of the results of hearings, motions or other interim proceeding or developments, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Risks Related to Our Finances and Capital Requirements

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

In recent years, we have focused primarily on developing, manufacturing and commercializing linaclotide. We and Forest launched LINZESS in the U.S. in December 2012, and we believe that it will take us some time to attain profitability and positive cash flow from operations. We have financed our operations to date primarily through the issuance of equity, our collaboration and license arrangements and our January 2013 issuance of debt securities related to the sales of LINZESS in the U.S., and we have incurred losses in each year since our inception in 1998. We incurred net losses of approximately $272.8 million, $72.6 million and $64.9 million in the years ended December 31, 2013, 2012 and 2011, respectively. As of December 31, 2013, we had an accumulated deficit of approximately $777.8 million. Our prior losses and expected future losses, have had and we expect will continue to have, an adverse effect on our stockholders' equity and working capital. We expect to continue to incur substantial expenses in connection with our efforts to commercialize linaclotide and our research and development of our product candidates. As a result, we expect to continue to incur significant operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when, or if, we will become profitable.

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

In the second quarter of 2013, we completed an offering of approximately 11.2 million shares of our Class A common stock at a public offering price of $13.00 per share. In January 2013, we

completed an offering of $175.0 million in debt securities related to the sales of LINZESS in the U.S. However, marketing and selling a primary care drug, purchasing commercial quantities of pharmaceutical products, and developing product candidates and conducting clinical trials are expensive and uncertain. Circumstances, our strategic imperatives, or opportunities to create or acquire new programs could require us to, or we may choose to, seek to raise additional funds. The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the level of underlying demand for LINZESS by prescribers and patients in the U.S. and for CONSTELLA by prescribers and patients in the E.U.;
- the costs associated with commercializing LINZESS in the U.S.;
- the costs of maintaining and expanding sales, marketing and distribution capabilities for linaclotide;
- the regulatory approval of linaclotide outside of the United States and E.U., and the timing of commercial launches in those countries, as well as the associated development and commercial milestones and royalties;
- the rate of progress and cost of our clinical trials and other product development programs, including our post-approval nonclinical and clinical studies of LINZESS in pediatrics and our investment to enhance the clinical profile of LINZESS within its indicated populations, as well as to study linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions;
- the costs and timing of in-licensing additional product candidates or acquiring other complementary companies;
- the status, terms and timing of any collaboration, licensing, co-commercialization or other arrangements; and
- the timing of any regulatory approvals of our product candidates.

Additional funding may not be available on acceptable terms or at all. If adequate funds are not available, we may be required to delay, reduce the scope of our commercialization efforts or reduce or eliminate one or more of our development programs.

Our ability to pay principal of and interest on our outstanding debt securities will depend in part on the receipt of payments from Forest under our collaboration agreement that are equal to or in excess of our quarterly payment obligations on each payment date.

In January 2013, we issued $175.0 million in debt securities bearing an annual interest rate of 11%. Quarterly interest payments on these securities commenced on June 15, 2013. Beginning in March 2014, we will make quarterly payments on the notes equal to the greater of (i) 7.5% of net sales of LINZESS in the U.S. for the preceding quarter and (ii) the quarterly interest amount. Principal on the notes will be repaid in an amount equal to the difference between (i) and (ii) above, when this is a positive number, until the principal has been paid in full. If the cash flows derived from the net quarterly payments that we receive from Forest under the collaboration agreement are insufficient on any particular payment date to fund the quarterly interest payment, at a minimum, we will be obligated to pay the amounts of such shortfall out of our general funds. We expect that for the next few years, at a minimum, the net quarterly payments from Forest will be our primary source of cash flow from operations. The determination of whether Forest will be obligated to make a net quarterly payment to us in respect of a particular quarterly period is a function of the revenue generated by LINZESS in the U.S. as well as the development, manufacturing and commercialization expenses incurred by each of us and Forest under the collaboration agreement. Accordingly, since we believe that it will take us some time to attain profitability and positive cash flow from operations, we cannot guarantee that (i) we will

have the available funds to fund the quarterly interest payment, at a minimum, in the event that there is a deficiency in the net quarterly payment received from Forest, (ii) there will be a net quarterly payment from Forest at all or (iii) we will not also be required to make a true-up payment to Forest under the collaboration agreement, in each case, in respect of a particular quarterly period.

Our indebtedness could adversely affect our financial condition or restrict our future operations.

As of December 31, 2013, we had total indebtedness of approximately $175.0 million. We chose to issue debt securities based on the additional strategic optionality that this creates for us, and the limited restrictions that these debt securities place on our ability to run our business compared to other potential available financing transactions. However, our indebtedness could have important consequences, including:

- limiting our ability to obtain additional financing to fund future working capital, capital expenditures, acquisitions or other general corporate requirements;
- requiring a substantial portion of our cash flow to be dedicated to debt service payments instead of other purposes, thereby reducing the amount of cash flow available for working capital, capital expenditures, corporate transactions and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and competitive conditions;
- limiting our flexibility in planning for and reacting to changes in the industry in which we compete;
- placing us at a disadvantage compared to other, less leveraged competitors or competitors with comparable debt at more favorable interest rates; and
- increasing our cost of borrowing.

Although we are not as restricted under these debt securities as we might have been under a more traditional secured credit facility provided by a bank, the indenture governing our debt securities contains a number of restrictive covenants that impose restrictions on us and may limit our ability to engage in certain acts, including restrictions on our ability to:

- amend our collaboration agreement with Forest in a way that would have a material adverse effect on the noteholders rights, or terminate this collaboration agreement with respect to the U.S.;
- transfer our rights to commercialize the product under our collaboration agreement with Forest; and
- incur certain liens.

Upon a breach of the covenants under our indenture, the noteholders could elect to declare all amounts outstanding under the outstanding debt securities to be immediately due and payable. If we are unable to repay those amounts, the noteholders could proceed against the collateral granted to them to secure the debt securities. If the noteholders under the indenture accelerate the repayment of the debt securities, we cannot be certain that we will have sufficient assets to repay them.

If we breach our covenants under our indenture and seek a waiver, we may not be able to obtain a waiver from the required noteholders. If this occurs we would be in default under our indenture, the noteholders could exercise their rights, as described above, and we could be forced into bankruptcy or liquidation.

Our quarterly and annual operating results may fluctuate significantly.

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

- the level of underlying demand for LINZESS in the U.S. and CONSTELLA in the E.U., and wholesalers' buying patterns;
- the costs associated with commercializing LINZESS in the U.S.;
- the achievement and timing of milestone payments under our existing collaboration and license agreements;
- our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- regulatory developments affecting linaclotide or our product candidates; and
- any material lawsuit in which we may become involved.

If our operating results fall below the expectations of investors or securities analysts, the price of our Class A common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and it is possible that certain transactions or a combination of certain transactions may result in material additional limitations on our ability to use our net operating loss and tax credit carryforwards.

Section 382 and 383 of the Internal Revenue Code of 1986, as amended, contain rules that limit the ability of a company that undergoes an ownership change, which is generally any change in ownership of more than 50% of its stock over a three-year period, to utilize its net operating loss and tax credit carryforwards and certain built-in losses recognized in years after the ownership change. These rules generally operate by focusing on ownership changes involving stockholders owning directly or indirectly 5% or more of the stock of a company and any change in ownership arising from a new issuance of stock by the company. Generally, if an ownership change occurs, the yearly taxable income limitation on the use of net operating loss and tax credit carryforwards and certain built-in losses is equal to the product of the applicable long term tax exempt rate and the value of the company's stock immediately before the ownership change. We may be unable to offset our taxable income with losses, or our tax liability with credits, before such losses and credits expire and therefore would incur larger federal income tax liability. We have completed several financings since our inception which may have resulted in a change in control as defined by Section 382, or could result in a change in control in the future.

Risks Relating to Securities Markets and Investment in Our Stock

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could negatively impact the market price of our Class A common stock.

Provisions in our certificate of incorporation and bylaws may have the effect of delaying or preventing a change of control. These provisions include the following:

- Our certificate of incorporation provides for a dual class common stock structure. As a result of this structure, holders of our Class B common stock have significant influence over certain matters requiring stockholder approval, including a merger involving Ironwood, a sale of

substantially all Ironwood assets and a dissolution or liquidation of Ironwood. This concentrated control could discourage others from initiating a change of control transaction that other stockholders may view as beneficial.

- Our board of directors is divided into three classes serving staggered three-year terms, such that not all members of the board are elected at one time. This staggered board structure prevents stockholders from replacing the entire board at a single stockholders' meeting.
- Our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors.
- Our board of directors may issue, without stockholder approval, shares of preferred stock. The ability to authorize preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.
- Stockholders must provide advance notice to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting. Furthermore, stockholders may only remove a member of our board of directors for cause. These provisions may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect such acquirer's own slate of directors or otherwise attempting to obtain control of our company.
- Our stockholders may not act by written consent. As a result, a holder, or holders, controlling a majority of our capital stock are not able to take certain actions outside of a stockholders' meeting.
- Special meetings of stockholders may be called only by the chairman of our board of directors, our chief executive officer or a majority of our board of directors. As a result, a holder, or holders, controlling a majority of our capital stock are not able to call a special meeting.
- A majority of the outstanding shares of Class B common stock are required to amend our certificate of incorporation and a super-majority (80%) of the outstanding shares of common stock are required to amend our bylaws, which make it more difficult to change the provisions described above.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our certificate of incorporation and our bylaws and in the Delaware General Corporation Law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors.

The concentration of voting control on certain corporate matters with our pre-IPO stockholders will limit the ability of the holders of our Class A common stock to influence such matters.

Because of our dual class common stock structure, the holders of our Class B common stock, who consist of our pre-IPO investors (and their affiliates), founders, directors, executives and certain of our employees, are able to control certain corporate matters listed below if any such matter is submitted to our stockholders for approval even though such stockholders own less than 50% of the outstanding shares of our common stock. As of December 31, 2013, the holders of our Class A common stock own approximately 85% and the holders of our Class B common stock own approximately 15% of the outstanding shares of Class A common stock and Class B common stock, combined. However, because of our dual class common stock structure these holders of our Class A common stock have approximately 36% and holders of our Class B common stock have approximately 64% of the total votes on each of the matters identified in the list below. This concentrated control of our Class B

common stockholders limits the ability of the Class A common stockholders to influence those corporate matters and, as a result, we may take actions that many of our stockholders do not view as beneficial, which could adversely affect the market price of our Class A common stock.

Each share of Class A common stock and each share of Class B common stock has one vote per share on all matters except for the following matters, for which each share of our Class B common stock has ten votes per share and each share of our Class A common stock has one vote per share:

- adoption of a merger or consolidation agreement involving Ironwood;
- a sale of all or substantially all of Ironwood's assets;
- a dissolution or liquidation of Ironwood; and
- every matter, if and when any individual, entity or "group" (as that term is used in Regulation 13D of the Exchange Act) has, or has publicly disclosed (through a press release or a filing with the SEC) an intent to have, beneficial ownership of 30% or more of the number of outstanding shares of Class A common stock and Class B common stock, combined.

If we identify a material weakness in our internal control over financial reporting, it could have an adverse effect on our business and financial results and our ability to meet our reporting obligations could be negatively affected, each of which could negatively affect the trading price of our Class A common stock.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Our system of internal controls, however well designed and operated, is based in part on certain assumptions and includes elements that rely on information from third parties, including our collaboration partners. Our system can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results, and the price of our Class A common stock could be negatively affected.

Further, we are dependent on our collaboration partners for information related to our results of operations. Our net profit or net loss generated from the sales of LINZESS in the U.S. is partially determined based on amounts provided by Forest and involves the use of estimates and judgments, which could be modified in the future. We also are highly dependent on our partners for timely and accurate information regarding any revenues realized from sales of linaclotide in their respective territories, and in the case of Forest and AstraZeneca, the costs incurred in developing and commercializing it in order to accurately report our results of operations. If we do not receive timely and accurate information or incorrectly estimate activity levels associated with the relevant collaboration at a given point in time, whether the result of a material weakness or not, we could be required to record adjustments in future periods. Such adjustments, if significant, could have an adverse effect on our financial results, which could lead to a decline in our Class A common stock price.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. Failure to

comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, The NASDAQ Stock Market or other regulatory authorities.

We expect that the price of our Class A common stock will fluctuate substantially.

The market price of our Class A common stock may be highly volatile due to many factors, including:

- the commercial performance of linaclotide in the U.S. and in the E.U.;
- any third-party coverage and reimbursement policies for linaclotide;
- market conditions in the pharmaceutical and biotechnology sectors;
- developments, litigation or public concern about the safety of linaclotide or our potential products;
- announcements of the introduction of new products by us or our competitors;
- announcements concerning product development results, including clinical trial results, or intellectual property rights of us or others;
- actual and anticipated fluctuations in our quarterly and annual operating results;
- deviations in our operating results from the estimates of securities analysts;
- sales of additional shares of our common stock;
- additions or departures of key personnel;
- developments concerning current or future strategic collaborations; and
- discussion of us or our stock price in the financial or scientific press or in online investor communities.

The realization of any of the risks described in these "Risk Factors" could have a dramatic and material adverse impact on the market price of our Class A common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced periods of volatility. Any such litigation brought against us could result in substantial costs and a diversion of management attention, which could hurt our business, operating results and financial condition.

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

None.

Item 2. ***Properties***

Our corporate headquarters and operations are located in Cambridge, Massachusetts, where, as of December 31, 2013, we lease and occupy approximately 234,000 rentable square feet of office and laboratory space at our Cambridge, Massachusetts facility. Under our lease, we are obligated to rent approximately 70,000 square feet of additional space at our Cambridge, Massachusetts facility in three equal stages, each commencing no later than June 1, 2014, June 1, 2015 and June 1, 2016, respectively. Our lease expires in January 2018. We believe that our facilities are suitable and adequate for our needs for the foreseeable future.

Item 3. ***Legal Proceedings***

None.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

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

Shares of our Class A common stock are traded on the NASDAQ Global Select Market under the symbol "IRWD." Our shares have been publicly traded since February 3, 2010.

	Class A Common Stock			
	2013		2012	
	High	Low	High	Low
First Quarter	$19.67	$11.11	$15.92	$10.65
Second Quarter	$18.38	$ 9.83	$15.00	$11.24
Third Quarter	$13.95	$ 9.83	$14.36	$11.29
Fourth Quarter	$12.19	$ 8.95	$13.70	$10.01

As of January 28, 2014, there were 45 stockholders of record of our Class A common stock and 99 stockholders of record of our Class B common stock. The number of record holders is based upon the actual number of holders registered on the books of the company at such date and does not include holders of shares in "street names" or persons, partnerships, associations, corporations or other entities identified in security position listings maintained by depositories.

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of Class A common stock and Class B common stock are entitled to share equally in any dividends that our board of directors may determine to issue from time to time. In the event a dividend is paid in the form of shares of common stock or rights to acquire shares of common stock, the holders of Class A common stock will receive Class A common stock, or rights to acquire Class A common stock, as the case may be, and the holders of Class B common stock will receive Class B common stock, or rights to acquire Class B common stock, as the case may be.

We have never declared or paid any cash dividends on our capital stock, and we do not currently anticipate declaring or paying cash dividends on our capital stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance operations. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and covenants and other factors that our board of directors may deem relevant.

The information required to be disclosed by Item 201(d) of Regulation S-K, "Securities Authorized for Issuance Under Equity Compensation Plans," is referenced under Item 12 of Part III of this Annual Report on Form 10-K.

Corporate Performance Graph

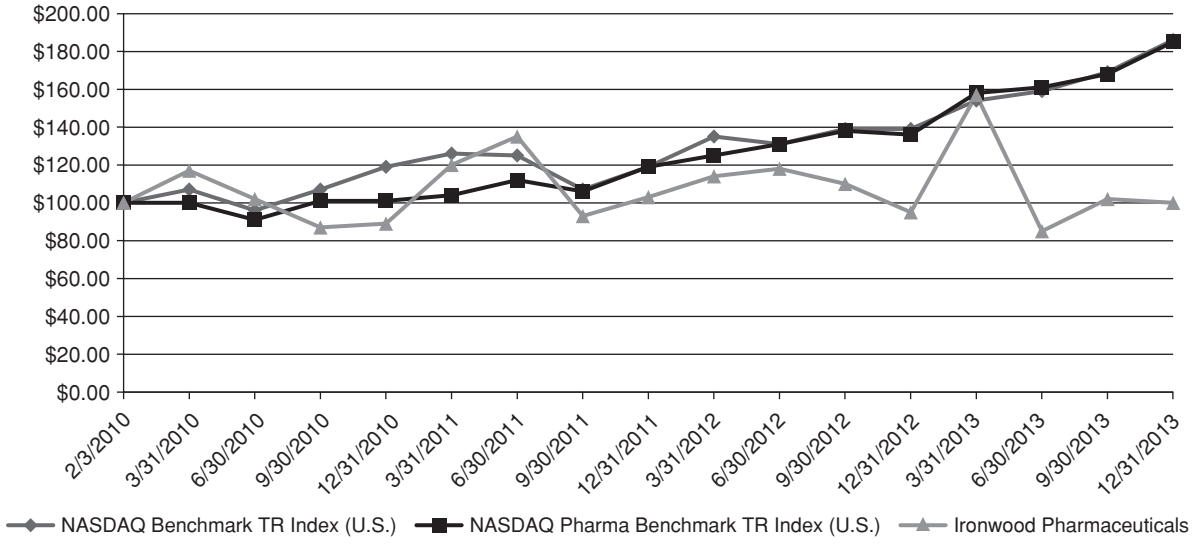
The following performance graphs and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The first graph below compares the performance of our Class A common stock to the NASDAQ Benchmark TR Index (U.S.) and to the NASDAQ Pharmaceutical Benchmark TR Index (U.S.) from February 3, 2010 (the first date that shares of our Class A common stock were publicly traded) through December 31, 2013. The second graph below compares the performance of our Class A common stock to the NASDAQ Stock Market (U.S.) and to the NASDAQ Pharmaceutical Index over the same period, which is consistent with the presentation we provided in our Form 10-K for the year ended

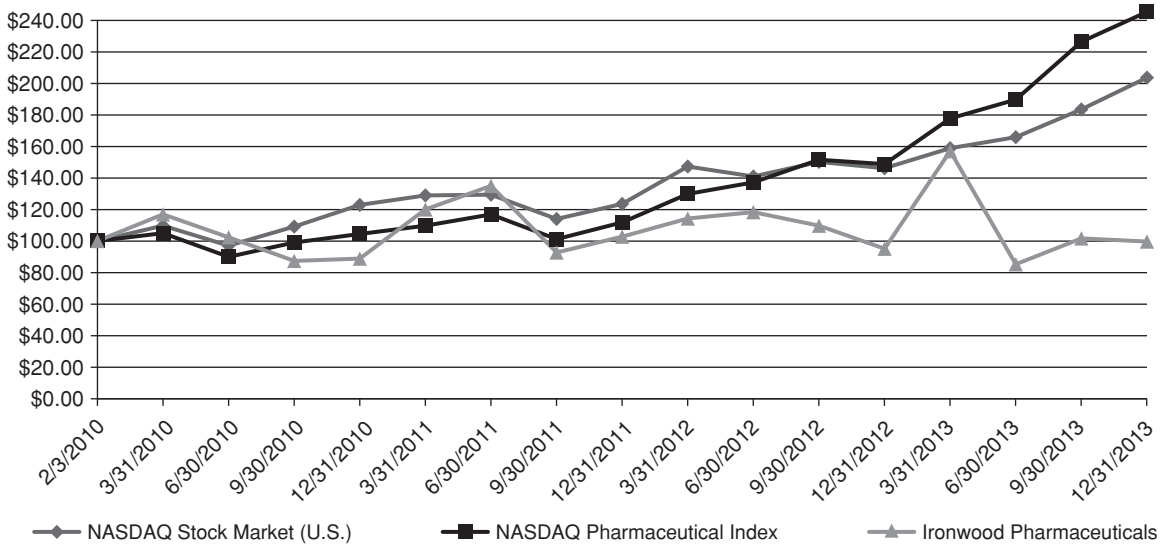
December 31, 2012. We have changed the indices presented in our corporate performance graph as a result of a change in the total return data made available to us by our third-party provider.

In each graph, the comparison assumes $100 was invested after the market closed on February 3, 2010 in our Class A common stock and in each of the presented indices, and it assumes reinvestment of dividends, if any.

COMPARISON OF QUARTERLY CUMULATIVE TOTAL RETURN
Among The NASDAQ Benchmark TR Index (U.S.),
the NASDAQ Pharmaceutical Benchmark TR Index (U.S.)
and Ironwood Pharmaceuticals, Inc.



COMPARISON OF QUARTERLY CUMULATIVE TOTAL RETURN
Among the NASDAQ Stock Market (U.S.),
the NASDAQ Pharmaceutical Index,
and Ironwood Pharmaceuticals, Inc.



Item 6. ***Selected Consolidated Financial Data***

You should read the following selected financial data together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statements of operations data for the years ended December 31, 2013, 2012 and 2011 and the consolidated balance sheet data as of December 31, 2013 and 2012 from our audited financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statements of operations data for the years ended December 31, 2010 and 2009 and the consolidated balance sheet data as of December 31, 2011, 2010 and 2009 from our audited financial

statements not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Years Ended December 31,				
	2013	2012	2011	2010	2009
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Collaborative arrangements revenue	$ 22,881	$150,245	$ 65,871	$ 43,857	$ 34,321
Cost and expenses:					
Cost of revenue	7,203	965	—	—	—
Research and development[1]	102,378	113,474	86,093	77,454	76,100
Selling, general and administrative[1]	123,228	92,538	45,920	27,169	19,037
Collaboration expense[2]	42,074	16,030	—	—	—
Total cost and expenses	274,883	223,007	132,013	104,623	95,137
Loss from operations	(252,002)	(72,762)	(66,142)	(60,766)	(60,816)
Other income (expense):					
Interest expense	(21,002)	(59)	(63)	(196)	(318)
Interest and investment income	192	197	456	614	240
Remeasurement of forward purchase contracts	—	—	—	—	600
Other income	—	—	900	993	—
Other income (expense), net	(20,810)	138	1,293	1,411	522
Net loss from continuing operations before income tax (benefit) expense	(272,812)	(72,624)	(64,849)	(59,355)	(60,294)
Income tax (benefit) expense	—	—	3	(2,944)	(296)
Net loss from continuing operations	(272,812)	(72,624)	(64,852)	(56,411)	(59,998)
Net income (loss) from discontinued operations[1]	—	—	—	4,551	(13,314)
Net loss	(272,812)	(72,624)	(64,852)	(51,860)	(73,312)
Net (income) loss from discontinued operations attributable to noncontrolling interest	—	—	—	(1,121)	2,127
Net loss attributable to Ironwood Pharmaceuticals, Inc.	$(272,812)	$(72,624)	$(64,852)	$(52,981)	$(71,185)
Net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted:					
Continuing operations	$ (2.35)	$ (0.68)	$ (0.65)	$ (0.63)	$ (8.43)
Discontinued operations	—	—	—	0.04	(1.57)
Net loss per share	$ (2.35)	$ (0.68)	$ (0.65)	$ (0.59)	$ (10.00)
Weighted average number of common shares used in net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	115,852	106,403	99,875	89,653	7,117

(1) Includes share-based compensation expense as indicated in the following table:

Research and development	$ 9,178	$9,080	$6,071	$4,112	$2,372
Selling, general and administrative	10,651	8,493	5,661	3,384	2,723
Discontinued operations	—	—	—	59	149

(2) Collaboration expense for the years ended December 31, 2011, 2010 and 2009 is included in selling, general and administrative expense and was not material.

	December 31,				
	2013	2012	2011	2010	2009
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents and available-for-sale securities	$197,602	$168,228	$164,016	$248,027	$ 122,306
Working capital of continuing operations (excluding deferred revenue)	193,162	132,883	138,724	234,699	107,485
Assets of discontinued operations	—	—	—	—	2,346
Total assets	278,962	229,907	208,977	301,365	162,451
Deferred revenue, including current portion	16,490	21,405	57,421	102,433	126,002
Long-term debt, including current portion	174,672	—	—	—	1,763
Capital lease obligations, including current portion	4,273	569	655	590	255
Liabilities of discontinued operations	—	—	—	—	2,301
Total liabilities	240,737	85,855	99,121	141,814	162,441
Convertible preferred stock	—	—	—	—	298,350
Noncontrolling interest	—	—	—	—	3,212
Total stockholders' equity (deficit)	38,225	144,052	109,856	159,551	(298,340)

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

Forward-Looking Information

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" in Item 1A of this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are an entrepreneurial pharmaceutical company focused on creating medicines that make a difference for patients, building value to earn the continued support of our fellow shareholders, and empowering our team to passionately pursue excellence. Our core strategy is to establish a leading gastrointestinal, or GI, therapeutics company, leveraging our development and commercial capabilities in addressing GI disorders as well as our pharmacologic expertise in guanylate cyclase, or GC, pathways.

We have one marketed product, linaclotide, which is available in the United States, or U.S., under the trademarked name LINZESS® and in the European Union, or E.U., under the trademarked name CONSTELLA®. Linaclotide is also being developed in other parts of the world by certain of our partners.

In August 2012, the United States Food and Drug Administration, or FDA, approved LINZESS as a once-daily treatment for adult men and women suffering from irritable bowel syndrome with constipation, or IBS-C, or chronic idiopathic constipation, or CIC. LINZESS is being commercialized in the U.S. by us and our collaboration partner, Forest Laboratories, Inc., or Forest. We and Forest began commercializing LINZESS in the U.S. during December 2012.

In November 2012, the European Commission granted marketing authorization to CONSTELLA for the symptomatic treatment of moderate to severe IBS-C in adults. CONSTELLA is the first and

only drug approved in the E.U. for IBS-C. Our European partner, Almirall, S.A., or Almirall, has exclusive marketing rights for CONSTELLA in Europe (including the Commonwealth of Independent States and Turkey). Currently, CONSTELLA is commercially available in certain European countries, including the United Kingdom and Germany.

In December 2013, the Health Canada granted approval of CONSTELLA as a once-daily, first-in-class treatment for adult women and men suffering from IBS-C or CIC. Forest has exclusive rights to develop and commercialize linaclotide in Canada.

Astellas Pharma Inc., or Astellas, our partner in Japan, is developing linaclotide for the treatment of patients with IBS-C. Astellas recently completed a double-blind, placebo-controlled, dose-ranging Phase II clinical trial of linaclotide in adult patients with IBS-C. In February 2014, we received preliminary top level data for the Phase II trial from Astellas indicating that, while all linaclotide dose groups showed numerically higher responder rates in the primary endpoint than placebo, the responder rates were not statistically significant compared to placebo in this study. Linaclotide was well tolerated in all dose groups in this study. Data analysis is still ongoing at Astellas to determine next steps.

In October 2012, we entered into a collaboration agreement with AstraZeneca AB, or AstraZeneca, to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. In the third quarter of 2013, we and AstraZeneca initiated a double-blind, placebo-controlled Phase III clinical trial of linaclotide in adult patients with IBS-C.

We continue to assess alternatives to bring linaclotide to IBS-C and CIC sufferers in the parts of the world outside of our partnered territories. We are also exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. In addition to linaclotide-based opportunities, we are advancing multiple GI development programs as well as further leveraging our GC expertise to advance a second GC program targeting soluble guanylate cyclase, or sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

We were incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc. We currently operate in one reportable business segment—human therapeutics.

To date, we have dedicated substantially all of our activities to the research, development and commercialization of linaclotide, our lead product and product candidate, as well as research and development of our other product candidates. We have incurred significant operating losses since our inception in 1998. As of December 31, 2013, we had an accumulated deficit of $777.8 million and we expect to continue to incur net losses for the foreseeable future.

In February 2012, we sold 6,037,500 shares of our Class A common stock through a firm commitment, underwritten public offering at a price to the public of $15.09 per share. As a result of the offering, we received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $85.2 million. On January 4, 2013, we closed a private placement of $175.0 million in aggregate principal amount of 11% notes due on or before June 15, 2024. As a result of the debt offering, we received aggregate net proceeds, after offering expenses, of approximately $167.3 million. During the second quarter of 2013, we sold 11,204,948 shares of our Class A common stock through a firm commitment, underwritten public offering at a price to the public of $13.00 per share. As a result of the offering, we received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $137.8 million.

On January 8, 2014, we announced a headcount reduction of approximately 10% to align our workforce with our strategy to grow a leading GI therapeutics company. As maximizing LINZESS is

core to our strategy, our field-based sales force and medical science liaison teams were excluded from this reduction in workforce. We estimate that we will incur aggregate charges in connection with this reduction in workforce of approximately $4.0 million to $4.5 million for employee severance and benefit costs, of which approximately 85% to 95% are expected to result in cash expenditures. We committed to this course of action on January 8, 2014, and expect to complete the reduction in workforce during the first quarter of 2014.

Financial Overview

Revenue. Revenue to date has been generated primarily through our collaboration agreements with Forest and AstraZeneca, and our license agreements with Almirall and Astellas. The terms of these agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, and (iii) the manufacture of finished drug product, active pharmaceutical ingredient, or API, or development materials for the collaborative partners. Payments to us may include one or more of the following: nonrefundable license fees; payments for research and development activities, payments for the manufacture of finished drug product, API or development materials, payments based upon the achievement of certain milestones and royalties on product sales. Additionally, we will receive our share of the net profits or bear our share of the net losses from the sale of linaclotide in the U.S. and China. LINZESS launched in the U.S. in December 2012 and CONSTELLA became commercially available in certain European countries in the second quarter of 2013.

We record our share of the net profits and losses from the sales of LINZESS in the U.S. on a net basis and present the settlement payments as collaborative arrangements revenue or collaboration expense, as applicable. Net profits or losses consist of net sales to third-party customers in the U.S. less the cost of goods sold as well as selling, general and administrative expenses. Although we expect net sales to increase over time, the settlement payments between Forest and us, resulting in collaborative arrangements revenue or collaboration expense, are subject to fluctuation based on the ratio of selling, general and administrative expenses incurred by each party. In addition, our collaborative arrangements revenue may fluctuate as a result of timing and amount of license fees and clinical and commercial milestones received and recognized under our current and future strategic partnerships as well as timing and amount of royalties from the sales of CONSTELLA in the European and Canadian market. One instance of this potential fluctuation relates to the challenging environment in the European pharmaceutical sector. As challenges in obtaining adequate pricing and reimbursement for pharmaceutical products in Europe have grown recently, it became clear to us and our partner, Almirall, that revising certain aspects of our current partnership would benefit the potential for linaclotide. Accordingly, in June 2013, we amended the Almirall license agreement to make the amount and timing of certain of the commercial launch milestones contingent on the reimbursement amount in such countries in exchange for additional new sales-based incentives and a more favorable royalty structure at certain sales thresholds.

Cost of Revenue. Cost of revenue is recognized upon shipment of linaclotide API to certain of our licensing partners. Our cost of revenue consists of the internal and external costs of producing such API. We expensed most of the manufacturing costs of API as research and development expenses in the periods prior to July 1, 2012, at which date we began capitalizing linaclotide-related inventory costs as their realizability became probable, based on our evaluation of, among other factors, the status of the linaclotide New Drug Applications, or NDA, in the U.S., the Committee for Medicinal Products for Human Use, or CHMP, positive recommendation to grant marketing approval for CONSTELLA in Europe, and the ability of our third-party suppliers to successfully manufacture commercial quantities of linaclotide API. As of December 31, 2012, the previously expensed commercial API inventory was substantially utilized. As demand for linaclotide is expected to increase over time, we expect our cost of revenue to increase in future periods.

Research and Development Expense. Research and development expense consists of expenses incurred in connection with the discovery, development, manufacture and distribution of our product candidates. These expenses consist primarily of compensation, benefits and other employee-related expenses, research and development related facility costs, third-party contract costs relating to nonclinical study and clinical trial activities, development of manufacturing processes, regulatory registration of third-party manufacturing facilities and costs associated with linaclotide API prior to meeting our inventory capitalization policy, as well as licensing fees for our product candidates. We charge all research and development expenses to operations as incurred. Under our Forest and AstraZeneca collaboration agreements, we are reimbursed for certain research and development expenses, and we net these reimbursements against our research and development expenses as incurred. Payments to Forest or AstraZeneca are recorded as incremental research and development expense.

Our lead product is linaclotide, and it represents the largest portion of our research and development expense for our product candidates. Linaclotide is the first and, to date, only FDA-approved guanylate cyclase type-C agonist and is our only product or product candidate that has demonstrated clinical proof of concept. NDAs for LINZESS with respect to both IBS-C and CIC were approved by the FDA in August 2012. In November 2012, the European Commission approved CONSTELLA for the treatment of IBS-C in adults.

We are also exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. In addition to linaclotide-based opportunities, we are advancing multiple GI development programs as well as further leveraging our GC expertise to advance a second GC program targeting sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

The following table sets forth our research and development expenses related to our product pipeline for the years ended December 31, 2013, 2012 and 2011. These expenses relate primarily to external costs associated with nonclinical studies and clinical trial costs, costs incurred to develop manufacturing processes and register manufacturing facilities with the FDA, costs associated with linaclotide API that was expensed prior to meeting our inventory capitalization policy and licensing fees for our product candidates. Beginning in the third quarter of 2013, we began to allocate costs related to facilities, depreciation, share-based compensation and research and development support services, laboratory supplies and certain other costs directly to programs. Prior-period amounts in the table below were reclassified to conform to the current period's presentation.

	Years Ended December 31,		
	2013	2012	2011
		(in thousands)	
Linaclotide	$ 46,048	$ 51,044	$37,913
Early development candidates:			
GI disorders (two compounds)[1]	11,068	15,547	8,707
Central nervous system disorders (three compounds)[1]	14,793	14,910	4,824
Allergic disorders (one compound)[1]	916	5,232	7,524
Total early development candidates	26,777	35,689	21,055
Discovery research	29,553	26,741	27,125
	$102,378	$113,474	$86,093

(1) Number of compounds is for the year ended December 31, 2013.

Since 2004, the date we began tracking costs by program, we have incurred approximately $258.4 million of research and development expenses related to linaclotide. For the periods prior to January 1, 2011, this amount excludes certain allocated costs related to facilities, depreciation, share-based compensation and research and development support services, laboratory supplies and certain other expenses. The expenses for linaclotide include both reimbursements to us by Forest and AstraZeneca as well as our portion of research and development costs incurred by Forest or AstraZeneca for linaclotide and invoiced to us under the cost-sharing provisions of our collaboration agreements.

The lengthy process of securing regulatory approvals for new drugs requires the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals would materially adversely affect our product development efforts and our business overall. In August 2012, the FDA approved our NDAs for LINZESS as a once-daily treatment for adult men and women suffering from IBS-C or CIC. In connection with the FDA approval, we are required to conduct certain nonclinical and clinical studies aimed at understanding: (a) whether orally administered linaclotide can be detected in breast milk, (b) the potential for antibodies to be developed to linaclotide, and if so, (c) whether antibodies specific for linaclotide could have any therapeutic or safety implications. In addition, we and Forest established a nonclinical and clinical post-marketing plan with the FDA to understand the efficacy and safety of LINZESS in pediatric patients. In October 2012, we entered into a collaboration agreement with AstraZeneca under which we will jointly develop and commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. We are also exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. Therefore, we cannot currently estimate with any degree of certainty the amount of time or money that we will be required to expend in the future on linaclotide in pediatrics, for other geographic markets, within its indicated population, in additional indications and populations, new formulations or in combination with other products. In addition to linaclotide-based opportunities, we are advancing multiple GI development programs as well as further leveraging our GC expertise to advance a second GC program targeting sGC, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development. Given the inherent uncertainties that come with the development of pharmaceutical products, we cannot estimate with any degree of certainty how these programs will evolve, and therefore the amount of time or money that would be required to obtain regulatory approval to market them. As a result of these uncertainties surrounding the timing and outcome of any approvals, we are currently unable to estimate precisely when, if ever, linaclotide will be developed in pediatrics or otherwise outside of its current markets, indications, populations or formulations, or when, if ever, any of our other product candidates will generate revenues and cash flows.

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. In addition, we are actively engaged in evaluating externally-discovered drug candidates at all stages of development that fit within our core strategy. In evaluating potential assets, we apply the same criteria as those used for investments in internally-discovered assets.

The successful development of our product candidates is highly uncertain and subject to a number of risks including, but not limited to:

- The duration of clinical trials may vary substantially according to the type, complexity and novelty of the product candidate.
- The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products, typically requiring lengthy and detailed

laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures.

- Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activity. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.
- The duration and cost of discovery, nonclinical studies and clinical trials may vary significantly over the life of a product candidate and are difficult to predict.
- The costs, timing and outcome of regulatory review of a product candidate may not be favorable.
- The emergence of competing technologies and products and other adverse market developments may negatively impact us.

As a result of the uncertainties discussed above, we are unable to determine the duration and costs to complete current or future nonclinical and clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the data of each product candidate, the competitive landscape and ongoing assessments of such product candidate's commercial potential. As a result of the regulatory approvals in 2012, LINZESS and CONSTELLA began generating sales in December 2012 and in the second quarter of 2013, respectively, upon commercial launch in the U.S. and certain European countries.

We expect our research and development costs will be substantial for the foreseeable future. We will continue to invest in linaclotide including the areas of its supply chain, the investigation of ways to enhance the clinical profile within its indicated population and the exploration of its utility in other indications and populations, new formulations and in combination with other products. We will also invest in our other product candidates as we advance them through nonclinical studies and clinical trials, in addition to funding full-time equivalents for research and development activities under our external collaboration and license agreements.

Selling, General and Administrative Expense. Selling, general and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resource functions. Other costs include the legal costs of pursuing patent protection of our intellectual property, general and administrative related facility costs and professional fees for accounting and legal services. As we continue to invest in the commercialization of LINZESS, we expect our selling, general and administrative expenses will be substantial for the foreseeable future. We charge all selling, general and administrative expenses to operations as incurred.

Under our Forest and AstraZeneca collaboration agreements, we are reimbursed for certain selling, general and administrative expenses and we net these reimbursements against our selling, general and administrative expenses as incurred. Beginning in the fourth quarter of 2012, we include Forest's selling, general and administrative cost-sharing payments in the calculation of the net profits and net losses from the sale of LINZESS in the U.S. and present the net payment to or from Forest as collaboration expense or collaborative arrangements revenue, respectively. The selling, general and administrative cost-sharing payments to Forest for the nine months ended September 30, 2012 were reclassified to conform to the current period's presentation. Prior to 2012, such selling, general and

administrative cost-sharing payments were presented within selling, general and administrative expenses and were not material to the consolidated financial statements.

Collaboration Expense. Collaboration expense represents 50% of LINZESS net sales in the U.S. as well as cost of goods sold and selling, general and administrative cost-sharing settlement between us and Forest. Prior to the fourth quarter of 2012, selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses. The cost-sharing payments to Forest for the nine months ended September 30, 2012 were reclassified to conform to the current period's presentation. Prior to 2012, such selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses and were not material to the consolidated financial statements.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the U.S. The preparation of these financial statements requires us to make certain estimates and assumptions that may affect the reported amounts of assets and liabilities, the reported amounts of revenues and expenses during the reported periods and related disclosures. These estimates and assumptions, including those related to revenue recognition, inventory valuation and related reserves, research and development expenses and share-based compensation are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on our historical experience, trends in the industry, and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from our estimates under different assumptions or conditions.

We believe that our application of the following accounting policies, each of which require significant judgments and estimates on the part of management, are the most critical to aid in fully understanding and evaluating our reported financial results. Our significant accounting policies are more fully described in Note 2, *Summary of Significant Accounting Policies*, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Revenue Recognition

Our revenue is generated primarily through collaborative research and development and license agreements. The terms of these agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, and (iii) the manufacture of finished drug product, API or development materials for the collaborative partner. Non-refundable payments to us under these agreements may include up-front license fees, payments for research and development activities, payments for the manufacture of finished drug product, API or development materials, payments based upon the achievement of certain milestones and royalties on product sales. Additionally, we may receive our share of the net profits or bear our share of the net losses from the sale of linaclotide in the U.S. and China through our collaborations with Forest and AstraZeneca, respectively.

We evaluate revenue from new agreements that have multiple elements under the guidance of Accounting Standards Update, or ASU, No. 2009-13, *Multiple-Deliverable Revenue Arrangements*, or ASU 2009-13, which we adopted in January 2011. We also evaluate whether amendments to our multiple element arrangements are considered material modifications that are subject to the application of ASU 2009-13. This evaluation requires us to assess all relevant facts and circumstances and to make subjective determinations and judgments. As part of this assessment, we consider whether the modification results in a material change to the arrangement, including whether there is a change in total arrangement consideration that is more than insignificant, whether there are changes in the

deliverables included in the arrangement, whether there is a change in the term of the arrangement and whether there is a significant modification to the delivery schedule for contracted deliverables.

We identify the deliverables included within multiple element agreements and evaluate which deliverables represent separate units of accounting. We account for those components as separate elements when the following criteria are met:

- the delivered items have value to the customer on a stand-alone basis; and
- if there is a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and within our control.

This evaluation requires subjective determinations and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, we evaluate certain criteria, including whether the deliverables have standalone value, based on consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research, manufacturing and commercialization capabilities of the partner and the availability of peptide research and manufacturing expertise in the general marketplace. In addition, we consider whether the collaborator can use the license or other deliverables for their intended purpose without the receipt of the remaining elements, and whether the value of the deliverable is dependent on the undelivered items and whether there are other vendors that can provide the undelivered items.

The consideration is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

We determine the estimated selling price for deliverables using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE nor TPE is available. Determining the BESP for a deliverable requires significant judgment. We use BESP to estimate the selling price for licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize BESP to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating our BESP, we evaluate whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

We recognize revenue when there is persuasive evidence that an arrangement exists, services have been rendered or delivery has occurred, the price is fixed or determinable, and collection is reasonably assured.

For certain of our arrangements, particularly our license agreement with Almirall, it is required that taxes be withheld on payments to us. We have adopted a policy to recognize revenue net of these tax withholdings.

Up-Front License Fees

We recognize revenues from nonrefundable, up-front license fees related to collaboration and license agreements entered into before January 1, 2011, including the $70.0 million up-front license fee under the Forest collaboration agreement entered into in September 2007, the $40.0 million up-front license fee, of which approximately $38.0 million was received net of foreign withholding taxes, under the Almirall license agreement entered into in April 2009 and the $30 million up-front license fee

under the Astellas license agreement entered into in November 2009, on a straight-line basis over the contracted or estimated period of performance since the license deliverables were not deemed to have value on a standalone basis under pre-ASU 2009-13 guidance and we could not determine the fair value of the undelivered elements. The period of performance over which the revenues are recognized is typically the period over which the research and/or development is expected to occur. As a result, we often are required to make estimates regarding drug development and commercialization timelines for compounds being developed pursuant to a collaboration or license agreement. Because the drug development process is lengthy and our collaboration and license agreements typically cover activities over several years, this approach has resulted in the deferral of significant amounts of revenue into future periods. In addition, because of the many risks and uncertainties associated with the development of drug candidates, our estimates regarding the period of performance may change in the future. Any change in our estimates could result in substantial changes to the period over which the revenues from an up-front license fee are recognized. In June 2011, we revised our estimate of the development period associated with our Almirall license agreement from 50 months to 41 months and adjusted the amortization of the remaining deferred revenue accordingly. In March 2013, we revised our estimate of the development period associated with our Astellas license agreement from 115 months to 85 months and adjusted the amortization of the remaining deferred revenue accordingly. Aside from these changes, we have had no other material changes to our estimated periods of continuing involvement under existing collaboration and license agreements. At September 30, 2012, the up-front license fees under the Forest and Almirall collaborations were fully amortized.

We recognize revenue allocated to the license related to collaboration and license agreements entered into or materially modified on or after January 1, 2011, including the amounts allocated to the license under the AstraZeneca collaboration agreement entered into in October 2012, upon delivery, when we believe the license to our intellectual property has stand-alone value. When we recognize revenue allocated to the license upon delivery under any of our collaborations, we may experience significant fluctuations in our collaborative arrangements revenues from quarter to quarter and year to year depending on the timing of transactions. When we believe the license to our intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, it is combined with other deliverables and the revenue of the combined unit of accounting is recorded based on the method appropriate for the last delivered item.

Milestones

At the inception of each arrangement that includes pre-commercial milestone payments, we evaluate whether each pre-commercial milestone is substantive, in accordance with ASU No. 2010-17, *Revenue Recognition—Milestone Method,* or ASU 2010-17, adopted on January 1, 2011. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. If a substantive pre-commercial milestone is achieved and collection of the related receivable is reasonably assured, we recognize revenue related to the milestone in its entirety in the period in which the milestone is achieved. At December 31, 2013, we had no pre-commercial milestones that were deemed substantive. If we were to achieve milestones that we consider substantive under any of our collaborations, we may experience significant fluctuations in our collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of achieving such substantive milestones. In those circumstances where a pre-commercial milestone is not

substantive, we recognize as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved, with the balance being deferred and recognized over the remaining period of performance.

Commercial milestones are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Net Profit or Net Loss Sharing

The determination of whether we should recognize revenue on a gross or net basis involves judgment based on the relevant facts and circumstances. In accordance with ASC 808 Topic, *Collaborative Arrangements*, and ASC 605-45, *Principal Agent Considerations*, we consider the nature and contractual terms of the arrangement and the nature of our business operations to determine the classification of the transactions under our collaboration agreements. We record revenue transactions gross in the consolidated statements of operations if we are deemed the principal in the transaction, which includes being the primary obligor and having the risks and rewards of ownership.

We recognize our share of the pre-tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are reported by Forest and related cost of goods sold and selling, general and administrative expenses are incurred by us and our collaboration partner. These amounts are partially determined based on amounts provided by Forest and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co-payment assistance costs, which could be adjusted based on actual results in the future. We are highly dependent on Forest for timely and accurate information regarding any net revenues realized from sales of LINZESS and the costs incurred in selling it, in order to accurately report our results of operations. For the periods covered in the consolidated financial statements presented, there have been no significant or material changes to prior period estimates of revenues, cost of goods sold and selling, general and administrative expenses associated with the sales of LINZESS in the U.S. However, if we do not receive timely and accurate information or incorrectly estimate activity levels associated with the collaboration at a given point in time, we could be required to record adjustments in future periods.

We record our share of the net profits or net losses from the sales of LINZESS on a net basis and present the settlement payments to and from Forest as collaboration expense or collaborative arrangements revenue, as applicable, as we are not the primary obligor and do not have the risks and rewards of ownership in the collaboration agreement with Forest. We and our collaboration partner settle the cost sharing quarterly and each payment represents 50% of LINZESS net sales in the U.S. as well as the cost sharing settlement of selling, general and administrative expenses and cost of goods sold between us and Forest. Prior to the fourth quarter of 2012, selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses. The cost-sharing payments to Forest for the nine months ended September 30, 2012 were reclassified to conform to the current period's presentation. Prior to 2012, such selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses and were not material to the consolidated financial statements.

Royalties on Product Sales

We receive or expect to receive in the future royalty revenues under certain of our license or collaboration agreements. If we do not have any future performance obligations under these license or collaborations agreements, we record these revenues as earned. To the extent we do not have access to the royalty reports from our partners or the ability to accurately estimate the royalty revenue in the period earned, we record such royalty revenues one quarter in arrears.

Other

We produce finished drug product, API and development materials for certain of our collaborators. We recognize revenue on finished drug product, API and development materials when the material has passed all quality testing required for collaborator acceptance, delivery has occurred, title and risk of loss have transferred to the collaborator, the price is fixed or determinable, and collection is reasonably assured. As it relates to development materials and API produced for Almirall and Astellas, we are reimbursed at a contracted rate. Such reimbursements are considered as part of revenue generated by Almirall and Astellas license agreements and presented as collaborative arrangements revenue. Any finished drug product, API and development materials currently produced for Forest or AstraZeneca are recognized in accordance with the cost-sharing provisions of the Forest and AstraZeneca collaboration agreements, respectively. We may experience fluctuations in our collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of such transactions.

Inventory Valuation and Related Reserves

Inventory is stated at the lower of cost or market with cost determined under the first-in, first-out basis.

We evaluate inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements or inventory that fails to meet commercial sale specifications is written down with a corresponding charge to cost of revenue in the period that the impairment is first identified.

We capitalize inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, we evaluate, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales, including the existence of current or anticipated competitive drugs and the availability of reimbursement. In addition, we evaluate risks associated with manufacturing the product candidate, including the ability of our third-party suppliers to complete the validation batches, and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred.

There is a risk inherent in these judgments and any changes in these judgments may have a material impact on our financial results in future periods.

Research and Development Expense

All research and development expenses are expensed as incurred. We defer and capitalize nonrefundable advance payments we make for research and development activities until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits and other employee-related expenses; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; costs associated with linaclotide API prior to us concluding that regulatory approval is probable and that its net realizable value is recoverable; licensing fees for our product candidates; and other outside expenses.

Clinical trial expenses include expenses associated with contract research organizations, or CROs. The invoicing from CROs for services rendered can lag several months. We accrue the cost of services rendered in connection with CRO activities based on our estimate of site management, monitoring costs, project management costs, and investigator fees. We maintain regular communication with our CRO vendors to gauge the reasonableness of our estimates. Differences between actual clinical trial expenses and estimated clinical trial expenses recorded have not been material and are adjusted for in the period in which they become known. However, if we incorrectly estimate activity levels associated with the CRO services at a given point in time, we could be required to record material adjustments in future periods. Under our Forest and AstraZeneca collaboration agreements, we are reimbursed for certain research and development expenses and we net these reimbursements against our research and development expenses as incurred. Payments to Forest or AstraZeneca are recorded as incremental research and development expense. Nonrefundable advance payments for research and development activities are capitalized and expensed over the related service period or as goods are received.

Share-based Compensation Expense

We make certain assumptions in order to value and record expense associated with awards made under our share-based compensation arrangements. We estimate the fair value of the share-based awards for employees and non-employees using the Black-Scholes option-pricing model. Determining the fair value of share-based awards requires the use of highly subjective assumptions, including expected term of the award and expected stock price volatility. For certain of these awards, we determine the appropriate amount to expense based on the anticipated achievement of performance targets, which requires judgment, including forecasting the achievement of future specified targets. Changes in these assumptions may lead to variability with respect to the amount of expense we recognize in connection with share-based payments.

We recognize compensation expense on a straight-line basis over the requisite service period based upon options that are ultimately expected to vest, and accordingly, such compensation expense is adjusted by the amount of estimated forfeitures. We estimate forfeitures over the requisite service period when recognizing share-based compensation expense based on historical rates and forward-looking factors; these estimates are adjusted to the extent that actual forfeitures differ, or are expected to materially differ, from our estimates.

We have also granted time-accelerated stock options with terms that allow the acceleration in vesting of the stock options upon the achievement of performance-based milestones specified in the grants. Share-based compensation expense associated with these time-accelerated stock options is recognized over the requisite service period of the awards or the implied service period, if shorter.

While the assumptions used to calculate and account for share-based compensation awards represents management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to our underlying assumptions and estimates, our share-based compensation expense could vary significantly from period to period.

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial statements.

	Years Ended December 31,		
	2013	2012	2011
	(in thousands)		
Collaborative arrangements revenue	$ 22,881	$150,245	$ 65,871
Cost and expenses:			
Cost of revenue	7,203	965	—
Research and development	102,378	113,474	86,093
Selling, general and administrative	123,228	92,538	45,920
Collaboration expense[1]	42,074	16,030	—
Total cost and expenses	274,883	223,007	132,013
Loss from operations	(252,002)	(72,762)	(66,142)
Other income (expense):			
Interest expense	(21,002)	(59)	(63)
Interest and investment income	192	197	456
Other income	—	—	900
Other income (expense), net	(20,810)	138	1,293
Net loss before income tax expense	(272,812)	(72,624)	(64,849)
Income tax expense	—	—	3
Net loss	$(272,812)	$(72,624)	$(64,852)

(1) Collaboration expense for the year ended December 31, 2011 is included in selling, general and administrative expense and was not material.

Year Ended December 31, 2013 Compared to Year Ended December 31, 2012

Revenue

	Years Ended December 31,		Change	
	2013	2012	$	%
	(dollars in thousands)			
Collaborative arrangements revenue	$22,881	$150,245	$(127,364)	(85)%

Collaborative Arrangements Revenue. The decrease in collaborative arrangements revenue of approximately $127.4 million for the year ended December 31, 2013 compared to the year ended December 31, 2012 was primarily related to an $85.0 million decrease in revenue related to the achievement of milestones under the Forest collaboration agreement related to the approval of the linaclotide NDAs for both IBS-C and CIC in August 2012, an approximately $33.2 million decrease in the amortization of deferred revenue associated with the development phase of the arrangements with Forest and Almirall as the performance periods ended in the third quarter of 2012, and an approximately $23.7 million decrease in revenue recognized under the AstraZeneca collaboration agreement primarily associated with revenue recognized upon delivery of the license in 2012. These decreases were partially offset by an approximately $8.0 million increase in revenue from shipments of linaclotide API, primarily to Almirall, an approximately $2.9 million increase in our share of the net profits and net losses from the sale of LINZESS in the U.S., an approximately $1.9 million increase in revenue related to the achievement of certain commercial launch milestones in our arrangement with

Almirall (net of foreign tax withholdings), an approximately $1.5 million increase in revenue related to the amortization of deferred revenue associated with the Astellas license agreement due to a change in estimate in the development period, and an approximately $0.2 million increase in royalty revenue based on sales of CONSTELLA in the European territory.

Cost and Expenses

	Years Ended December 31,		Change	
	2013	2012	$	%
	(dollars in thousands)			
Cost and expenses:				
Cost of revenue	$ 7,203	$ 965	$ 6,238	646%
Research and development	102,378	113,474	(11,096)	(10)%
Selling, general and administrative	123,228	92,538	30,690	33%
Collaboration expense	42,074	16,030	26,044	162%
Total cost and expenses	$274,883	$223,007	$ 51,876	23%

Cost of Revenue. The increase in cost of revenue of approximately $6.2 million for the year ended December 31, 2013 compared to the year ended December 31, 2012 was primarily related to the cost of linaclotide API sold to our licensing partners. We expensed most of the manufacturing costs of linaclotide API as research and development expenses in the periods prior to July 1, 2012. In the third quarter of 2012, we began capitalizing inventory costs for linaclotide API manufactured in preparation for our planned launch in the U.S. and Europe based on our evaluation of, among other factors, the status of linaclotide NDAs in the U.S., the CHMP positive recommendation to grant marketing approval for CONSTELLA in Europe, and the ability of our third-party suppliers to successfully manufacture commercial quantities of linaclotide API, which provided us with reasonable assurance that the net realizable value of the inventory would be recoverable. As of December 31, 2012, the previously expensed commercial API inventory was substantially utilized.

Research and Development Expense. The decrease in research and development expense of approximately $11.1 million for the year ended December 31, 2013 compared to the year ended December 31, 2012 was primarily related to a decrease of approximately $7.9 million in research costs related to our early stage pipeline candidates, an approximately $4.8 million decrease in external costs related to the development of linaclotide, an approximately $2.4 million decrease in operating costs, including facility costs such as rent and amortization of leasehold improvements allocated to research and development, and an approximately $1.6 million decrease in costs related to the collaboration with Forest. These decreases were partially offset by an increase of approximately $2.8 million in information technology and other operating costs allocated to research and development, an approximately $1.9 million increase in costs related to the collaboration with AstraZeneca, which was executed in October 2012, an approximately $0.6 million increase related to the development of manufacturing processes and costs associated with linaclotide API prior to meeting our inventory capitalization policy, an approximately $0.2 million increase in compensation, benefits, and employee related expenses primarily related to increased average headcount and increased healthcare costs, and an approximately $0.1 million increase in share-based compensation expense primarily related to our new hire grants and our annual stock option grant made in February 2013.

Selling, General and Administrative Expense. Selling, general and administrative expenses increased approximately $30.7 million for the year ended December 31, 2013 compared to the year ended December 31, 2012 primarily as a result of increases in our workforce expenses and infrastructure due to the launch and commercialization of LINZESS in the U.S. These increases include approximately $26.5 million in compensation, benefits and other employee related expenses associated with increased

average headcount, primarily due to our field sales force, approximately $9.4 million in costs associated with selling expenses and marketing programs, approximately $4.0 million in selling, general and administrative expenses related to facilities and information technology infrastructure costs associated with operating our Cambridge, Massachusetts facility, including rent and amortization of leasehold improvements; and approximately $2.2 million in share-based compensation expense primarily related to increased average headcount and our annual stock option grant made in February 2013. These increases were partially offset by an approximately $11.4 million decrease in external consulting and other service costs primarily associated with developing and maintaining the infrastructure to support linaclotide.

Collaboration Expense. Collaboration expense increased approximately $26.0 million for the year ended December 31, 2013 compared to the year ended December 31, 2012, primarily as a result of higher selling, general and administrative expenses incurred by us and Forest and higher cost of goods sold reported by Forest under our collaboration agreement, partially offset by our share of higher LINZESS net sales in the U.S.

Other Income (Expense), Net

	Years Ended December 31,		Change	
	2013	2012	$	%
	(dollars in thousands)			
Other income (expense):				
Interest expense	$(21,002)	$(59)	$(20,943)	35,497%
Interest and investment income	192	197	(5)	(3)%
Total other income (expense), net	$(20,810)	$138	$(20,948)	(15,180)%

Interest Expense. Interest expense increased approximately $20.9 million for the year ended December 31, 2013 compared to the year ended December 31, 2012, primarily due to interest on our $175.0 million in aggregate principal amount notes issued in January 2013.

Year Ended December 31, 2012 Compared to Year Ended December 31, 2011

Revenue

	Years Ended December 31,		Change	
	2012	2011	$	%
	(dollars in thousands)			
Collaborative arrangements revenue	$150,245	$65,871	$84,374	128%

Collaborative Arrangements Revenue. The increase in collaborative arrangements revenue of approximately $84.4 million for the year ended December 31, 2012 compared to the year ended December 31, 2011 was primarily related to the additional $65.0 million in milestone payments we earned under the Forest collaboration agreement and approximately $24.7 million in revenue earned under the AstraZeneca collaboration agreement, principally related to the license for linaclotide in China. In August 2012, we achieved two milestones totaling $85.0 million under the Forest collaboration agreement due to the FDA's approval of the linaclotide NDAs for both IBS-C and CIC. In 2011, we achieved two milestones totaling $20.0 million upon the FDA's acceptance of the linaclotide NDA for both IBS-C and CIC. Additionally, during 2012, we recognized approximately $3.4 million more in shipments of linaclotide API, primarily to Almirall in anticipation of a potential commercial launch in Europe in the first half of 2013. These increases were partially offset by an approximately $8.7 million decrease in the amortization of deferred revenue associated with the development phase of

the collaboration and license agreements with Forest and Almirall as the performance periods ended in September 2012.

Cost and Expenses

	Years Ended December 31,		Change	
	2012	2011	$	%
	(dollars in thousands)			
Cost and expenses:				
Cost of revenue	$ 965	$ —	$ 965	100%
Research and development	113,474	86,093	27,381	32%
Selling, general and administrative	92,538	45,920	46,618	102%
Collaboration expense	16,030	—	16,030	100%
Total cost and expenses	$223,007	$132,013	$90,994	69%

Cost of Revenue. The increase in cost of revenue of approximately $1.0 million for the year ended December 31, 2012 compared to the year ended December 31, 2011 was related to our inventory capitalization policy. We expensed most of the manufacturing costs of API for linaclotide as research and development expenses in the periods prior to July 1, 2012. In the third quarter of 2012, we began capitalizing inventory costs for linaclotide API manufactured in preparation for our planned launch in the U.S. and Europe based on our evaluation of, among other factors, the status of linaclotide NDAs in the U.S., the CHMP positive recommendation to grant marketing approval for CONSTELLA in Europe, and the ability of our third-party suppliers to successfully manufacture commercial quantities of linaclotide API, which provided us with reasonable assurance that the net realizable value of the inventory would be recoverable.

Research and Development Expense. The increase in research and development expense of approximately $27.4 million for the year ended December 31, 2012 compared to the year ended December 31, 2011 was primarily related to an increase of approximately $10.8 million in compensation, benefits, and employee-related expenses associated mainly with increased headcount; an increase of approximately $6.7 million associated with linaclotide development, consisting of increased contract manufacturing costs associated with validation of batches of linaclotide API in anticipation of a potential commercial launch, higher collaboration expenses from Forest and decreased reimbursements from Forest, partially offset by a decrease in contract research associated with lower clinical trial expenses; an increase of approximately $3.8 million in research and development related facilities costs, including rent, property taxes and amortization of leasehold improvements, associated with additional space we leased and improved in our Cambridge, Massachusetts facility; an increase of approximately $3.1 million in research costs related to our other pipeline candidates, including research and development fees, and up-front and milestone payments associated with our licensing agreements; and an increase of approximately $3.0 million in share-based compensation expense primarily related to our new hire grants and our annual stock option grant made in February 2012.

Selling, General and Administrative Expense. Selling, general and administrative expenses increased approximately $46.6 million for the year ended December 31, 2012 compared to the year ended December 31, 2011 primarily as a result of increases in our workforce expenses and infrastructure due to the commercial launch of LINZESS in the U.S. These increases include approximately $25.3 million in compensation, benefits and other employee-related expenses associated with increased headcount, mainly due to our field sales force; external consulting costs of approximately $13.7 million primarily associated with developing the infrastructure to commercialize and support LINZESS, including sales training and conferences; approximately $2.1 million in selling, general and administrative expenses related to facilities and information technology infrastructure costs associated with operating our

Cambridge, Massachusetts facility, including rent and amortization of leasehold improvements; approximately $3.0 million in corporate legal, patent and other professional service fees; and approximately $2.8 million in share-based compensation expense primarily related to our new hire grants and our annual stock option grant made in February 2012. These increases were offset by an approximately $0.3 million decrease in amounts related to the cost-sharing arrangement with Forest, which are presented as collaboration expense in the year ended December 31, 2012 and were not reclassified from selling, general and administrative expense in 2011 as the amount was not material to the consolidated financial statements.

Collaboration Expense. Collaboration expense increased approximately $16.0 million for the year ended December 31, 2012 compared to the year ended December 31, 2011, primarily as a result of a net increase in selling and marketing expenses incurred by Forest under our collaboration agreement, partially offset by our share of LINZESS net sales in the U.S. Prior to 2012, such selling and marketing cost-sharing payments were presented within selling, general and administrative expenses.

Other Income (Expense), Net

	Years Ended December 31,		Change	
	2012	2011	$	%
	(dollars in thousands)			
Other income (expense):				
Interest expense	$(59)	$ (63)	$ 4	(6)%
Interest and investment income	197	456	(259)	(57)%
Other income	—	900	(900)	(100)%
Total other income (expense), net	$138	$1,293	$(1,155)	(89)%

Other Income. The decrease in other income for the year ended December 31, 2012 compared to the year ended December 31, 2011 was primarily due to the timing of tax incentives or awards we received. In 2011, we recognized a Life Sciences Tax Incentive Program award of $0.9 million from the Massachusetts Life Sciences Center.

Liquidity and Capital Resources

We have incurred losses since our inception on January 5, 1998 and, as of December 31, 2013, we had an accumulated deficit of approximately $777.8 million. We have financed our operations to date primarily through the sale of preferred stock and common stock, including approximately $203.2 million of net proceeds from our initial public offering and approximately $223.0 million of net proceeds from our follow-on public stock offerings, payments received under collaborative arrangements, including up-front and milestone payments as well as reimbursement of certain expenses, debt financings, including approximately $167.3 million in net proceeds from our debt financing in January 2013 and interest earned on investments. At December 31, 2013, we had approximately $197.6 million of unrestricted cash, cash equivalents and available-for-sale securities. Our cash equivalents include amounts held in money market funds and U.S. government sponsored securities. Our available-for-sale securities include amounts held in U.S. Treasury securities and U.S. government sponsored securities. We invest cash in excess of immediate requirements in accordance with our investment policy, which limits the amounts we may invest in any one type of investment and requires all investments held by us to be at least A+ rated, with a remaining maturity when purchased of less than twelve months, so as to primarily achieve liquidity and capital preservation.

During the year ended December 31, 2013, our balances of cash, cash equivalents and available-for-sale securities decreased approximately $29.4 million. This decrease is primarily due to the cash used to operate our business, as we made payments related to, among other things, research and

development and selling, general and administrative expenses as we continued to invest in our research pipeline and support the continued commercialization of LINZESS in the U.S. We also invested approximately $9.6 million in capital expenditures and made payments of approximately $0.8 million on our capital leases. These uses of cash were partially offset by approximately $167.3 million in net proceeds from our debt financing in January 2013, approximately $137.8 million in net proceeds from our follow-on public stock offering in the second quarter of 2013, and approximately $9.3 million in proceeds from the exercise of stock options and the issuance of shares pursuant to our employee stock purchase plan.

Cash Flows From Operating Activities

Net cash used in operating activities totaled approximately $273.4 million for the year ended December 31, 2013. The primary uses of cash were our net loss of approximately $272.8 million and changes in assets and liabilities of approximately $35.7 million resulting primarily from a decrease in accounts payable and accrued expenses, including accrued research and development costs due to timing of payments, an increase in inventory for linaclotide API, a decrease in deferred revenue associated with the Astellas license agreement, a decrease in deferred rent and an increase accounts receivable. These uses of cash were partially offset by non-cash items of approximately $35.1 million, including approximately $19.8 million in share-based compensation expense, approximately $11.7 million in depreciation and amortization expense of property and equipment, approximately $1.7 million in non-cash interest expense, approximately $1.3 million in accretion of discounts and premiums on available-for-sale securities and approximately $0.6 million in losses on the disposal of property and equipment.

Net cash used in operating activities totaled approximately $69.6 million for the year ended December 31, 2012. The primary uses of cash were our net loss of approximately $72.6 million and changes in assets and liabilities of approximately $27.1 million resulting primarily from a decrease in deferred revenue associated mainly with the recognition of collaborative arrangements revenue from our Forest and Almirall agreements, an increase in inventory for linaclotide API manufactured in preparation for its sales launch in the U.S. and Europe, an increase in prepaid expenses and other current assets due to timing of payments, offset by increases in accounts payable and accrued expenses. These uses of cash were partially offset by non-cash items of approximately $30.1 million, including approximately $11.3 million in depreciation and amortization expense of property and equipment, approximately $17.6 million in share-based compensation expense and approximately $1.2 million in accretion of discounts and premiums on available-for-sale securities.

Net cash used in operating activities totaled approximately $75.2 million for the year ended December 31, 2011. The primary uses of cash were our net loss of approximately $64.9 million and changes in assets and liabilities of approximately $34.3 million resulting primarily from changes in deferred revenue associated with the recognition of revenue from our Forest collaboration agreement and our Almirall and Astellas license agreements, as well as the achievement of the milestone associated with the Almirall agreement. These uses of cash were partially offset by non-cash items of approximately $24.0 million, including approximately $10.0 million in depreciation and amortization expense of property and equipment, approximately $11.7 million in share-based compensation expense and approximately $2.2 million in accretion of discounts and premiums on available-for-sale securities.

Cash Flows From Investing Activities

Cash used in investing activities for the year ended December 31, 2013 totaled approximately $101.4 million and resulted primarily from the purchase of approximately $287.9 million of available-for-sale securities and the purchase of $9.6 million of property and equipment, primarily manufacturing and laboratory equipment as well as software to improve our information technology infrastructure. This was partially offset by the maturity of approximately $196.1 million in available-for-sale securities.

Cash provided by investing activities for the year ended December 31, 2012 totaled approximately $30.1 million and resulted primarily from the sale and maturity of approximately $140.8 million in available-for-sale securities. This was partially offset by the purchase of approximately $96.7 million of available-for-sale securities and the purchase of approximately $14.0 million of property and equipment, primarily leasehold improvements, associated with the expansion of our Cambridge, Massachusetts facility and software to improve our information technology infrastructure.

Cash provided by investing activities for the year ended December 31, 2011 totaled approximately $115.1 million and resulted primarily from the sale and maturity of approximately $222.3 million in available-for-sale securities. This was partially offset by the purchase of approximately $97.5 million of available-for-sale securities and the purchase of approximately $9.7 million of property and equipment, primarily leasehold improvements, associated with the expansion of our Cambridge, Massachusetts facility and software to improve our information technology infrastructure.

Cash Flows From Financing Activities

Cash provided by financing activities for the year ended December 31, 2013 totaled approximately $313.6 million and resulted primarily from approximately $167.3 million in net proceeds from our debt financing in January 2013, approximately $137.8 million in net proceeds from our follow-on public stock offering in the second quarter of 2013 and approximately $9.3 million in cash provided by stock option exercises and the issuance of shares under the employee stock purchase plan, partially offset by approximately $0.8 million in cash used for payments on our capital leases.

Cash provided by financing activities for the year ended December 31, 2012 totaled approximately $89.0 million and resulted primarily from approximately $85.2 million in net proceeds from our follow-on public stock offering in February 2012, approximately $4.0 million in cash provided by stock option exercises and the purchase of shares under the employee stock purchase plan, partially offset by approximately $0.3 million in cash used for payments on our capital leases.

Cash provided by financing activities for the year ended December 31, 2011 totaled approximately $3.1 million and resulted primarily from the approximately $3.4 million in cash provided by stock option exercises and the purchase of shares under the employee stock purchase plan, partially offset by approximately $0.3 million in cash used for payments on our capital leases.

Funding Requirements

In August 2012, we received regulatory approval for LINZESS in the U.S. for the treatment of IBS-C or CIC in adults and, in December 2012, commenced our commercial launch with our collaboration partner, Forest. While we began commercializing LINZESS in the fourth quarter of 2012, we have not achieved profitability. In November 2012, our European partner, Almirall, received approval for CONSTELLA for the treatment of IBS-C in adults, which is currently being commercialized in certain European countries by Almirall. Our partnership with Forest requires total net sales of LINZESS to be reduced by commercial costs incurred by each party, and such resulting net profit or net loss attributable to LINZESS is shared equally between us and Forest. Additionally, we receive royalties which escalate based on sales volume for CONSTELLA. We cannot anticipate when, if ever, proceeds generated from sales of LINZESS and CONSTELLA will enable the Company to become cash flow positive. We anticipate that we will continue to incur substantial expenses for the next several years as we further develop and commercialize linaclotide in the U.S., China and other markets, and continue to invest in our pipeline and potentially other external opportunities. In addition, we are generally required to make cash expenditures to manufacture linaclotide API in advance of selling it to our collaboration partners and collecting payments for such inventory sales, which may result in significant periodic uses of cash. We believe that our cash on hand as of December 31, 2013 will be sufficient to meet our projected operating needs at least through the next twelve months.

Our forecast of the period of time through which our financial resources will be adequate to support our operations, including the underlying estimates regarding the costs to obtain regulatory approval and the costs to commercialize linaclotide in the U.S., China and other markets, is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially and negatively as a result of a number of factors, including the factors discussed in the "Risk Factors" section of this Annual Report on Form 10-K. We have based our estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Due to the numerous risks and uncertainties associated with the development of our product candidates, we are unable to estimate precisely the amounts of capital outlays and operating expenditures necessary to complete the development of, and to obtain regulatory approval for, linaclotide (other than in the U.S. and E.U.) and our other product candidates for all of the markets, indications, populations and formulations for which we believe each product candidate is suited. Our funding requirements will depend on many factors, including, but not limited to, the following:

- the rate of progress and cost of our commercialization activities;
- the expenses we incur in marketing and selling LINZESS and any other products;
- the revenue generated by sales of LINZESS, CONSTELLA and any other products;
- the success of our third-party manufacturing activities;
- the time and costs involved in obtaining regulatory approvals for our product candidates;
- the success of our research and development efforts;
- the emergence of competing or complementary developments;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish; and
- the acquisition of businesses, products and technologies.

Financing Strategy

We may, from time to time, consider additional funding through a combination of new collaborative arrangements, strategic alliances, and additional equity and debt financings or from other sources. We will continue to manage our capital structure and to consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. Any such capital transactions may or may not be similar to transactions in which we have engaged in the past. There can be no assurance that any such financing opportunities will also be available on acceptable terms, if at all.

Contractual Commitments and Obligations

Lease and Commercial Supply Obligations

The following table summarizes our lease and commercial supply obligations at December 31, 2013 (excluding interest):

	Payments Due by Period				
	Total	Less Than 1 Year	1–3 Years	3–5 Years	More Than 5 Years
			(in thousands)		
Commercial supply obligations[1]	$ 37,886	$ 8,656	$13,750	$10,420	$5,060
Capital lease obligations[2]	4,856	1,434	3,422	—	—
Operating lease obligations[3]	58,861	13,072	29,407	16,382	—
Total contractual obligations	$101,603	$23,162	$46,579	$26,802	$5,060

(1) We have multiple commercial supply agreements with contract manufacturing organizations for the purchase of linaclotide finished drug product and API. The table above reflects our minimum purchase requirements under these commercial supply agreements, as well as any outstanding non-cancellable purchase orders, related to the supply contracts associated with the territories not covered by our collaboration with Forest. In addition, we and Forest are jointly obligated to make minimum purchases of linaclotide API for the territories covered by our collaboration with Forest. Currently, Forest fulfills all such minimum purchase commitments and, as a result, they are excluded from the table above.

(2) Our commitment for capital lease obligations principally relates to leased automobiles for our field-based sales force and medical science liaisons, and computer and office equipment.

(3) Our commitments for operating leases relate to our lease of office and laboratory space in Cambridge, Massachusetts and our data storage space in Boston, Massachusetts.

Notes Payable

In addition, on January 4, 2013, we closed a private placement of $175.0 million in aggregate principal amount of notes due on or before June 15, 2024. The notes bear an annual interest rate of 11%, with interest payable March 15, June 15, September 15 and December 15 of each year (each a "Payment Date") beginning June 15, 2013. From and after March 15, 2014, we will make quarterly payments on the notes equal to the greater of (i) 7.5% of net sales of LINZESS in the U.S. for the preceding quarter (the "Synthetic Royalty Amount") and (ii) accrued and unpaid interest on the notes (the "Required Interest Amount"). Principal on the notes will be repaid in an amount equal to the Synthetic Royalty Amount minus the Required Interest Amount, when this is a positive number, until the principal has been paid in full. Given the principal payments on the notes are based on the net sales of LINZESS in the U.S., which will vary from quarter to quarter, the notes may be repaid prior to June 15, 2024, the final legal maturity date. Since we are unable to reliably estimate the exact timing and amounts of the principal payments, as discussed under "Risk Factors" in Item 1A of this Annual Report on Form 10-K, the notes-related commitments are not included in the table above.

Commitments Related to Our Collaboration and License Agreements

Under our collaborative agreements with Forest and AstraZeneca, we share with Forest and AstraZeneca all development and commercialization costs related to linaclotide in the U.S. and China, respectively. The actual amounts that we pay our partners or that partners pay to us will depend on numerous factors outside of our control, including the success of our clinical development efforts with respect to linaclotide, the content and timing of decisions made by the regulators, the reimbursement

and competitive landscape around linaclotide and our other product candidates, and other factors described under "Risk Factors" in Item 1A of this Annual Report on Form 10-K.

In addition, we have commitments to make potential future milestone payments to third parties under certain of our license and collaboration arrangements totaling $364.0 million, which include $98.5 million for development milestones and $265.5 million for regulatory milestones. We are also committed to make potential future milestone payments of up to $114.5 million per product to one of our collaboration partners, including $21.5 million for development milestones, $58.0 million for regulatory milestones and $35.0 million for sales-based milestones. These milestones primarily include the commencement and results of clinical trials, obtaining regulatory approval in various jurisdictions and the future commercial success of development programs, the outcome and timing of which are difficult to predict and subject to significant uncertainty. In addition to the milestones discussed above, we are obligated to pay royalties on future sales, which are contingent on generating levels of sales of future products that have not been achieved and may never be achieved. Since we are unable to reliably estimate the timing and amounts of such milestone and royalty payments, or whether they will occur at all, these contingent payments have been excluded from the table above. See Note 4, "Collaboration and License Agreements," in the accompanying notes to consolidated financial statements for additional information regarding our license and collaboration arrangements.

Other Funding Commitments

As of December 31, 2013, we have several on-going studies in various clinical trial stages. Our most significant clinical trial expenditures are to CROs. The contracts with CROs generally are cancellable, with notice, at our option and do not have any significant cancellation penalties. These items are not included in the table above.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, that would have been established for the purpose of facilitating off-balance sheet arrangements (as that term is defined in Item 303(a)(4)(ii) of Regulation S-K) or other contractually narrow or limited purposes. As such, we are not exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in those types of relationships. We enter into guarantees in the ordinary course of business related to the guarantee of our own performance and the performance of our subsidiaries.

New Accounting Pronouncements

For a discussion of new accounting pronouncements please refer to Note 2, "Summary of Significant Accounting Policies", to our consolidated financial statements included in this report.

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

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies and money market instruments. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates, particularly because our investments are in short-term marketable securities. Due to the short-term duration of our investment portfolio and the low risk profile of our

investments, an immediate 1% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

We do not believe our cash, cash equivalents and available-for-sale securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and available-for-sale securities 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, cash equivalents and available-for-sale securities at one or more financial institutions that are in excess of federally insured limits. Given the recent instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits.

Our capital lease and debt obligations bear interest at a fixed rate and therefore have minimal exposure to changes in interest rates; however, because these interest rates are fixed, we may be paying a relatively higher interest rate in the future if our credit rating improves or other circumstances change.

Foreign Currency Risk

We have no significant operations outside the U.S. and we do not expect to be impacted significantly by foreign currency fluctuations.

Effects of Inflation

We do not believe that inflation and changing prices over the years ended December 31, 2013, 2012 and 2011 had a significant impact on our results of operations.

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

Our consolidated financial statements, together with the independent registered public accounting firm report thereon, appear at pages F-1 through F-47, of this Annual Report on Form 10-K.

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

As required by Rule 13a-15(b) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation as of the end of the period covered by this Annual Report on Form 10-K of the effectiveness of the design and operation of our disclosure controls and procedures. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures are effective at the reasonable assurance level in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of assets;

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with the authorizations of management and directors; and

(3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2013.

The effectiveness of our internal control over financial reporting as of December 31, 2013 has been audited by Ernst and Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

Changes in Internal Control

As required by Rule 13a-15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the quarter ended December 31, 2013 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. Based on that evaluation, our principal executive officer and principal financial officer concluded no such changes during the quarter ended December 31, 2013 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Ironwood Pharmaceuticals, Inc.

We have audited Ironwood Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) (the COSO criteria). Ironwood Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, Ironwood Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2013, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Ironwood Pharmaceuticals, Inc. as of December 31, 2013 and 2012, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2013 of Ironwood Pharmaceuticals, Inc. and our report dated February 7, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 7, 2014

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

None.

PART III

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

We have adopted a code of business conduct and ethics applicable to our directors, executive officers and all other employees. A copy of that code is available on our corporate website at http://www.ironwoodpharma.com. Any amendments to the code of business conduct and ethics, and any waivers thereto involving our executive officers, also will be available on our corporate website. A printed copy of these documents will be made available upon request. The content on our website is not incorporated by reference into this Annual Report on Form 10-K.

Certain information regarding our executive officers is set forth at the end of Part I, Item 1 of this Form 10-K under the heading, "Executive Officers of the Registrant." The other information required by this item is incorporated by reference from our proxy statement for our 2014 Annual Meeting of Stockholders.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference from our proxy statement for our 2014 Annual Meeting of Stockholders.

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

The information relating to security ownership of certain beneficial owners of our common stock and information relating to the security ownership of our management required by this item is incorporated by reference from our proxy statement for our 2014 Annual Meeting of Stockholders.

The table below sets forth information with regard to securities authorized for issuance under our equity compensation plans as of December 31, 2013. As of December 31, 2013, we had three active equity compensation plans, each of which was approved by our stockholders:

- Our Amended and Restated 2005 Stock Incentive Plan;
- Our Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan; and
- Our Amended and Restated 2010 Employee Stock Purchase Plan.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants, and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders	20,927,874	$8.87	7,868,767
Equity compensation plans not approved by security holders	—	—	—
Total	20,927,874	$8.87	7,868,767

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

The information required by this item is incorporated by reference from our proxy statement for our 2014 Annual Meeting of Stockholders.

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

The information required by this item is incorporated by reference from our proxy statement for our 2014 Annual Meeting of Stockholders.

PART IV

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

(a) List of documents filed as part of this report

(1) Consolidated Financial Statements listed under Part II, Item 8 and included herein by reference.

(2) Consolidated Financial Statement Schedules

No schedules are submitted because they are not applicable, not required or because the information is included in the Consolidated Financial Statements or Notes to Consolidated Financial Statements.

(3) Exhibits

		Incorporated by reference herein	
Number	**Description**	**Form**	**Date**
3.1	Eleventh Amended and Restated Certificate of Incorporation	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
3.2	Fifth Amended and Restated Bylaws	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
4.1	Specimen Class A common stock certificate	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 20, 2010
4.2	Eighth Amended and Restated Investors' Rights Agreement, dated as of September 1, 2009, by and among Ironwood Pharmaceuticals, Inc., the Founders and the Investors named therein	Registration Statement on Form S-1, as amended (File No. 333-163275)	November 20, 2009
4.3	Indenture, dated as of January 4, 2013, by and between Ironwood Pharmaceuticals, Inc., as issuer of the Notes, and U.S. Bank National Association, as initial trustee of the Notes and as Operating Bank	Form 8-K (File No. 001-34620)	January 8, 2013
10.1#	Amended and Restated 2002 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.2#	Amended and Restated 2005 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 29, 2010
10.3#	Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Registration Statement on Form S-8, as amended (File No. 333-184396)	October 12, 2012

Number	Description	Incorporated by reference herein	
		Form	Date
10.3.1#	Form of Stock Option Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
10.3.2#*	Form of Non-employee Director Restricted Stock Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan		
10.4#	Amended and Restated 2010 Employee Stock Purchase Plan	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.5#	Change of Control Severance Benefit Plan	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.6#*	Director Compensation Plan effective January 1, 2014		
10.7#	Form of Indemnification Agreement with Directors and Officers	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.8#	Consulting Agreement, dated as of November 30, 2009, by and between Christopher Walsh and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.9+	Collaboration Agreement, dated as of September 12, 2007, as amended on November 3, 2009, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.9.1	Amendment No. 2 to the Collaboration Agreement, dated as of January 8, 2013, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.10+	License Agreement, dated as of April 30, 2009, by and between Almirall, S.A. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.10.1+	Amendment No. 1 to License Agreement, dated as of June 11, 2013, by and between Almirall, S.A. and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 8, 2013

Number	Description	Incorporated by reference herein	
		Form	Date
10.11+	License Agreement, dated as of November 10, 2009, by and among Astellas Pharma Inc. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.12+	Collaboration Agreement, dated as of October 23, 2012, by and between AstraZeneca AB and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.13+	Commercial Supply Agreement, dated as of June 23, 2010, by and among PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB, Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 10, 2010
10.14+	Commercial Supply Agreement, dated as of March 28, 2011, by and among Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	May 13, 2011
10.14.1++*	Amendment No. 3 to Commercial Supply Agreement, dated as of November 26, 2013, by and between Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.		
10.15	Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 12, 2007, as amended on April 9, 2009, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.15.1	Second Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 9, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010

Number	Description	Incorporated by reference herein	
		Form	Date
10.15.2	Third Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 1, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2011
10.15.3	Fourth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 3, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2011
10.15.4	Fifth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 18, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 29, 2012
10.15.5	Sixth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 19, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.15.6	Seventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 30, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
21.1*	Subsidiaries of Ironwood Pharmaceuticals, Inc.		
23.1*	Consent of Independent Registered Public Accounting Firm		
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		

Number	Description	Incorporated by reference herein	
		Form	Date
32.1‡	Certification of Chief Executive Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
32.2‡	Certification of Chief Financial Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
101.INS*	XBRL Instance Document		
101.SCH*	XBRL Taxonomy Extension Schema Document		
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document		
101.LAB*	XBRL Taxonomy Extension Label Linkbase Database		
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document		
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document		

* Filed herewith.

‡ Furnished herewith.

\+ Confidential treatment granted under 17 C.F.R. §§200.80(b)(4) and 230.406. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

++ Confidential treatment requested under 17 C.F.R. §200.80(b)(4) and Rule 24b-2. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

\# Management contract or compensatory plan, contract, or arrangement.

(b) Exhibits.

The exhibits required by this Item are listed under Item 15(a)(3).

(c) Financial Statement Schedules.

The financial statement schedules required by this Item are listed under Item 15(a)(2).

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on the 7th day of February 2014.

Ironwood Pharmaceuticals, Inc.

By: /s/ PETER M. HECHT
Peter M. Hecht, Ph.D.
Chief Executive Officer

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the date indicated.

Signature	Title	Date
/s/ PETER M. HECHT Peter M. Hecht	Chief Executive Officer and Director *(Principal Executive Officer)*	February 7, 2014
/s/ MICHAEL J. HIGGINS Michael J. Higgins	Chief Operating Officer & Chief Financial Officer *(Principal Financial Officer & Principal Accounting Officer)*	February 7, 2014
/s/ BRYAN E. ROBERTS Bryan E. Roberts	Chairman of the Board	February 7, 2014
/s/ GEORGE H. CONRADES George H. Conrades	Director	February 7, 2014
/s/ JOSEPH C. COOK, JR. Joseph C. Cook, Jr.	Director	February 7, 2014
/s/ DAVID A. EBERSMAN David A. Ebersman	Director	February 7, 2014
/s/ MARSHA H. FANUCCI Marsha H. Fanucci	Director	February 7, 2014

Signature	Title	Date
/s/ TERRANCE G. MCGUIRE Terrance G. McGuire	Director	February 7, 2014
/s/ EDWARD P. OWENS Edward P. Owens	Director	February 7, 2014
/s/ DAVID E. SHAW David E. Shaw	Director	February 7, 2014
/s/ CHRISTOPHER T. WALSH Christopher T. Walsh	Director	February 7, 2014

Index to Consolidated Financial Statements of
Ironwood Pharmaceuticals, Inc.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Shareholders of
Ironwood Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Ironwood Pharmaceuticals, Inc. as of December 31, 2013 and 2012, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Ironwood Pharmaceuticals, Inc. at December 31, 2013 and 2012, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the consolidated financial statements, effective January 1, 2011, the Company adopted Financial Accounting Standards Board Accounting Standards Update No. 2010-17, *Revenue Recognition—Milestone Method*.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Ironwood Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) and our report dated February 7, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 7, 2014

Ironwood Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2013	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$ 75,490	$ 136,700
Available-for-sale securities	122,112	31,528
Accounts receivable	513	457
Related party accounts receivable, net	2,700	1,030
Inventory	22,145	6,699
Prepaid expenses and other current assets	6,168	8,026
Total current assets	229,128	184,440
Restricted cash	8,147	7,647
Property and equipment, net	37,376	37,537
Other assets	4,311	283
Total assets	$ 278,962	$ 229,907
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,139	$ 14,217
Related party accounts payable, net	48	7,509
Accrued research and development costs	3,412	5,664
Accrued expenses	18,438	21,171
Current portion of capital lease obligations	1,139	261
Current portion of deferred rent	2,790	2,735
Current portion of deferred revenue	5,074	3,381
Total current liabilities	41,040	54,938
Capital lease obligations, net of current portion	3,134	308
Deferred rent, net of current portion	8,822	11,593
Deferred revenue, net of current portion	11,416	18,024
Notes payable	174,672	—
Other liabilities	1,653	992
Commitments and contingencies (Note 4, 10 and 11)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 75,000,000 shares authorized, no shares issued and outstanding	—	—
Class A common stock, $0.001 par value, 500,000,000 shares authorized and 102,803,093 and 78,253,074 shares issued and outstanding at December 31, 2013 and 2012, respectively	103	78
Class B common stock, $0.001 par value, 100,000,000 shares authorized and 18,362,037 and 29,512,253 shares issued and outstanding at December 31, 2013 and 2012, respectively	18	30
Additional paid-in capital	815,930	648,955
Accumulated deficit	(777,828)	(505,016)
Accumulated other comprehensive income	2	5
Total stockholders' equity	38,225	144,052
Total liabilities and stockholders' equity	$ 278,962	$ 229,907

The accompanying notes are an integral part of these consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Operations

(In thousands, except per share amounts)

	Years Ended December 31,		
	2013	2012	2011
Collaborative arrangements revenue	$ 22,881	$150,245	$ 65,871
Cost and expenses:			
Costs of revenue	7,203	965	—
Research and development	102,378	113,474	86,093
Selling, general and administrative	123,228	92,538	45,920
Collaboration expense	42,074	16,030	—
Total cost and expenses	274,883	223,007	132,013
Loss from operations	(252,002)	(72,762)	(66,142)
Other income (expense):			
Interest expense	(21,002)	(59)	(63)
Interest and investment income	192	197	456
Other income	—	—	900
Other income (expense), net	(20,810)	138	1,293
Net loss before income tax expense	(272,812)	(72,624)	(64,849)
Income tax expense	—	—	3
Net loss	$(272,812)	$(72,624)	$(64,852)
Net loss per share—basic and diluted	$ (2.35)	$ (0.68)	$ (0.65)
Weighted average number of common shares used in net loss per share—basic and diluted:	115,852	106,403	99,875

The accompanying notes are an integral part of these consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Comprehensive Loss

(In thousands)

	Years Ended December 31,		
	2013	2012	2011
Net loss	$(272,812)	$(72,624)	$(64,852)
Other comprehensive income (loss):			
Unrealized gains (losses) on available-for-sale securities	(3)	(1)	5
Total other comprehensive income (loss)	(3)	(1)	5
Comprehensive loss	$(272,815)	$(72,625)	$(64,847)

The accompanying notes are an integral part of these consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Class A common stock		Class B common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive income (loss)	Total stockholders' equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2010	48,202,089	$ 48	50,970,247	$ 51	$526,991	$(367,540)	$ 1	$ 159,551
Issuance of common stock upon exercise of stock options and employee stock purchase plan	112,433	—	1,463,449	2	3,391	—	—	3,393
Issuance of common stock awards	2,328	—	—	—	30	—	—	30
Cancellation of restricted common stock awards	—	—	(27,500)	—	—	—	—	—
Conversion of Class B common stock to Class A common stock	13,484,920	14	(13,484,920)	(14)	—	—	—	—
Share-based compensation expense related to issuance of stock options to non-employees	—	—	—	—	152	—	—	152
Share-based compensation expense related to issuance of stock options to employees and employee stock purchase plan	—	—	—	—	11,550	—	—	11,550
Repurchase and retirement of shares of common stock	—	—	(7,196)	—	—	—	—	—
Restricted common stock no longer subject to repurchase	—	—	—	—	27	—	—	27
Unrealized gain on short-term investments	—	—	—	—	—	—	5	5
Net loss	—	—	—	—	—	(64,852)	—	(64,852)
Balance at December 31, 2011	61,801,770	62	38,914,080	39	542,141	(432,392)	6	109,856
Issuance of common stock upon exercise of stock options and employee stock purchase plan	226,658	—	782,955	1	4,019	—	—	4,020
Issuance of common stock awards	2,364	—	—	—	30	—	—	30
Issuance of common stock upon public offering, net of offering costs of $5.9 million	6,037,500	6	—	—	85,222	—	—	85,228
Conversion of Class B common stock to Class A common stock	10,184,782	10	(10,184,782)	(10)	—	—	—	—
Share-based compensation expense related to issuance of stock options to non-employees	—	—	—	—	60	—	—	60
Share-based compensation expense related to issuance of stock options to employees and employee stock purchase plan	—	—	—	—	17,483	—	—	17,483
Restricted common shares subject to repurchase	—	—	—	—	(7)	—	—	(7)
Restricted common stock no longer subject to repurchase	—	—	—	—	7	—	—	7
Unrealized loss on short-term investments	—	—	—	—	—	—	(1)	(1)
Net loss	—	—	—	—	—	(72,624)	—	(72,624)

The accompanying notes are an integral part of these consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity (Continued)

(In thousands, except share amounts)

	Class A common stock		Class B common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive income (loss)	Total stockholders' equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2012	78,253,074	78	29,512,253	30	648,955	(505,016)	5	144,052
Issuance of common stock upon exercise of stock options and employee stock purchase plan	645,196	1	1,538,887	1	9,295	—	—	9,297
Issuance of common stock awards	10,772	—	—	—	28	—	—	28
Issuance of common stock upon public offering, net of offering costs of $7.9 million	11,204,948	11	—	—	137,755	—	—	137,766
Conversion of Class B common stock to Class A common stock	12,689,103	13	(12,689,103)	(13)	—	—	—	—
Share-based compensation expense related to issuance of stock options to non-employees	—	—	—	—	272	—	—	272
Share-based compensation expense related to issuance of stock options to employees and employee stock purchase plan	—	—	—	—	19,624	—	—	19,624
Restricted common stock no longer subject to repurchase	—	—	—	—	1	—	—	1
Unrealized loss on short-term investments	—	—	—	—	—	—	(3)	(3)
Net loss	—	—	—	—	—	(272,812)	—	(272,812)
Balance at December 31, 2013	102,803,093	$103	18,362,037	$ 18	$815,930	$(777,828)	$ 2	$ 38,225

The accompanying notes are an integral part of these consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(In thousands)

	Years Ended December 31,		
	2013	**2012**	**2011**
Cash flows from operating activities:			
Net loss	$(272,812)	$(72,624)	$(64,852)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	11,729	11,325	9,999
Loss on disposal of property and equipment	610	20	7
Share-based compensation expense	19,829	17,573	11,732
Accretion of discount/premium on investment securities	1,254	1,157	2,234
Non-cash interest expense	1,719	—	—
Changes in assets and liabilities:			
Accounts receivable and related party accounts receivable	(1,726)	(835)	2,243
Restricted cash	(500)	—	2,833
Prepaid expenses and other current assets	(52)	(5,127)	2,421
Inventory	(11,915)	(6,699)	—
Other assets	116	(145)	136
Accounts payable and accrued expenses	(11,724)	24,241	5,086
Accrued research and development costs	(2,252)	(1,346)	(1,130)
Deferred revenue	(4,915)	(36,016)	(45,012)
Deferred rent	(2,716)	(2,149)	(934)
Other liabilities	—	992	—
Net cash used in operating activities	(273,355)	(69,633)	(75,237)
Cash flows from investing activities:			
Purchases of available-for-sale securities	(287,943)	(96,709)	(97,511)
Sales and maturities of available-for-sale securities	196,102	140,757	222,254
Purchases of property and equipment	(9,592)	(13,979)	(9,682)
Proceeds from sale of property and equipment	—	9	4
Net cash provided by (used in) investing activities	(101,433)	30,078	115,065
Cash flows from financing activities:			
Proceeds from issuance of common stock	137,766	85,228	—
Proceeds from issuance of notes payable	175,000	—	—
Costs associated with issuance of notes payable	(7,717)	—	—
Proceeds from exercise of stock options, stock purchase plan	9,297	4,020	3,393
Payments on capital lease obligations	(768)	(275)	(260)
Net cash provided by financing activities	313,578	88,973	3,133
Net increase (decrease) in cash and cash equivalents	(61,210)	49,418	42,961
Cash and cash equivalents, beginning of period	136,700	87,282	44,321
Cash and cash equivalents, end of period	$ 75,490	$136,700	$ 87,282
Supplemental cash flow disclosures:			
Cash paid for interest	$ 18,428	$ 55	$ 64
Cash paid for income taxes	$ —	$ —	$ 3
Purchases under capital leases	$ 4,472	$ 247	$ 325

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of Business

Ironwood Pharmaceuticals, Inc. (the "Company") is an entrepreneurial pharmaceutical company focused on creating medicines that make a difference for patients, building value to earn the continued support of its fellow shareholders, and empowering its team to passionately pursue excellence. The Company's core strategy is to establish a leading gastrointestinal ("GI") therapeutics company, leveraging its development and commercial capabilities in addressing GI disorders as well as its pharmacologic expertise in guanylate cyclase ("GC") pathways.

The Company's lead product, linaclotide, is being marketed in the United States ("U.S.") under the trademarked name of LINZESS®. In August 2012, the United States Food and Drug Administration ("FDA") approved LINZESS as a once-daily treatment for adult men and women suffering from irritable bowel syndrome with constipation ("IBS-C") or chronic idiopathic constipation ("CIC"). LINZESS is the first and, to date, only FDA-approved guanylate cyclase type-C ("GC-C") agonist. The Company and its collaboration partner, Forest Laboratories, Inc. ("Forest"), began commercializing LINZESS in December 2012.

In November 2012, the European Commission granted marketing authorization to linaclotide (CONSTELLA®) for the symptomatic treatment of moderate to severe IBS-C in adults. CONSTELLA is the first and only drug approved in the European Union ("E.U.") for IBS-C. The Company's European partner, Almirall, S.A. ("Almirall"), has exclusive marketing rights for CONSTELLA in Europe (including the Commonwealth of Independent States and Turkey). Currently, CONSTELLA is commercially available in certain European countries, including the United Kingdom and Germany.

In December 2013, the Health Canada granted approval of CONSTELLA as a once-daily, first-in-class treatment for adult women and men suffering from IBS-C or CIC. Forest has exclusive rights to develop and commercialize linaclotide in Canada.

Astellas Pharma Inc. ("Astellas"), the Company's partner in Japan, is developing linaclotide for the treatment of patients with IBS-C in its territory. Astellas recently completed a double-blind, placebo-controlled, dose-ranging Phase II clinical trial of linaclotide in adult patients with IBS-C. In February 2014, the Company received preliminary top level data for the Phase II trial from Astellas indicating that, while all linaclotide dose groups showed numerically higher responder rates in the primary endpoint than placebo, the responder rates were not statistically significant compared to placebo in this study. Linaclotide was well tolerated in all dose groups in this study. Data analysis is still ongoing at Astellas to determine next steps.

In October 2012, the Company entered into a collaboration agreement with AstraZeneca AB ("AstraZeneca") to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. In the third quarter of 2013, the Company and AstraZeneca initiated a double-blind, placebo-controlled Phase III clinical trial of linaclotide in adult patients with IBS-C.

The Company continues to assess alternatives to bring linaclotide to IBS-C and CIC sufferers in the parts of the world outside of its partnered territories.

The Company is also exploring development opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various GI conditions. In addition to linaclotide-based opportunities, the Company is advancing multiple GI development programs as well as further leveraging its GC expertise

1. Nature of Business (Continued)

to advance a second GC program targeting soluble guanylate cyclase, a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

The Company was incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, the Company changed its name to Ironwood Pharmaceuticals, Inc. To date, the Company has dedicated substantially all of its activities to the research, development and commercialization of linaclotide, the Company's lead product and product candidate, as well as research and development of other product candidates. The Company has incurred significant operating losses since its inception in 1998. As of December 31, 2013, the Company had an accumulated deficit of $777.8 million.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Ironwood Pharmaceuticals, Inc. and its wholly owned subsidiaries, Ironwood Pharmaceuticals Securities Corporation and Ironwood Pharmaceuticals GmbH. All intercompany transactions and balances are eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in accordance with generally accepted accounting principles in the U.S. requires the Company's management to make estimates and judgments that may affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. On an on-going basis, the Company's management evaluates its estimates, including those related to revenue recognition, available-for-sale securities, inventory valuation and related reserves, impairment of long-lived assets, balance sheet classification of notes payable, income taxes including the valuation allowance for deferred tax assets, research and development expense, contingencies and share-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ from these estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

Cash and Cash Equivalents

The Company considers all highly liquid investment instruments with a remaining maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents primarily consist of money market funds and U.S. government-sponsored securities. The carrying amount of cash equivalents approximates fair value. The amount of cash equivalents included in cash and cash equivalents was approximately $67.3 million and approximately $113.9 million at December 31, 2013 and 2012, respectively.

Restricted Cash

The Company is contingently liable under unused letters of credit with a bank, related to the Company's facility and automobile lease agreements and credit card arrangements, in the amount of approximately $8.1 million and approximately $7.6 million as of December 31, 2013 and 2012,

2. Summary of Significant Accounting Policies (Continued)

respectively. As a result, the Company has restricted cash of approximately $8.1 million and approximately $7.6 million as of December 31, 2013 and 2012, respectively, securing these letters of credit. The cash will be restricted until the termination of the leases and credit card arrangements.

Available-for-Sale Securities

The Company classifies all short-term investments with a remaining maturity when purchased of greater than three months as available-for-sale. Available-for-sale securities are recorded at fair value, with the unrealized gains and losses reported in other comprehensive income (loss). The amortized cost of debt securities in this category is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, interest, dividends, and declines in value judged to be other than temporary on available-for-sale securities are included in interest and investment income.

The cost of securities sold is based on the specific identification method for purposes of recording realized gains and losses. To determine whether an other-than-temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary. There were no other-than-temporary impairments for the years ended December 31, 2013, 2012 and 2011.

Inventory

Inventory is stated at the lower of cost or market with cost determined under the first-in, first-out basis.

The Company evaluates inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements or inventory that fails to meet commercial sale specifications is written down with a corresponding charge to cost of revenue in the period that the impairment is first identified.

The Company capitalizes inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, the Company evaluates, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales, including the existence of current or anticipated competitive drugs and the availability of reimbursement. In addition, the Company evaluates risks associated with manufacturing the product candidate, including the ability of the Company's third-party suppliers to complete the validation batches, and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred.

Concentrations of Suppliers

The Company relies on third-party manufacturers and its collaboration partners to manufacture the linaclotide active pharmaceutical ingredient ("API") and final linaclotide drug product. Currently,

2. Summary of Significant Accounting Policies (Continued)

there are two third-party manufacturers approved for the production of the linaclotide API in three facilities. The Company's collaboration partners, except AstraZeneca in China, (Forest, Almirall and Astellas) are responsible for drug product manufacturing of linaclotide into finished product for their respective territories. The Company also has an agreement with another independent third party to serve as a second source of drug product manufacturing of linaclotide for its partnered territories. The Company and AstraZeneca also continue to explore manufacturing alternatives for China. If any of the Company's suppliers were to limit or terminate production or otherwise fail to meet the quality or delivery requirements needed to satisfy the supply commitments, the process of locating and qualifying alternate sources could require up to several months, during which time the Company's production could be delayed. Such delays could have a material adverse effect on the Company's business, financial position and results of operations.

Accounts Receivable and Related Valuation Account

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company's receivables primarily relate to amounts reimbursed under its collaboration and license agreements. The Company believes that credit risks associated with these collaborators are not significant. To date, the Company has not had any write-offs of bad debt, and as such, the Company does not have an allowance for doubtful accounts as of December 31, 2013 and 2012.

Concentrations of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents, restricted cash, available-for-sale securities, and accounts receivable. The Company maintains its cash and cash equivalent balances with high-quality financial institutions and, consequently, the Company believes that such funds are subject to minimal credit risk. The Company's available-for-sale investments primarily consist of U.S. Treasury securities and certain U.S. government sponsored securities and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy which limits the amounts the Company may invest in any one type of investment, and requires all investments held by the Company to be at least A+ rated, thereby reducing credit risk exposure.

Accounts receivable, including related party accounts receivable, primarily consist of amounts due under the collaboration agreement with Forest and license agreement with Astellas (Note 4) for which the Company does not obtain collateral. Accounts receivable or payable to or from Forest and Almirall are presented as related party transactions on the consolidated balance sheets as both entities own common stock of the Company.

2. Summary of Significant Accounting Policies (Continued)

The percentages of revenue recognized from significant customers of the Company in the years ended December 31, 2013, 2012 and 2011 as well as the account receivable balances, net of any payables due, at December 31, 2013 and 2012 are included in the following table:

	Accounts Receivable		Revenue		
	December 31,		Years Ended December 31,		
	2013	2012	2013	2012	2011
Collaborative Partner:					
Forest	84%	—%	13%	67%	64%
Almirall	—%	69%	57%	14%	31%
Astellas	16%	31%	25%	3%	5%
AstraZeneca	—%	—%	5%	16%	—%

As of December 31, 2013, the Company was in a net payable position with AstraZeneca; as such, there was no accounts receivable due from AstraZeneca as of December 31, 2013. As of December 31, 2012, the Company was in a net payable position with Forest; as such, there was no accounts receivable due from Forest as of December 31, 2012.

For the years ended December 31, 2013, 2012 and 2011, no additional customers accounted for more than 10% of the Company's revenue.

Revenue Recognition

The Company's revenue is generated through collaborative research and development and licensing agreements. The terms of these agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, including participation on joint steering committees, and (iii) the manufacture of finished drug product, API, or development materials for the collaborative partner which are reimbursed at a contractually determined rate. Non-refundable payments to the Company under these agreements may include (i) up-front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API, or development materials, (iv) payments based upon the achievement of certain milestones, and (v) royalties on product sales. Additionally, the Company may receive its share of the net profits or bear its share of the net losses from the sale of linaclotide in the U.S. and China through its collaborations with Forest and AstraZeneca, respectively.

At December 31, 2013, the Company had collaboration agreements with Forest and AstraZeneca and license agreements with Almirall and Astellas. Refer to Note 4, "Collaboration and License Agreements," for additional discussion of these agreements.

The Company recognizes revenue when there is persuasive evidence that an arrangement exists, services have been rendered or delivery has occurred, the price is fixed or determinable, and collection is reasonably assured.

For certain of our arrangements, particularly the license agreement with Almirall, it is required that taxes be withheld on payments to the Company. The Company has adopted a policy to recognize revenue net of these tax withholdings.

2. Summary of Significant Accounting Policies (Continued)

Agreements Entered into Prior to January 1, 2011

For arrangements that include multiple deliverables, the Company follows the provisions of the Accounting Standards Codification ("ASC") Topic 605-25, *Revenue Recognition—Multiple-Element Arrangements* ("ASC 605-25"), in accounting for these agreements. Under ASC 605-25, the Company was required to identify the deliverables included within the agreement and evaluate which deliverables represent separate units of accounting. Collaborative research and development and licensing agreements that contained multiple deliverables were divided into separate units of accounting when the following criteria were met:

- Delivered element(s) had value to the collaborator on a standalone basis,
- There was objective and reliable evidence of the fair value of the undelivered obligation(s), and
- If the arrangement included a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) was considered probable and substantially within the Company's control.

The Company allocated arrangement consideration among the separate units of accounting either on the basis of each unit's respective fair value or using the residual method, and applied the applicable revenue recognition criteria to each of the separate units. If the separation criteria were not met, revenue of the combined unit of accounting was recorded based on the method appropriate for the last delivered item.

Up-Front License Fees

The Company recognizes revenue from nonrefundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance, which is typically the period over which the research and development is expected to occur or manufacturing services are expected to be provided. Accordingly, the Company is required to make estimates regarding the drug development and commercialization timelines for drugs and drug candidates being developed pursuant to the applicable agreement. The determination of the length of the period over which to recognize the revenue is subject to judgment and estimation and can have an impact on the amount of revenue recognized in a given period. Quarterly, the Company reassesses its period of substantial involvement over which the Company amortizes its up-front license fees and makes adjustments as appropriate. The Company's estimates regarding the period of performance under its collaborative research and development and licensing agreements have changed in the past and may change in the future. In the event that a license were to be terminated, the Company would recognize as revenue any portion of the up-front fee that had not previously been recorded as revenue, but was classified as deferred revenue at the date of such termination. At December 31, 2013, only a portion of Astellas' up-front license fee remains deferred as the period of performance under the Forest and Almirall arrangements ended in the quarter ended September 30, 2012.

Agreements Entered into or Materially Modified on or after January 1, 2011

The Company evaluates revenue from new multiple element agreements entered into on or after January 1, 2011 under ASU No. 2009-13, *Multiple-Deliverable Revenue Arrangements* ("ASU 2009-13"), which was adopted on a prospective basis in January 2011. The Company also evaluates whether amendments to its multiple element arrangements are considered material modifications that are

2. Summary of Significant Accounting Policies (Continued)

subject to the application of ASU 2009-13. This evaluation requires management to assess all relevant facts and circumstances and to make subjective determinations and judgments. As part of this assessment, the Company considers whether the modification results in a material change to the arrangement, including whether there is a change in total arrangement consideration that is more than insignificant, whether there are changes in the deliverables included in the arrangement, whether there is a change in the term of the arrangement and whether there is a significant modification to the delivery schedule for contracted deliverables.

When evaluating multiple element arrangements under ASU 2009-13, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research, manufacturing and commercialization capabilities of the partner and the availability of peptide research and manufacturing expertise in the general marketplace. In addition, the Company considers whether the collaborator can use the license or other deliverables for their intended purpose without the receipt of the remaining elements, and whether the value of the deliverable is dependent on the undelivered items and whether there are other vendors that can provide the undelivered items.

The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. Determining the BESP for a deliverable requires significant judgment. The Company uses BESP to estimate the selling price for licenses to the Company's proprietary technology, since the Company often does not have VSOE or TPE of selling price for these deliverables. In those circumstances where the Company utilizes BESP to determine the estimated selling price of a license to the Company's proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company's BESP, the Company evaluates whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

At December 31, 2013, the Company has one collaboration agreement with AstraZeneca that is being accounted for under ASU 2009-13.

Up-Front License Fees

When management believes the license to its intellectual property has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. When management believes the license to its intellectual property does not have stand-alone value from the other

2. Summary of Significant Accounting Policies (Continued)

deliverables to be provided in the arrangement, it is combined with other deliverables and the revenue of the combined unit of accounting is recorded based on the method appropriate for the last delivered item.

Milestones

At the inception of each arrangement that includes pre-commercial milestone payments, the Company evaluates whether each pre-commercial milestone is substantive, in accordance with ASU No. 2010-17, *Revenue Recognition—Milestone Method ("*ASU 2010-17"), adopted on January 1, 2011. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. At December 31, 2013, the Company had no pre-commercial milestones that were deemed substantive. If a substantive pre-commercial milestone is achieved and collection of the related receivable is reasonably assured, the Company recognizes revenue related to the milestone in its entirety in the period in which the milestone is achieved. If the Company were to achieve milestones that are considered substantive under any of the Company's collaborations, the Company may experience significant fluctuations in collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of achieving such substantive milestones. In those circumstances where a pre-commercial milestone is not substantive, the Company recognizes as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved, with the balance being deferred and recognized over the remaining period of performance. Pre-commercial milestone payments received prior to the adoption of ASU 2010-17 continue to be recognized over the remaining period of performance.

Commercial milestones are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Net Profit or Net Loss Sharing

In accordance with ASC 808 Topic, *Collaborative Arrangements*, and ASC 605-45, *Principal Agent Considerations*, the Company considers the nature and contractual terms of the arrangement and the nature of the Company's business operations to determine the classification of the transactions under the Company's collaboration agreements. The Company records revenue transactions gross in the consolidated statements of operations if it is deemed the principal in the transaction, which includes being the primary obligor and having the risks and rewards of ownership.

The Company recognizes its share of the pre-tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are reported by Forest and related cost of goods sold and selling, general and administrative expenses are incurred by the Company and its collaboration partner. These amounts are partially determined based on amounts provided by Forest

2. Summary of Significant Accounting Policies (Continued)

and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co-payment assistance costs, which could be adjusted based on actual results in the future. The Company is highly dependent on Forest for timely and accurate information regarding any net revenues realized from sales of LINZESS and the costs incurred in selling it, in order to accurately report its results of operations. For the periods covered in the consolidated financial statements presented, there have been no material changes to prior period estimates of revenues, cost of goods sold or selling, general and administrative expenses associated with the sales of LINZESS in the U.S. However, if the Company does not receive timely and accurate information or incorrectly estimates activity levels associated with the collaboration at a given point in time, the Company could be required to record adjustments in future periods.

The Company records its share of the net profits or net losses from the sales of LINZESS in the U.S. on a net basis and presents the settlement payments to and from Forest as collaboration expense or collaborative arrangements revenue, as applicable, as the Company is not the primary obligor and does not have the risks and rewards of ownership in the collaboration agreement with Forest. The Company and Forest settle the cost sharing quarterly, such that the Company's statement of operations reflects 50% of the pre-tax net profit or loss generated from sales of LINZESS in the U.S. Prior to the fourth quarter of 2012, selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses. The cost-sharing payments to Forest for the nine months ended September 30, 2012 were reclassified to conform to the current period's presentation. Prior to 2012, such selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses and were not material to the consolidated financial statements.

Royalties on Product Sales

The Company receives or expects to receive in the future royalty revenues under certain of the Company's license or collaboration agreements. If the Company does not have any future performance obligations under these license or collaborations agreements, the Company records these revenues as earned. To the extent the Company does not have access to the royalty reports from the Company's partners or the ability to accurately estimate the royalty revenue in the period earned, the Company records such royalty revenues one quarter in arrears.

Other

The Company produces finished drug product, API and development materials for certain of its collaborators. The Company recognizes revenue on finished drug product, API and development materials when the material has passed all quality testing required for collaborator acceptance, delivery has occurred, title and risk of loss have transferred to the collaborator, the price is fixed or determinable, and collection is reasonably assured. As it relates to development materials and API produced for Almirall and Astellas, the Company is reimbursed at a contracted rate. Such reimbursements are considered as part of revenue generated pursuant to the Almirall and Astellas license agreements and are presented as collaborative arrangements revenue. Any finished drug product, API and development materials currently produced for Forest or AstraZeneca are recognized in accordance with the cost-sharing provisions of the Forest and AstraZeneca collaboration agreements, respectively.

2. Summary of Significant Accounting Policies (Continued)

Cost of Revenue

Cost of revenue is recognized upon shipment of linaclotide API to certain of the Company's collaboration partners and consists of the costs of producing such API. The costs of API were primarily recorded as research and development expenses in the periods prior to July 1, 2012. In the third quarter of 2012, the Company began capitalizing inventory costs for linaclotide API manufactured in preparation for its launch of linaclotide in the U.S. and Europe based on its evaluation of, among other factors, the status of the LINZESS NDAs in the U.S., the Committee for Medicinal Products for Human Use ("CHMP") positive recommendation to grant marketing approval for CONSTELLA in Europe, and the ability of the Company's third-party suppliers to successfully manufacture commercial quantities of linaclotide API, which provided the Company with reasonable assurance that the net realizable value of the inventory would be recoverable. As of December 31, 2012, the previously expensed commercial API inventory was substantially utilized.

Research and Development Costs

The Company expenses research and development costs to operations as incurred. The Company defers and capitalizes nonrefundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits and other employee-related expenses; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; costs associated with linaclotide API prior to the Company concluding that regulatory approval is probable and that its net realizable value is recoverable; licensing fees for our product candidates; and other outside expenses.

The Company has entered into collaboration agreements with Forest and AstraZeneca pursuant to which it shares research and development expenses with the collaborators. The Company records expenses incurred under the collaboration arrangements for such work as research and development expense. Because the collaboration arrangements are cost-sharing arrangements, the Company concluded that when there is a period during the collaboration arrangements during which the Company receives payments from Forest or AstraZeneca, the Company records the payments by Forest or AstraZeneca for their share of the development effort as a reduction of research and development expense. Payments to Forest or AstraZeneca are recorded as incremental research and development expense.

Selling, General and Administrative Expenses

The Company expenses selling, general and administrative costs to operations as incurred. Selling, general and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resource functions. Other costs include the legal costs of pursuing patent protection of the Company's intellectual property, general and administrative related facility costs and professional fees for accounting and legal services.

2. Summary of Significant Accounting Policies (Continued)

Under the Forest and AstraZeneca collaboration agreements, the Company is reimbursed for certain selling, general and administrative expenses and it nets these reimbursements against selling, general and administrative expenses as incurred. Payments to Forest or AstraZeneca are recorded as incremental selling, general and administrative expense.

Beginning in the fourth quarter of 2012, the Company includes Forest's selling, general and administrative cost-sharing payments in the calculation of the net profits and net losses from the sale of LINZESS in the U.S. and presents the net payment to or from Forest as collaboration expense or collaborative arrangements revenue, as applicable. The selling, general and administrative cost-sharing payments to Forest for the nine months ended September 30, 2012 were reclassified to conform to the current presentation. Prior to 2012, such Forest-related selling, general and administrative cost-sharing payments were presented within selling, general and administrative expenses and were not material to the consolidated financial statements.

Share-Based Compensation

The Company's stock-based compensation programs grant awards which have included stock awards, restricted stock, and stock options. Share-based compensation is recognized as an expense in the financial statements based on the grant date fair value over the requisite service period. For awards that vest based on service conditions, the Company uses the straight-line method to allocate compensation expense to reporting periods. The grant date fair value of options granted is calculated using the Black-Scholes option-pricing model, which requires the use of subjective assumptions including volatility and expected term, among others.

The Company records the expense for stock option grants subject to performance-based milestone vesting using the accelerated attribution method over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

The Company records the expense of services rendered by non-employees based on the estimated fair value of the stock option using the Black-Scholes option-pricing model. The fair value of unvested non-employee awards is remeasured at each reporting period and expensed over the vesting term of the underlying stock options.

Patent Costs

The Company incurred and recorded as operating expense legal and other fees related to patents of approximately $3.2 million, approximately $3.5 million, and approximately $2.2 million for the years ended December 31, 2013, 2012 and 2011, respectively. These costs were charged to selling, general and administrative expenses as incurred.

Net Income (Loss) Per Share

The Company calculates basic net income (loss) per common share and diluted net loss per common share by dividing the net income (loss) by the weighted average number of common shares outstanding during the period. Diluted net income per common share is computed by dividing net income by the diluted number of shares outstanding during the period. Except where the result would

2. Summary of Significant Accounting Policies (Continued)

be antidilutive to net income, diluted net income per share is computed assuming the exercise of common stock options and the vesting of restricted stock (using the treasury stock method), as well as their related income tax effects. The Company allocates undistributed earnings between the classes on a one-to-one basis when computing net income (loss) per share. As a result, basic and diluted net income (loss) per Class A and Class B shares are equivalent.

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost, and are depreciated when placed into service using the straight-line method based on their estimated useful lives as follows:

Asset Description	Estimated Useful Life (In Years)
Manufacturing equipment	10
Laboratory equipment	5
Computer and office equipment	3
Furniture and fixtures	7
Software	3

Included in property and equipment are certain costs of software obtained for internal use. Costs incurred during the preliminary project stage are expensed as incurred, while costs incurred during the application development stage are capitalized and amortized over the estimated useful life of the software. The Company also capitalizes costs related to specific upgrades and enhancements when it is probable the expenditures will result in additional functionality. Maintenance and training costs related to software obtained for internal use are expensed as incurred.

Leasehold improvements are amortized over the shorter of the estimated useful life of the asset or the lease term. Capital lease assets are amortized over the lease term. However, if ownership was transferred by the end of the capital lease, or there was a bargain purchase option, such capital lease assets would be amortized over the useful life that would be assigned if such assets were owned.

Costs for capital assets not yet placed into service have been capitalized as construction in progress, and will be depreciated in accordance with the above guidelines once placed into service. Maintenance and repair costs are expensed as incurred.

Income Taxes

The Company provides for income taxes under the liability method. Deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates in effect when the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to reflect the uncertainty associated with their ultimate realization.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return.

2. Summary of Significant Accounting Policies (Continued)

Impairment of Long-Lived Assets

The Company regularly reviews the carrying amount of its long-lived assets to determine whether indicators of impairment may exist, which warrant adjustments to carrying values or estimated useful lives. If indications of impairment exist, projected future undiscounted cash flows associated with the asset are compared to the carrying amount to determine whether the asset's value is recoverable. If the carrying value of the asset exceeds such projected undiscounted cash flows, the asset will be written down to its estimated fair value. There were no significant impairments of long-lived assets for the years ended December 31, 2013, 2012 or 2011.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions, and other events and circumstances from non-owner sources and currently consists of net loss and changes in unrealized gains and losses on available-for-sale securities.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's chief operating decision-maker in deciding how to allocate resources and in assessing performance. The Company currently operates in one reportable business segment—human therapeutics.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board or other standard setting bodies that are adopted by the Company as of the specified effective date. The Company did not adopt any new accounting pronouncements during the year ended December 31, 2013 that had a material effect on its consolidated financial statements.

3. Net Loss Per Share

The following table sets forth the computation of basic and diluted net loss per share (in thousands, except per share amounts):

	Years Ended December 31,		
	2013	2012	2011
Numerator:			
Net loss	$(272,812)	$(72,624)	$(64,852)
Denominator:			
Weighted average number of common shares used in net loss per share—basic and diluted	115,852	106,403	99,875
Net loss per share—basic and diluted	$ (2.35)	$ (0.68)	$ (0.65)

3. Net Loss Per Share (Continued)

The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding as they would be anti-dilutive (in thousands):

	Years Ended December 31,		
	2013	2012	2011
Options to purchase common stock	20,928	19,540	16,425
Shares subject to repurchase	—	80	160
	20,928	19,620	16,585

The number of shares issuable under the Company's employee stock purchase plan that were excluded from the calculation of diluted weighted average shares outstanding because their effects would be anti-dilutive was insignificant.

4. Collaboration and License Agreements

Forest Laboratories, Inc.

In September 2007, the Company entered into a collaboration agreement with Forest to develop and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in North America. Under the terms of this collaboration agreement, the Company shares equally with Forest all development costs as well as future net profits or losses from the development and sale of linaclotide in the U.S. The Company will also receive royalties in the mid-teens percent based on net sales in Canada and Mexico. Forest is solely responsible for the further development, regulatory approval and commercialization of linaclotide in those countries and funding any costs. In September 2012, Forest sublicensed its commercialization rights in Mexico to Almirall. Forest made non-refundable, up-front payments totaling $70.0 million to the Company in order to obtain rights to linaclotide in North America. Because the license to jointly develop and commercialize linaclotide did not have a standalone value without research and development activities provided by the Company, the Company recorded the up-front license fee as collaborative arrangements revenue on a straight-line basis through September 30, 2012, the period over which linaclotide was jointly developed under the collaboration. The collaboration agreement also includes contingent milestone payments, as well as a contingent equity investment, based on the achievement of specific development and commercial milestones. At December 31, 2013, $205.0 million in license fees and development milestone payments had been received by the Company, as well as a $25.0 million equity investment in the Company's capital stock. The Company can also achieve up to $100.0 million in a sales related milestone if certain conditions are met.

The collaboration agreement included a contingent equity investment, in the form of a forward purchase contract, which required Forest to purchase shares of the Company's convertible preferred stock upon achievement of a specific development milestone. At the inception of the arrangement, the Company valued the contingent equity investment and recorded an approximately $9.0 million asset and incremental deferred revenue. The $9.0 million of incremental deferred revenue was recognized as collaborative arrangements revenue on a straight-line basis over the period of the Company's continuing involvement through September 30, 2012. In July 2009, the Company achieved the development milestone triggering the equity investment and reclassified the forward purchase contract

4. Collaboration and License Agreements (Continued)

as a reduction to convertible preferred stock. On September 1, 2009, the Company issued 2,083,333 shares of convertible preferred stock to Forest (Note 16).

The Company achieved all six development milestones under this agreement. In September 2008 and July 2009, the Company achieved development milestones which triggered $10.0 million and $20.0 million milestone payments, respectively. These development milestones were recognized as collaborative arrangements revenue through September 2012. In October 2011, the Company achieved two development milestones upon the FDA's acceptance of the linaclotide New Drug Applications ("NDA") for both IBS-C and CIC in adults and received milestone payments totaling $20.0 million from Forest. In August 2012, the Company achieved two additional development milestones upon the FDA's approval of the linaclotide NDAs for both IBS-C and CIC in adults and received milestone payments totaling $85.0 million from Forest in September 2012, accordingly. In accordance with ASU 2010-17, these four development milestones were recognized as collaborative arrangements revenue in their entirety upon achievement. The remaining milestone payment that could be received from Forest upon the achievement of sales targets will be recognized as collaborative arrangements revenue as earned.

As a result of the research and development cost-sharing provisions of the collaboration, the Company recognized approximately $2.2 million and approximately $2.1 million in incremental research and development costs during the years ended December 31, 2013 and 2012, respectively, and offset approximately $7.9 million against research and development costs in the year ended December 31, 2011, to reflect its obligation under the collaboration to bear half of the development costs incurred by both parties.

The Company receives 50% of the net profits and bears 50% of the net losses from the commercial sale of LINZESS in the U.S., provided, however, that if either party provides fewer calls on physicians in a particular year than it is contractually required to provide, such party's share of the net profits will be reduced as stipulated by the collaboration agreement. Net profits or net losses consist of net sales to third-party customers and sublicense income in the U.S. less cost of goods sold as well as selling, general and administrative expenses. Net sales are calculated and recorded by Forest and may include gross sales net of discounts, rebates, allowances, sales taxes, freight and insurance charges, and other applicable deductions. The Company and Forest began commercializing LINZESS in December 2012.

The Company recognized collaborative arrangements revenue from the Forest collaboration agreement totaling approximately $2.9 million, approximately $100.4 million and approximately $41.8 million during the years ended December 31, 2013, 2012 and 2011, respectively. The collaborative arrangements revenue recognized in the year ended December 31, 2013 represents the Company's share of the net profits and net losses on the sale of LINZESS in the U.S. The collaborative arrangements revenue recognized in the years ended December 2012 and 2011 related to the substantive pre-commercial milestones earned and the amortization of deferred revenue.

4. Collaboration and License Agreements (Continued)

The following table presents the amounts recorded by the Company for commercial efforts related to LINZESS in the years ended December 31, 2013 and 2012 (in thousands):

	Year Ended December 31,	
	2013	2012
Collaborative arrangements revenue[1]	$ 2,914	$ —
Collaboration expense	(42,074)	(16,030)
Selling, general and administrative costs incurred by the Company[1]	(33,839)	(5,092)
The Company's share of net loss	$(72,999)	$(21,122)

(1) Includes only collaborative arrangement revenue or selling, general and administrative costs attributable to the cost-sharing arrangement with Forest.

Prior to 2012, selling, general and administrative cost-sharing payments presented within selling, general and administrative expenses were not material.

Almirall, S.A.

In April 2009, the Company entered into a license agreement with Almirall to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States and Turkey) for the treatment of IBS-C, CIC and other GI conditions. Under the terms of the license agreement, Almirall is responsible for the expenses associated with the development and commercialization of linaclotide in the European territory and the Company was required to participate on a joint development committee over linaclotide's development period.

In May 2009, the Company received an approximately $38.0 million payment from Almirall representing a $40.0 million non-refundable up-front payment net of foreign withholding taxes. The Company elected to record the non-refundable up-front payment net of taxes withheld. The Company recognized the up-front license fee as collaborative arrangements revenue on a straight-line basis through September 30, 2012, the period over which linaclotide was developed under the license agreement.

The license agreement also included a $15.0 million contingent equity investment, in the form of a forward purchase contract, which required Almirall to purchase shares of the Company's convertible preferred stock upon achievement of a specific development milestone. At the inception of the arrangement, the Company valued the contingent equity investment and recorded an approximately $6.0 million asset and incremental deferred revenue. The $6.0 million of incremental deferred revenue was recognized as collaborative arrangements revenue through September 2012. In November 2009, the Company achieved the development milestone triggering the equity investment and reclassified the forward purchase contract as a reduction to convertible preferred stock. On November 13, 2009, the Company received $15.0 million from Almirall for the purchase of 681,819 shares of convertible preferred stock (Note 16).

The original license agreement also included contingent milestone payments that could total up to $40.0 million upon achievement of specific development and commercial launch milestones. In

4. Collaboration and License Agreements (Continued)

November 2010, the Company achieved a development milestone, which resulted in a $19.0 million payment, representing a $20.0 million milestone, net of foreign withholding taxes. This development milestone was recognized as collaborative arrangements revenue through September 2012. Commercial milestone payments under the original license agreement consisted of $4.0 million due upon the first commercial launch in each of the five major E.U. countries set forth in the agreement.

In June 2013, the Company and Almirall amended the original license agreement. Pursuant to the terms of the amendment, (i) the commercial launch milestones were reduced to $17.0 million; (ii) new sales-based milestone payments were added to the agreement; and (iii) the escalating royalties based on sales of linaclotide were modified such that they begin in the low-twenties percent and escalate to the mid-forties percent through April 2017, and thereafter begin in the mid-twenties percent and escalate to the mid-forties percent at lower sales thresholds. In each case, these royalty payments are reduced by the transfer price paid for the API included in the product actually sold in the Almirall territory and other contractual deductions. The Company concluded that the amendment was not a material modification of the license agreement. The commercial launch and sales-based milestones are recognized as revenue as earned. The Company records royalties on sales of CONSTELLA one quarter in arrears as it does not have access to the royalty reports from Almirall or the ability to estimate the royalty revenue in the period earned.

During the second quarter of 2013, the Company achieved two milestones under the amended Almirall license agreement, which resulted in payments of approximately $1.9 million from Almirall to the Company related to the commercial launches in two of the five major E.U. countries, the United Kingdom and Germany. The approximately $1.9 million payment represented the two $1.0 million milestones, net of foreign tax withholdings.

The Company recognized approximately $13.1 million, approximately $21.2 million and approximately $20.6 million in total collaborative arrangements revenue from the Almirall license agreement during the years ended December 31, 2013, 2012 and 2011, respectively, including approximately $11.1 million, approximately $3.5 million and approximately $0.5 million, respectively, in revenue from the sale of API to Almirall as well as approximately $0.2 million in royalty revenue and approximately $1.9 million in commercial launch milestones in the year ended December 31, 2013.

Astellas Pharma Inc.

In November 2009, the Company entered into a license agreement with Astellas to develop and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in Japan, South Korea, Taiwan, Thailand, the Philippines and Indonesia. As a result of an amendment executed in March 2013, the Company regained rights to linaclotide in South Korea, Taiwan, Thailand, the Philippines and Indonesia. The Company concluded that the amendment was not a material modification of the license agreement. Astellas continues to be responsible for all activities relating to development, regulatory approval and commercialization in Japan as well as funding any costs and the Company is required to participate on a joint development committee over linaclotide's development period.

In 2009, Astellas paid the Company a non-refundable, up-front licensing fee of $30.0 million, which is being recognized as collaborative arrangements revenue on a straight-line basis over the Company's estimate of the period over which linaclotide will be developed under the license agreement. In March 2013, the Company revised its estimate of the development period from

4. Collaboration and License Agreements (Continued)

115 months to 85 months based on the Company's assessment of regulatory approval timelines for Japan. This resulted in the recognition of an additional approximately $1.5 million of revenue in the year ended December 31, 2013.

The agreement also includes additional development milestone payments that could total up to $45.0 million. These milestone payments, none of which the Company considers substantive, consist of $15.0 million upon initiation of a Phase III study for linaclotide in Japan, $15.0 million upon filing of the Japanese equivalent of an NDA with the relevant regulatory authority in Japan, and $15.0 million upon approval of such equivalent by the relevant regulatory authority. In addition, the Company will receive royalties which escalate based on sales volume, beginning in the low-twenties percent, less the transfer price paid for the API included in the product actually sold and other contractual deductions.

At December 31, 2013, approximately $16.5 million of the up-front license fee remains deferred. During the years ended December 31, 2013, 2012 and 2011, the Company recognized approximately $5.8 million, approximately $3.9 million and approximately $3.5 million, respectively, in revenue from the Astellas license agreement, including approximately $1.2 million, approximately $0.8 million, and approximately $0.4 million, respectively, from the sale of API to Astellas.

AstraZeneca AB

In October 2012, the Company entered into a collaboration agreement with AstraZeneca (the "AstraZeneca Collaboration Agreement") to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau (the "License Territory"). The collaboration provides AstraZeneca with an exclusive nontransferable license to exploit the underlying technology in the License Territory. The parties will share responsibility for continued development and commercialization of linaclotide under a joint development plan and a joint commercialization plan, respectively, with AstraZeneca having primary responsibility for the local operational execution.

The parties agreed to an Initial Development Plan ("IDP") which includes the planned development of linaclotide in China, including the lead responsibility for each activity and the related internal and external costs. The IDP indicates that AstraZeneca is responsible for a multinational Phase III clinical trial, the Company is responsible for nonclinical development and supplying clinical trial material and both parties are responsible for the regulatory submission process. The IDP indicates that the party specifically designated as being responsible for a particular development activity under the IDP shall implement and conduct such activities. The activities are governed by a Joint Development Committee ("JDC"), with equal representation from each party. The JDC is responsible for approving, by unanimous consent, the joint development plan and development budget, as well as approving protocols for clinical studies, reviewing and commenting on regulatory submissions, and providing an exchange of data information.

The AstraZeneca Collaboration Agreement will continue until there is no longer a development plan or commercialization plan in place, however, it can be terminated by AstraZeneca at any time upon 180 days' prior written notice. Under certain circumstances, either party may terminate the AstraZeneca Collaboration Agreement in the event of bankruptcy or an uncured material breach of the other party. Upon certain change in control scenarios of AstraZeneca, the Company may elect to terminate the AstraZeneca Collaboration Agreement and may re-acquire its product rights in a lump sum payment equal to the fair market value of such product rights.

4. Collaboration and License Agreements (Continued)

In connection with the AstraZeneca Collaboration Agreement, the Company and AstraZeneca also executed a co-promotion agreement (the "Co-Promotion Agreement"), pursuant to which the Company will utilize its existing sales force to co-promote NEXIUM® (esomeprazole magnesium), one of AstraZeneca's products, in the U.S. The Co-Promotion Agreement expires upon the earlier of May 27, 2014 or the date on which a generic version of AstraZeneca's product is first sold in the U.S. The Company may terminate the Co-Promotion Agreement on or after December 31, 2013 upon written notice to AstraZeneca.

There are no refund provisions in the AstraZeneca Collaboration Agreement and the Co-Promotion Agreement (together, the "AstraZeneca Agreements").

Under the terms of the AstraZeneca Collaboration Agreement, the Company received a $25.0 million non-refundable upfront payment upon execution. The Company is also eligible for $125.0 million in additional commercial milestone payments contingent on the achievement of certain sales targets. The parties will also share in the net profits and losses associated with the development and commercialization of linaclotide in the License Territory, with AstraZeneca receiving 55% of the net profits or incurring 55% of the net losses until a certain specified commercial milestone is achieved, at which time profits and losses will be shared equally thereafter.

Activities under the AstraZeneca Agreements were evaluated in accordance with ASC 605-25 to determine if they represented a multiple element revenue arrangement. The Company identified the following deliverables in the AstraZeneca Agreements:

- an exclusive license to develop and commercialize linaclotide in the License Territory (the "License Deliverable"),
- research, development and regulatory services pursuant to the IDP (the "R&D Services"),
- JDC services,
- obligation to supply clinical trial material, and
- co-promotion services for AstraZeneca's product (the "Co-Promotion Deliverable").

The License Deliverable is nontransferable and has certain sublicense restrictions. The Company determined that the License Deliverable had standalone value as a result of AstraZeneca's internal product development and commercialization capabilities, which would enable it to use the License Deliverable for its intended purposes without the involvement of the Company. The remaining deliverables were deemed to have standalone value based on their nature and all deliverables met the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in this determination included, among other things, whether any other vendors sell the items separately and if the customer could use the delivered item for its intended purpose without the receipt of the remaining deliverables.

The Company identified the supply of linaclotide drug product for commercial requirements and commercialization services as contingent deliverables because these services are contingent upon the receipt of regulatory approval to commercialize linaclotide in the License Territory, and there were no binding commitments or firm purchase orders pending for commercial supply. As these deliverables are contingent, and are not at an incremental discount, they are not evaluated as deliverables at the inception of the arrangement. These contingent deliverables will be evaluated and accounted for

4. Collaboration and License Agreements (Continued)

separately as each related contingency is resolved. As of December 31, 2013, no contingent deliverables were provided by the Company under the AstraZeneca Agreements.

The total amount of the non-contingent consideration allocable to the AstraZeneca Agreements of approximately $26.9 million ("Arrangement Consideration") includes the $25.0 million non-refundable upfront payment and 55% of the costs for clinical trial material supply services and research, development and regulatory activities allocated to the Company in the IDP, or approximately $1.9 million. The Company allocated the Arrangement Consideration of approximately $26.9 million to the non-contingent deliverables based on management's BESP of each deliverable using the relative selling price method as the Company did not have VSOE or TPE of selling price for such deliverables. The Company estimated the BESP for the License Deliverable using a multi-period excess-earnings method under the income approach which utilized cash flow projections, the key assumptions of which included the following market conditions and entity-specific factors: (a) the specific rights provided under the license to develop and commercialize linaclotide; (b) the potential indications for linaclotide pursuant to the license; (c) the likelihood linaclotide will be developed for more than one indication; (c) the stage of development of linaclotide for IBS-C and CIC and the projected timeline for regulatory approval; (d) the development risk by indication; (f) the market size by indication; (g) the expected product life of linaclotide assuming commercialization; (h) the competitive environment, and (i) the estimated development and commercialization costs of linaclotide in the License Territory. The Company utilized a discount rate of 11.5% in its analysis, representing the weighted average cost of capital derived from returns on equity for comparable companies. The Company determined its BESP for the remaining deliverables based on the nature of the services to be performed and estimates of the associated effort and cost of the services adjusted for a reasonable profit margin such that they represented estimated market rates for similar services sold on a standalone basis.

The Company concluded that a change in key assumptions used to determine BESP for each deliverable would not have a significant effect on the allocation of the Arrangement Consideration, as the estimated selling price of the License Deliverable significantly exceeds the other deliverables.

Of the approximately $26.9 million Arrangement Consideration, approximately $24.7 million was allocated to the License Deliverable, approximately $0.3 million to the R&D Services, approximately $28,000 to the JDC services, approximately $0.1 million to the clinical trial material supply services, and approximately $1.8 million to the Co-Promotion Deliverable in the relative selling price model. The Company recognized all $24.7 million allocated to the License Deliverable as revenue upon the execution of the AstraZeneca Agreements as the associated unit of accounting had been delivered and there is no general right of return. At inception, the remaining approximately $0.3 million of the Arrangement Consideration received and allocated to the remaining deliverables based on their relative selling prices, was deferred.

Because the Company shares development costs with AstraZeneca, payments from AstraZeneca with respect to both research and development and selling, general and administrative costs incurred by the Company prior to the commercialization of linaclotide in the License Territory are recorded as a reduction to expense, in accordance with the Company's policy, which is consistent with the nature of the cost reimbursement. Development costs incurred by the Company that pertain to the IDP are recorded as research and development expense as incurred. Payments to AstraZeneca are recorded as incremental research and development expense.

4. Collaboration and License Agreements (Continued)

The Company will perform the R&D Services, JDC services and supply clinical trial materials during the estimated development period of approximately 44 months. All Arrangement Consideration allocated to such services is being recognized as a reduction of research and development costs, using the proportional performance method, by which the amounts are recognized in proportion to the costs incurred. As a result of the cost-sharing arrangements under the collaboration, the Company recognized approximately $1.9 million in incremental research and development costs during the year ended December 31, 2013. Research and development costs incurred during the year ended December 31, 2012 were not significant.

The amount allocated to the Co-Promotion Deliverable is being recognized as collaborative arrangements revenue using the proportional performance method, which approximates recognition on a straight-line basis beginning on the date that the Company began to co-promote AstraZeneca's product, through December 31, 2013 (the earliest cancellation date). Through December 31, 2013, the Company earned all consideration allocated to the Co-Promotion Deliverable but recognized approximately $1.0 million as collaborative arrangement revenue. The revenue recognized in the statement of operations was limited to the non-contingent consideration at December 31, 2013 in accordance with ASC 605-25.

The Company reassesses the periods of performance for each deliverable at the end of each reporting period.

Milestone payments received from AstraZeneca upon the achievement of sales targets will be recognized as earned.

Other Collaboration and License Agreements

The Company has other collaboration and license agreements that are not individually significant to its business. In connection with entering into these agreements, the Company made aggregate up-front payments of approximately $5.8 million, which were expensed as research and development expense. Pursuant to the terms of certain of those agreements, the Company may be required to pay $99.5 million for development milestones, of which $1.0 million had been paid, and $265.5 million for regulatory milestones, none of which had been paid, in each case as of December 31, 2013. In addition, pursuant to the terms of another agreement, the contingent milestones could total up to $114.5 million per product to one of the Company's collaboration partners, including $21.5 million for development milestones, $58.0 million for regulatory milestones and $35.0 million for sales-based milestones. Further, under such agreements, the Company is also required to fund certain research activities and, if any product related to these collaborations is approved for marketing, to pay significant royalties on future sales. During the years ended December 31, 2013, 2012 and 2011, the Company incurred approximately $3.6 million, approximately $8.2 million and approximately $6.0 million, respectively, in research and development expense associated with the Company's other collaboration and license agreements.

5. Fair Value of Financial Instruments

The tables below present information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2013 and 2012 and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize observable inputs such as quoted prices in active markets for

5. Fair Value of Financial Instruments (Continued)

identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are either directly or indirectly observable, such as quoted prices, interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points in which there is little or no market data, which require the Company to develop its own assumptions for the asset or liability.

The Company's investment portfolio includes many fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. In addition, model processes were used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data.

The following tables present the assets the Company has measured at fair value on a recurring basis (in thousands):

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2013	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents:				
Money market funds	$ 59,747	$59,747	$ —	$—
U.S. government-sponsored securities	7,505	—	7,505	—
Available-for-sale securities:				
U.S. Treasury securities	7,253	7,253	—	—
U.S. government-sponsored securities	114,859	—	114,859	—
Total	$189,364	$67,000	$122,364	$—

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2012	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents:				
Money market funds	$111,368	$111,368	$ —	$—
U.S. government-sponsored securities	2,500	—	2,500	—
Available-for-sale securities:				
U.S. Treasury securities	15,052	15,052	—	—
U.S. government-sponsored securities	16,476	—	16,476	—
Total	$145,396	$126,420	$18,976	$—

There were no transfers between Level 1 and Level 2 of the fair value hierarchy during the years ended December 31, 2013 or 2012.

5. Fair Value of Financial Instruments (Continued)

Cash equivalents, accounts receivable, including related party accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses and the current portion of capital lease obligations at December 31, 2013 and 2012 are carried at amounts that approximate fair value due to their short-term maturities.

The non-current portion of the capital lease obligations at December 31, 2013 and 2012 approximates fair value as it bears interest at a rate approximating a market interest rate.

6. Available-for-Sale Securities

The following tables summarize the available-for-sale securities held at December 31, 2013 and 2012 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2013:				
U.S. government-sponsored securities	$114,857	$6	$(4)	$114,859
U.S. Treasury securities	7,253	—	—	7,253
Total	$122,110	$6	$(4)	$122,112

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2012:				
U.S. government-sponsored securities	$16,472	$5	$(1)	$16,476
U.S. Treasury securities	15,051	1	—	15,052
Total	$31,523	$6	$(1)	$31,528

The contractual maturities of all securities held at December 31, 2013 are one year or less. There were 12 and 3 investments classified as available-for-sale securities in an unrealized loss position at December 31, 2013 and 2012, respectively, none of which had been in an unrealized loss position for more than twelve months. The aggregate fair value of these securities at December 31, 2013 and 2012 was approximately $38.7 million and approximately $3.0 million, respectively. The Company reviews its investments for other-than-temporary impairment whenever the fair value of an investment is less than amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity. The Company did not hold any securities with other-than-temporary impairment at December 31, 2013.

There were no sales of available-for-sale securities during the year ended December 31, 2013. The proceeds from maturities and sales of available-for-sale securities were approximately $89.8 million and approximately $51.0 million for the year ended December 31, 2012, respectively, and approximately

6. Available-for-Sale Securities (Continued)

$212.3 million and approximately $10.0 million for the year ended December 31, 2011, respectively. Gross realized gains and losses on the sales of available-for-sale securities that have been included in other income (expense), net unrealized holding gains or losses for the period that have been included in accumulated other comprehensive income as well as gains and losses reclassified out of accumulated other comprehensive income into other income (expense) were not material to the Company's consolidated results of operations. The cost of securities sold or the amount reclassified out of the accumulated other comprehensive income into other income (expense) is based on the specific identification method for purposes of recording realized gains and losses.

7. Inventory

Inventory consisted of the following (in thousands):

	December 31,	
	2013	2012
Raw materials	$22,145	$6,699

In the third quarter of 2012, the Company began capitalizing inventory costs for linaclotide manufactured in preparation for its launch in the U.S. and Europe based on its evaluation of, among other factors, the status of the LINZESS NDAs in the U.S., the CHMP positive recommendation to grant marketing approval for CONSTELLA in Europe, and the ability of its third-party suppliers to successfully manufacture commercial quantities of linaclotide API, which provided the Company with reasonable assurance that the net realizable value of the inventory would be recoverable. As of December 31, 2012, the previously expensed commercial API inventory was substantially utilized. Inventory at December 31, 2013 and 2012 represents API that is available for commercial sale.

8. Property and Equipment

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2013	2012
Manufacturing equipment	$ 2,812	$ —
Laboratory equipment	14,039	16,315
Computer and office equipment	5,202	6,476
Furniture and fixtures	2,365	2,449
Software	12,352	11,047
Construction in process	996	1,460
Leased vehicles	4,472	—
Leasehold improvements	36,827	36,770
	79,065	74,517
Less accumulated depreciation and amortization	(41,689)	(36,980)
	$ 37,376	$ 37,537

The Company has entered into capital leases for certain computer, vehicles and office equipment (Note 11). As of December 31, 2013 and 2012, the Company had approximately $5.5 million and

8. Property and Equipment (Continued)

approximately $1.4 million, respectively, of assets under capital leases with accumulated amortization balances of approximately $1.2 million and approximately $0.9 million, respectively.

Depreciation and amortization expense of property and equipment, including equipment recorded under capital leases, was approximately $11.7 million, approximately $11.3 million, and approximately $10.0 million for the years ended December 31, 2013, 2012 and 2011, respectively.

In October 2012, the Company entered into an amendment to its Cambridge, Massachusetts building lease, pursuant to which the term of the lease was extended by 24 months. As a result of this amendment, the Company extended on a prospective basis the period over which it amortizes its leasehold improvements.

9. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2013	2012
Salaries and benefits	$13,784	$14,594
Professional fees	531	1,031
Accrued interest	856	—
Other	3,267	5,546
	$18,438	$21,171

10. Notes Payable

On January 4, 2013, the Company closed a private placement of $175.0 million in aggregate principal amount of notes due on or before June 15, 2024. The notes bear an annual interest rate of 11%, with interest payable March 15, June 15, September 15 and December 15 of each year (each a "Payment Date") beginning June 15, 2013. From and after March 15, 2014, the Company will make quarterly payments on the notes equal to the greater of (i) 7.5% of net sales of LINZESS in the U.S. for the preceding quarter (the "Synthetic Royalty Amount") and (ii) accrued and unpaid interest on the notes (the "Required Interest Amount"). Principal on the notes will be repaid in an amount equal to the Synthetic Royalty Amount minus the Required Interest Amount, when this is a positive number, until the principal has been paid in full. Given the principal payments on the notes are based on the Synthetic Royalty Amount, which will vary from quarter to quarter, the notes may be repaid prior to June 15, 2024, the final legal maturity date. The Company has not made any principal payments since January 4, 2013 and does not expect to make significant principal payments within twelve months following December 31, 2013. As such, the outstanding principal balance was classified as a long term liability as of December 31, 2013.

The notes are secured solely by a security interest in a segregated bank account established to receive the required quarterly payments. Up to the amount of the required quarterly payments under the notes, Forest will deposit its quarterly profit (loss) sharing payments due to the Company under the collaboration agreement, if any, into the segregated bank account. If the funds deposited by Forest into the segregated bank account are insufficient to make a required payment of interest or principal on a

10. Notes Payable (Continued)

particular Payment Date, the Company is obligated to deposit such shortfall out of the Company's general funds into the segregated bank account.

The notes may be redeemed at any time prior to maturity, in whole or in part, at the option of the Company. If the applicable redemption of the notes occurred prior to January 1, 2014, the Company would have paid a redemption price equal to the greater of (i) the outstanding principal balance of the notes being redeemed or (ii) the present value, discounted at the rate on U.S. Treasury obligations with a comparable maturity to the remaining expected terms of the notes being redeemed plus 1.00%, of such principal payment amounts and interest on the outstanding principal balance, plus the accrued and unpaid interest to the redemption date on the notes being redeemed. If the applicable redemption of the notes occurs on or after January 1, 2014, the Company will pay a redemption price equal to the percentage of outstanding principal balance of the notes being redeemed specified below for the period in which the redemption occurs (plus the accrued and unpaid interest to the redemption date on the notes being redeemed):

Payment Dates	Redemption Percentage
From and including January 1, 2014 to and including December 31, 2014	112.00%
From and including January 1, 2015 to and including December 31, 2015	105.50%
From and including January 1, 2016 to and including December 31, 2016	102.75%
From and including January 1, 2017 and thereafter	100.00%

The notes contain certain covenants related to the Company's obligations with respect to the commercialization of LINZESS and the related collaboration agreement with Forest, as well as certain customary covenants, including covenants that limit or restrict the Company's ability to incur certain liens, merge or consolidate or make dispositions of assets. The notes also specify a number of events of default (some of which are subject to applicable cure periods), including, among other things, covenant defaults, other non-payment defaults, and bankruptcy and insolvency defaults. Upon the occurrence of an event of default, subject to cure periods in certain circumstances, all amounts outstanding may become immediately due and payable.

The upfront cash proceeds of $175.0 million, less a discount of approximately $0.4 million for payment of legal fees incurred on behalf of the noteholders, were recorded as notes payable at issuance. The Company also capitalized approximately $7.3 million of debt issuance costs, which are included in prepaid expenses and other current assets and in other assets on the Company's consolidated balance sheet. The debt issuance costs and discount are being amortized over the estimated term of the obligation using the effective interest method. The repayment provisions represent embedded derivatives that are clearly and closely related to the notes and as such do not require separate accounting treatment.

The accounting for the notes requires the Company to make certain estimates and assumptions about the future net sales of LINZESS in the U.S. LINZESS has been marketed since December 2012 and the estimates of the magnitude and timing of LINZESS net sales are subject to significant variability due to the recent product launch and the extended time period associated with the financing transaction, and thus subject to significant uncertainty. Therefore, these estimates and assumptions are likely to change as the Company gains additional experience marketing LINZESS, which may result in future adjustments to the portion of the debt that is classified as a current liability, the amortization of

10. Notes Payable (Continued)

debt issuance costs and discounts as well as the accretion of the interest expense. Any such adjustments could be material.

The fair value of the notes was estimated to be approximately $183.8 million as of December 31, 2013, and was determined using Level 3 inputs, including a quoted rate.

11. Commitments and Contingencies

Lease Commitments

The Company leases its facility, offsite data storage location, vehicles and various equipment under leases that expire at varying dates through 2018. Certain of these leases contain renewal options, and require the Company to pay operating costs, including property taxes, insurance, maintenance and other operating expenses.

As of December 31, 2013, the Company rents office and laboratory space at its corporate headquarters in Cambridge, Massachusetts under a non-cancelable operating lease, entered into in January 2007, as amended ("2007 Lease Agreement"). The 2007 Lease Agreement contains various provisions for renewal at our option and, in certain cases, free rent periods and rent escalation tied to the Consumer Price Index. The rent expense, inclusive of the escalating rent payments and free rent periods, is recognized on a straight-line basis over the lease term through January 2018. The Company maintains a letter of credit securing its obligations under the lease agreement of approximately $7.6 million, which is recorded as restricted cash. In addition to rents due under this lease, the Company is obligated to pay facilities charges, including utilities and taxes. In connection with the 2007 Lease Agreement, the Company was provided allowances totaling approximately $17.5 million as reimbursement for financing capital improvements to the facility. The reimbursement amount is recorded as deferred rent on the consolidated balance sheets and is being amortized as a reduction to rent expense over the lease term, as applicable. As of December 31, 2013, the Company was also obligated to rent a total of approximately 70,000 square feet of additional space in three equal stages commencing no later than June 1, 2014, June 1, 2015 and June 1, 2016.

In 2013, the Company also entered into 36-month capital leases for the vehicle fleet for its field-based sales force and medical science liaisons. The capital leases expire at various times through September 2016. At December 31, 2013, the weighted average interest rate on the outstanding capital lease obligations was approximately 7.7%. In accordance with the terms of these arrangements, the Company maintains a letter of credit securing its obligations under the lease agreements of $0.5 million, which is recorded as restricted cash.

The Company has also entered into capital leases for certain computer and office equipment. These capital leases expire at various times through June 2015. At December 31, 2013, the weighted average interest rate on the outstanding capital lease obligations was approximately 8.0%.

11. Commitments and Contingencies (Continued)

At December 31, 2013, future minimum lease payments under all non-cancelable lease arrangements were as follows (in thousands):

	Operating Leases	Capital Leases
2014	$13,072	$ 1,434
2015	14,152	1,265
2016	15,255	2,157
2017	15,778	—
2018	604	—
Total future minimum lease payments	$58,861	4,856
Less amounts representing interest		(583)
Capital lease obligations at December 31, 2013		4,273
Less current portion of capital lease obligations		(1,139)
Capital lease obligations, net of current portion		$ 3,134

Rental expense under the operating leases amounted to approximately $8.8 million, approximately $7.2 million, and approximately $6.6 million for the years ended December 31, 2013, 2012 and 2011, respectively.

Commercial Supply Commitments

The Company has entered into multiple commercial supply agreements for the purchase of linaclotide finished drug product and API. Certain of the agreements contain minimum purchase commitments, the earliest of which commenced in 2012. As of December 31, 2013, the Company's minimum purchase requirements and other firm commitments related to the supply contracts associated with the territories not covered by the collaboration with Forest were approximately $8.7 million, approximately $5.9 million, approximately $7.9 million, approximately $7.9 million, approximately $2.5 million and approximately $5.0 million for the years ending December 31, 2014, 2015, 2016, 2017, 2018 and 2019 and thereafter, respectively. In addition, the Company and Forest are jointly obligated to make minimum purchases of linaclotide API for the territories covered by the Company's collaboration with Forest. Currently, Forest fulfills all such minimum purchase commitments and, as a result, they are excluded from the amounts above.

Commitments Related to the Collaboration and License Agreements

Under the collaborative agreements with Forest and AstraZeneca, the Company shares with Forest and AstraZeneca all development and commercialization costs related to linaclotide in the U.S. and China, respectively. The actual amounts that the Company pays its partners or that partners pay to the Company will depend on numerous factors outside of the Company's control, including the success of certain clinical development efforts with respect to linaclotide, the content and timing of decisions made by the regulators, the reimbursement and competitive landscape around linaclotide and our other product candidates, and other factors.

11. Commitments and Contingencies (Continued)

In addition, the Company has commitments to make potential future milestone payments to third parties under certain of its license and collaboration arrangements. These milestones primarily include the commencement and results of clinical trials, obtaining regulatory approval in various jurisdictions and the future commercial success of development programs, the outcome and timing of which are difficult to predict and subject to significant uncertainty. In addition to the milestones discussed above, the Company is obligated to pay royalties on future sales, which are contingent on generating levels of sales of future products that have not been achieved and may never be achieved.

See Note 4, "Collaboration and License Agreements," for additional information regarding the license and collaboration arrangements.

Other Funding Commitments

As of December 31, 2013, the Company has several on-going studies in various clinical trial stages. The Company's most significant clinical trial expenditures are to contract research organizations ("CRO"). The contracts with CROs generally are cancellable, with notice, at the Company's option and do not have any significant cancellation penalties.

Guarantees

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that is intended to limit its exposure and enable it to recover a portion of any future amounts paid.

The Company enters into certain agreements with other parties in the ordinary course of business that contain indemnification provisions. These typically include agreements with directors and officers, business partners, contractors, landlords, clinical sites and customers. Under these provisions, the Company generally indemnifies and holds harmless the indemnified party for losses suffered or incurred by the indemnified party as a result of the Company's activities. These indemnification provisions generally survive termination of the underlying agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification provisions is unlimited. However, to date the Company has not incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. As a result, the estimated fair value of these obligations is minimal. Accordingly, the Company had no liabilities recorded for these obligations as of December 31, 2013 and 2012.

Litigation

From time to time, the Company is involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. While the outcome of these other claims cannot be predicted with certainty, management does not believe that the outcome of any of these ongoing legal matters, individually and in aggregate, will have a material adverse effect on the Company's consolidated financial statements.

12. Stockholders' Equity

Preferred Stock

The Company's preferred stock may be issued from time to time in one or more series, with each such series to consist of such number of shares and to have such terms as adopted by the board of directors. Authority is given to the board of directors to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitation or restrictions thereof, including without limitation, dividend rights, conversion rights, redemption privileges and liquidation preferences.

Common Stock

The Company has designated two series of common stock, Series A Common Stock, which is referred to as "Class A Common Stock," and Series B Common Stock, which is referred to as "Class B Common Stock." All shares of common stock that were outstanding immediately prior to August 2008 were converted into shares of Class B Common Stock. The holders of Class A Common Stock and Class B Common Stock vote together as a single class. Class A Common Stock is entitled to one vote per share. Class B Common Stock is also entitled to one vote per share with the following exceptions: (1) after the completion of an initial public offering ("IPO") of the Company's stock, the holders of the Class B Common Stock are entitled to ten votes per share if the matter is an adoption of an agreement of merger or consolidation, an adoption of a resolution with respect to the sale, lease, or exchange of the Company's assets or an adoption of dissolution or liquidation of the Company, and (2) Class B common stockholders are entitled to ten votes per share on any matter if any individual, entity, or group seeks to obtain or has obtained beneficial ownership of 30% or more of the Company's outstanding shares of common stock. Class B Common Stock can be sold at any time and irrevocably converts to Class A Common Stock, on a one-for-one basis, upon sale or transfer. The Class B Common Stock is also entitled to a separate class vote for the issuance of additional shares of Class B Common Stock (except pursuant to dividends, splits or convertible securities), or any amendment, alteration or repeal of any provision of the Company's charter. All Class B Common Stock will automatically convert into Class A Common Stock upon the earliest of:

- the later of (1) the first date on which the number of shares of Class B Common Stock then outstanding is less than 19,561,556 which represents 25% of the number of shares of Class B Common Stock outstanding immediately following the completion of the Company's IPO or (2) December 31, 2018;
- December 31, 2038; or
- a date agreed to in writing by a majority of the holders of the Class B Common Stock.

The Company has reserved such number of shares of Class A Common Stock as there are outstanding shares of Class B Common Stock solely for the purpose of effecting the conversion of the Class B Common Stock.

The holders of shares of Class A Common Stock and Class B Common Stock are entitled to dividends if and when declared by the board of directors. In the event that dividends are paid in the form of common stock or rights to acquire common stock, the holders of shares of Class A Common Stock shall receive Class A Common Stock or rights to acquire Class A Common Stock and the holders of shares of Class B Common Stock shall receive Class B Common Stock or rights to acquire Class B Common Stock, as applicable.

12. Stockholders' Equity (Continued)

In the event of a voluntary or involuntary liquidation, dissolution, distribution of assets, or winding up of the Company, the holders of shares of Class A Common Stock and the holders of shares of Class B Common Stock are entitled to share equally, on a per share basis, in all assets of the Company of whatever kind available for distribution to the holders of common stock.

In February 2012, the Company sold 6,037,500 shares of its Class A common stock through a firm commitment, underwritten public offering at a price to the public of $15.09 per share. As a result of the offering, the Company received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $85.2 million.

During the second quarter of 2013, the Company sold 11,204,948 shares of its Class A common stock through a firm commitment, underwritten public offering at a price to the public of $13.00 per share. As a result of this offering, the Company received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $137.8 million.

13. Stock Benefit Plans

The following table summarizes the expense recognized for share-based compensation arrangements in the consolidated statements of operations (in thousands):

	Years Ended December 31,		
	2013	2012	2011
Employee stock options	$17,981	$16,582	$10,904
Restricted stock awards	552	429	431
Non-employee stock options	271	60	152
Employee stock purchase plan	995	472	215
Stock award	30	30	30
	$19,829	$17,573	$11,732

Share-based compensation is reflected in the consolidated statements of operations as follows for the years ended December 31, 2013, 2012 and 2011 (in thousands):

	Years Ended December 31,		
	2013	2012	2011
Research and development	$ 9,178	$ 9,080	$ 6,071
Selling, general and administrative	10,651	8,493	5,661
	$19,829	$17,573	$11,732

Stock Benefit Plans

The Company has two share-based compensation plans pursuant to which awards are currently being made: the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan ("2010 Equity Plan") and the Amended and Restated 2010 Employee Stock Purchase Plan ("2010 Purchase Plan"). The Company also has two share-based compensation plans under which there are outstanding awards, but from which no further awards will be made: the Amended and Restated 2005 Stock Incentive Plan ("2005 Equity Plan") and the Amended and Restated 2002 Stock Incentive Plan

13. Stock Benefit Plans (Continued)

("2002 Equity Plan"). At December 31, 2013, there were 7,868,767 shares available for future grant under all such plans.

2010 Equity Plan

During 2010, the Company's stockholders approved the 2010 Equity Plan under which stock options, restricted stock, restricted stock units, and other stock-based awards may be granted to employees, officers, directors, or consultants of the Company. There were 6,000,000 shares of common stock initially reserved for issuance under the 2010 Equity Plan. The number of shares available for future grant may be increased on the first day of each fiscal year by an amount equal to the lesser of: (i) 6,600,000; (ii) 4% of the number of outstanding shares of common stock on the first day of each fiscal year; and (iii) an amount determined by the board of directors. Awards that are returned to the Company's other equity plans as a result of their expiration, cancellation, termination or repurchase are automatically made available for issuance under the 2010 Equity Plan. At December 31, 2013, there were 7,263,256 shares available for future grant under the 2010 Equity Plan.

2010 Purchase Plan

During 2010, the Company's stockholders approved the 2010 Purchase Plan, which gives eligible employees the right to purchase shares of common stock at the lower of 85% of the fair market value on the first or last day of an offering period. Each offering period is six months. There were 400,000 shares of common stock initially reserved for issuance pursuant to the 2010 Purchase Plan. The number of shares available for future grant under the 2010 Purchase Plan may be increased on the first day of each fiscal year by an amount equal to the lesser of: (i) 1,000,000 shares, (ii) 1% of the Class A shares of common stock outstanding on the last day of the immediately preceding fiscal year, or (iii) such lesser number of shares as is determined by the board of directors. At December 31, 2013, there were 574,658 shares available for future grant under the 2010 Purchase Plan.

2005 Equity Plan and 2002 Equity Plan

The 2005 Equity Plan and 2002 Equity Plan provided for the granting of stock options, restricted stock, restricted stock units, and other share-based awards to employees, officers, directors, consultants, or advisors of the Company. At December 31, 2013, there were 30,853 shares available for future grant under the 2005 Equity Plan and no shares available for future grant under the 2002 Equity Plan.

Restricted Stock

In 2009, the Company granted an aggregate of 515,549 shares of common stock to independent members of the board of directors under restricted stock agreements in accordance with the terms of the 2005 Equity Plan and the Company's director compensation program, effective in October 2009. 115,549 shares of this restricted common stock vested on December 31, 2009 and the remainder vested ratably over a four-year period ended December 31, 2013. In 2013, upon election of a new independent member of the Company's board of directors, the Company granted 8,333 shares of common stock in accordance with the terms of the 2010 Equity Plan and the Company's director compensation program. Of this restricted common stock, 833 shares vested on March 31, 2013 and the remainder vested ratably over the period ended December 31, 2013.

13. Stock Benefit Plans (Continued)

A summary of the unvested shares of restricted stock as of December 31, 2013 is presented below:

	Shares	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2012	80,000	$ 5.72
Granted	8,333	$14.94
Vested	(88,333)	$ 6.59
Forfeited	—	$ 0.00
Unvested at December 31, 2013	—	$ 0.00

Stock Options

Stock options granted under the Company's equity plans generally have a ten-year term and vest over a period of four years, provided the individual continues to serve at the Company through the vesting dates. Options granted under all equity plans are exercisable at a price per share not less than the fair market value of the underlying common stock on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the vesting period of each option.

The weighted average assumptions used to estimate the fair value of the stock options using the Black-Scholes option pricing model were as follows for the years ended December 31, 2013, 2012 and 2011:

	Years Ended December 31,		
	2013	2012	2011
Fair value of common stock	$12.57	$13.44	$11.98
Expected volatility	46.3%	49.2%	49.8%
Expected term (in years)	6.5	6.5	6.5
Risk-free interest rate	1.6%	1.2%	2.4%
Expected dividend yield	—%	—%	—%

Prior to February 3, 2010, the Company was not publicly traded and therefore had no trading history. Therefore, the Company uses a blended volatility rate that blends its own historical volatility with that of comparable public companies. For purposes of identifying comparable companies, the Company selected publicly-traded companies that are in the biopharmaceutical industry, have products or product candidates in similar therapeutic areas and stages of nonclinical and clinical development, have sufficient trading history to derive a historic volatility rate and have similar vesting terms as the Company's options. The expected term is estimated using the "simplified method" since the Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The risk-free interest rate used for each grant is based on a zero-coupon U.S. Treasury instrument with a remaining term similar to the expected term of the share-based award. The Company has not paid and does not anticipate paying cash dividends on its shares of common stock in the foreseeable future; therefore, the expected dividend yield is assumed to be zero.

13. Stock Benefit Plans (Continued)

The Company's Class B Common Stock is issuable upon exercise of options granted prior to the closing of the Company's IPO under the 2002 Equity Plan and the 2005 Equity Plan, and Class A Common Stock is issuable upon exercise of all options granted after the closing of the Company's IPO under the Company's equity plans. At December 31, 2013, options exercisable into 7,918,040 shares of Class B Common Stock and 13,009,834 shares of Class A Common Stock were outstanding.

Subject to approval by the board of directors, option grantees under the 2002 Equity Plan and the 2005 Equity Plan may have the right to exercise an option prior to vesting. The exercise of these shares is not substantive and as a result, the cash paid for the exercise prices is considered a deposit or prepayment of the exercise price and is recorded as a liability. Amounts received upon the exercise of these shares were not material to the consolidated financial statements at December 31, 2013 and 2012.

The Company, from time to time, issues certain time-accelerated stock options to certain employees. The vesting of these options accelerates upon the achievement of certain performance-based milestones. If these criteria are not met, such options will vest between six and ten years after the date of grant. During the year ended December 31, 2013, 253,334 shares vested as a result of milestone or service period achievements. At December 31, 2013 and 2012, there were 570,000 and 823,334 shares, respectively, issuable under the unvested time-accelerated options. When achievement of the milestone is not deemed probable, the Company recognizes compensation expense associated with time-accelerated stock options initially over the vesting period of the respective stock option. When deemed probable of achievement, the Company expenses the remaining unrecognized compensation over the implicit service period. The Company recorded share-based compensation related to these time-accelerated options of less than $0.1 million, approximately $0.5 million and approximately $0.8 million during the years ended December 31, 2013, 2012 and 2011, respectively. At December 31, 2013, the Company had approximately $0.2 million in unrecognized share-based compensation, net of estimated forfeitures, related to these options.

The Company also grants to certain employees performance-based options to purchase shares of common stock. These options are subject to performance-based milestone vesting. During the year ended December 31, 2013, 15,000 shares vested as a result of performance milestone achievements. The Company recorded share-based compensation related to these performance-based options of approximately $0.1 million, approximately $1.0 million and approximately $0.5 million, respectively, during the years ended December 31, 2013, 2012 and 2011. At December 31, 2013, the unrecognized share-based compensation related to these performance-based options was approximately $3.9 million.

13. Stock Benefit Plans (Continued)

The following table summarizes stock option activity under the Company's share-based compensation plans, including performance-based options:

	Shares of Common Stock Attributable to Options	Weighted-Average Exercise Price	Weighted-Average Contractual Life	Aggregate Intrinsic Value
			(in years)	(in thousands)
Outstanding at December 31, 2012	19,539,429	$ 7.75	6.33	$79,140
Granted	3,857,370	$12.57		
Exercised	(1,823,141)	$ 3.37		
Cancelled	(645,784)	$12.50		
Outstanding at December 31, 2013	20,927,874	$ 8.87	6.14	$71,616
Vested or expected to vest at December 31, 2013	19,873,836	$ 8.82	6.07	$68,903
Exercisable at December 31, 2013[1]	11,537,396	$ 6.89	4.77	$59,014

(1) All stock options granted under the 2002 Equity Plan and the 2005 Equity Plan contain provisions allowing for the early exercise of such options into restricted stock. The exercisable shares disclosed above represent those that were vested as of December 31, 2013.

The weighted-average grant date fair value per share of options granted during the years ended December 31, 2013, 2012 and 2011 was $5.96, $6.62 and $6.21, respectively. The total intrinsic value of options exercised during the years ended December 31, 2013, 2012 and 2011 was approximately $19.7 million, approximately $8.6 million, and approximately $17.4 million, respectively. The intrinsic value was calculated as the difference between the fair value of the Company's common stock and the exercise price of the option issued.

As of December 31, 2013, there was approximately $34.8 million of unrecognized share-based compensation, net of estimated forfeitures, related to stock option grants with time-based vesting, which is expected to be recognized over a weighted average period of approximately 2.78 years. The total unrecognized share-based compensation cost will be adjusted for future changes in estimated forfeitures. There was no unrecognized share-based compensation related to restricted stock awards as of December 31, 2013.

14. Income Taxes

In general, the Company has not recorded a provision for federal or state income taxes as it has had cumulative net operating losses since inception. However, the Company recorded an approximately $3,000 provision for state taxes for the year ended December 31, 2011.

14. Income Taxes (Continued)

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows (in thousands):

	Years Ended December 31,		
	2013	2012	2011
Income tax benefit using U.S. federal statutory rate	$(92,756)	$(24,692)	$(22,050)
Permanent differences	1,413	288	245
State income taxes, net of federal benefit	(13,684)	(3,835)	(3,531)
Stock compensation	3,830	3,531	2,104
Tax credits	(5,089)	(10,420)	509
Expiring net operating losses and tax credits	—	564	803
Effect of change in state tax rate on deferred tax assets and deferred tax liabilities	1,057	—	98
Change in the valuation allowance	105,186	34,577	20,955
Other	43	(13)	870
	$ —	$ —	$ 3

Components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2013	2012
Deferred tax assets:		
Net operating loss carryforwards	$ 231,660	$ 127,928
Tax credit carryforwards	29,533	24,444
Capitalized research and development	11,939	17,305
Deferred revenue	6,433	8,300
Other	29,223	25,036
Total deferred tax assets	308,788	203,013
Valuation allowance	(308,788)	(203,013)
Net deferred tax asset	$ —	$ —

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Management has considered the Company's history of operating losses and concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of its deferred tax assets. Accordingly, the deferred tax assets have been fully reserved at December 31, 2013 and 2012. Management reevaluates the positive and negative evidence on a quarterly basis.

The valuation allowance increased approximately $105.8 million during the year ended December 31, 2013, due primarily to the increase in the net operating loss carryforwards and tax credits. The valuation allowance increased approximately $34.8 million during the year ended December 31, 2012, due primarily to the increase in the net operating loss carryforwards and tax credits.

14. Income Taxes (Continued)

Subject to the limitations described below at December 31, 2013 and 2012, the Company has net operating loss carryforwards of approximately $600.9 million and approximately $334.1 million, respectively, to offset future federal taxable income, which expire beginning in 2018 continuing through 2033. The federal net operating loss carryforwards exclude approximately $37.3 million of deductions related to the exercise of stock options. This amount represents an excess tax benefit and has not been included in the gross deferred tax asset reflected for net operating losses. This amount will be recorded as an increase in additional paid in capital on the consolidated balance sheet once the excess benefits are "realized" in accordance with ASC 718. As of December 31, 2013 and 2012, the Company has state net operating loss carryforwards of approximately $545.3 million and approximately $271.4 million, respectively, to offset future state taxable income, which have begun to expire and will continue to expire through 2033. The Company also has tax credit carryforwards of approximately $32.1 million and approximately $26.4 million as of December 31, 2013 and 2012, respectively, to offset future federal and state income taxes, which expire at various times through 2033.

Utilization of net operating loss carryforwards and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future in accordance with Section 382 of the Internal Revenue Code of 1986 ("IRC Section 382") and with Section 383 of the Internal Revenue Code of 1986, as well as similar state provisions. These ownership changes may limit the amount of net operating loss carryforwards and research and development credit carryforwards that can be utilized annually to offset future taxable income and taxes, respectively. In general, an ownership change, as defined by IRC Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. The Company has completed several financings since its inception which may have resulted in a change in control as defined by IRC Section 382, or could result in a change in control in the future.

The Company applies ASC 740, *Income Taxes*. ASC 740 provides guidance on the accounting for uncertainty in income taxes recognized in financial statements and requires the impact of a tax position to be recognized in the financial statements if that position is more likely than not of being sustained by the taxing authority. As a result of the implementation of the new guidance, the Company recognized no material adjustment for unrecognized income tax benefits. At December 31, 2013 and 2012, the Company had no unrecognized tax benefits.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2013, 2012 and 2011, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations.

The statute of limitations for assessment by the Internal Revenue Service ("IRS") and state tax authorities is open for tax years ended December 31, 2012, 2011 and 2010, although carryforward attributes that were generated prior to tax year 2011 may still be adjusted upon examination by the IRS or state tax authorities if they either have been, or will be, used in a future period. There are currently no federal or state income tax audits in progress.

During 2012, the Company completed a study of its research and development credit carryforwards for the years 2003 through 2011. This study resulted in an increase in the Company's research and development credit carryforwards of approximately $9.9 million. These research and development credit carryforwards are subject to a full valuation allowance.

15. Defined Contribution Plan

The Ironwood Pharmaceuticals, Inc. 401(k) Savings Plan is a defined contribution plan in the form of a qualified 401(k) plan in which substantially all employees are eligible to participate upon employment. Subject to certain IRS limits, eligible employees may elect to contribute from 1% to 100% of their compensation. Company contributions to the plan are at the sole discretion of the Company's board of directors. Currently, the Company provides a matching contribution of 75% of the employee's contributions, up to $6,000 annually. During the years ended December 31, 2013, 2012 and 2011, the Company recorded approximately $2.8 million, approximately $1.9 million and approximately $0.6 million of expense related to its 401(k) company match, respectively.

16. Related Party Transactions

The Company has and currently obtains legal services from a law firm that is an investor of the Company. The Company paid approximately $0.1 million, approximately $0.2 million and approximately $0.2 million in legal fees to this investor during the years ended December 31, 2013, 2012 and 2011, respectively. At both December 31, 2013 and 2012, the Company had less than $0.1 million of accounts payable due to this related party.

In September 2009, Forest became a related party when the Company sold to Forest 2,083,333 shares of the Company's convertible preferred stock and in November 2009, Almirall became a related party when the Company sold to Almirall 681,819 shares of the Company's convertible preferred stock (Note 4). These shares of preferred stock converted to the Company's Class B common stock on a 1:1 basis upon the completion of the Company's IPO in February 2010. Amounts due to and due from Forest and Almirall are reflected as related party accounts payable and related party accounts receivable, respectively. These balances are reported net of any balances due to or from the related party. At December 31, 2013, the Company had less than $0.1 million in related party accounts receivable associated with Almirall and approximately $2.7 million in related party accounts receivable, net of related party accounts payable, associated with Forest. At December 31, 2012, the Company had approximately $1.0 million in related party accounts receivable associated with Almirall and approximately $7.5 million in related party accounts payable, net of related party accounts receivable, associated with Forest.

17. State Grants

In the years ended December 31, 2012 and 2011, the Company was awarded an approximately $1.7 million and approximately $0.9 million tax incentive, respectively, associated with the Life Sciences Tax Incentive Program from the Massachusetts Life Sciences Center. The program was established in 2008 in order to incentivize life sciences companies to create new sustained jobs in Massachusetts. Jobs must be maintained for at least five years, during which time the grant proceeds can be recovered by the Massachusetts Department of Revenue ("DOR") if the Company does not meet and maintain its job creation commitments. The award received in July 2011 was recognized as other income in the consolidated statement of operations in the third quarter of 2011, as the Company believed it had satisfied its job creation commitments. The $1.7 million in funds received in 2012 are recorded as other liabilities and no amount has been recognized in the statement of operations through December 31, 2013.

18. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for the years ended December 31, 2013 and 2012. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2013					
Collaborative arrangements revenue	$ 3,255	$ 9,663	$ 4,932	$ 5,031	$ 22,881
Total cost and expenses	92,088	69,543	61,483	51,769	274,883
Other income (expense), net	(5,069)	(5,269)	(5,224)	(5,248)	(20,810)
Net loss	(93,902)	(65,149)	(61,775)	(51,986)	(272,812)
Net loss per share—basic and diluted	$ (0.87)	$ (0.57)	$ (0.51)	$ (0.43)	$ (2.35)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2012					
Collaborative arrangements revenue	$ 12,248	$ 14,604	$96,413	$ 26,980	$150,245
Total cost and expenses	47,884	55,438	48,805	70,880	223,007
Other income (expense), net	35	31	27	45	138
Net income (loss)	(35,601)	(40,803)	47,635	(43,855)	(72,624)
Basic net income (loss) per share	$ (0.34)	$ (0.38)	$ 0.44	$ (0.41)	$ (0.68)
Diluted net income (loss) per share	$ (0.34)	$ (0.38)	$ 0.42	$ (0.41)	$ (0.68)

19. Subsequent Events

On January 8, 2014, the Company announced a headcount reduction of approximately 10% to align its workforce with its strategy to grow a leading GI therapeutics company. As maximizing LINZESS is core to the Company's strategy, its field-based sales force and medical science liaison team were excluded from the workforce reduction. The Company estimates that it will incur aggregate charges in connection with its reduction in workforce of approximately $4.0 million to $4.5 million for employee severance and benefit costs, of which approximately 85% to 95% are expected to result in cash expenditures. The Company committed to this course of action on January 8, 2014, and expects to complete the reduction in workforce during the first quarter of 2014.

Exhibit Index

Number	Description	Incorporated by reference herein	
		Form	Date
3.1	Eleventh Amended and Restated Certificate of Incorporation	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
3.2	Fifth Amended and Restated Bylaws	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
4.1	Specimen Class A common stock certificate	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 20, 2010
4.2	Eighth Amended and Restated Investors' Rights Agreement, dated as of September 1, 2009, by and among Ironwood Pharmaceuticals, Inc., the Founders and the Investors named therein	Registration Statement on Form S-1, as amended (File No. 333-163275)	November 20, 2009
4.3	Indenture, dated as of January 4, 2013, by and between Ironwood Pharmaceuticals, Inc., as issuer of the Notes, and U.S. Bank National Association, as initial trustee of the Notes and as Operating Bank	Form 8-K (File No. 001-34620)	January 8, 2013
10.1#	Amended and Restated 2002 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.2#	Amended and Restated 2005 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 29, 2010
10.3#	Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Registration Statement on Form S-8, as amended (File No. 333-184396)	October 12, 2012
10.3.1#	Form of Stock Option Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
10.3.2#*	Form of Non-employee Director Restricted Stock Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan		
10.4#	Amended and Restated 2010 Employee Stock Purchase Plan	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013

Number	Description	Incorporated by reference herein	
		Form	Date
10.5#	Change of Control Severance Benefit Plan	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.6#*	Director Compensation Plan effective January 1, 2014		
10.7#	Form of Indemnification Agreement with Directors and Officers	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.8#	Consulting Agreement, dated as of November 30, 2009, by and between Christopher Walsh and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.9+	Collaboration Agreement, dated as of September 12, 2007, as amended on November 3, 2009, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.9.1	Amendment No. 2 to the Collaboration Agreement, dated as of January 8, 2013, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.10+	License Agreement, dated as of April 30, 2009, by and between Almirall, S.A. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.10.1+	Amendment No. 1 to License Agreement, dated as of June 11, 2013, by and between Almirall, S.A. and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 8, 2013
10.11+	License Agreement, dated as of November 10, 2009, by and among Astellas Pharma Inc. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.12+	Collaboration Agreement, dated as of October 23, 2012, by and between AstraZeneca AB and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013

Number	Description	Incorporated by reference herein	
		Form	Date
10.13+	Commercial Supply Agreement, dated as of June 23, 2010, by and among PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB, Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 10, 2010
10.14+	Commercial Supply Agreement, dated as of March 28, 2011, by and among Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	May 13, 2011
10.14.1++*	Amendment No. 3 to Commercial Supply Agreement, dated as of November 26, 2013, by and between Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.		
10.15	Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 12, 2007, as amended on April 9, 2009, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.15.1	Second Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 9, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
10.15.2	Third Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 1, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2011
10.15.3	Fourth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 3, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2011

Number	Description	Incorporated by reference herein	
		Form	Date
10.15.4	Fifth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 18, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 29, 2012
10.15.5	Sixth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 19, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.15.6	Seventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 30, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
21.1*	Subsidiaries of Ironwood Pharmaceuticals, Inc.		
23.1*	Consent of Independent Registered Public Accounting Firm		
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		
32.1‡	Certification of Chief Executive Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
32.2‡	Certification of Chief Financial Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
101.INS*	XBRL Instance Document		
101.SCH*	XBRL Taxonomy Extension Schema Document		
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document		

Number	Description	Incorporated by reference herein	
		Form	Date
101.LAB*	XBRL Taxonomy Extension Label Linkbase Database		
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document		
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document		

* Filed herewith.

‡ Furnished herewith.

\+ Confidential treatment granted under 17 C.F.R. §§200.80(b)(4) and 230.406. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

++ Confidential treatment requested under 17 C.F.R. §200.80(b)(4) and Rule 24b-2. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

\# Management contract or compensatory plan, contract, or arrangement.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Form S-3 No. 333-179430 and Form S-8 Nos. 333-184396, 333-165227, 333-165228, 333-165229, 333-165230, 333-165231, 333-189339, and 333-189340) of Ironwood Pharmaceuticals, Inc. and in the related Prospectus of our reports dated February 7, 2014, with respect to the consolidated financial statements of Ironwood Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Ironwood Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2013.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 7, 2014

EXHIBIT 31.1

CERTIFICATION PURSUANT
TO RULE 13a-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934

I, Peter M. Hecht, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ironwood Pharmaceuticals, Inc. (the "registrant");

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

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

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

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

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

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

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

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

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

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

Date: February 7, 2014

/s/ PETER M. HECHT

Peter M. Hecht, Ph.D.
Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION PURSUANT
TO RULE 13a-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934

I, Michael J. Higgins, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ironwood Pharmaceuticals, Inc. (the "registrant");

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

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

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

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

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

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

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

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

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

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

Date: February 7, 2014

/s/ MICHAEL J. HIGGINS

Michael J. Higgins
Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Ironwood Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Peter M. Hecht, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ PETER M. HECHT

Peter M. Hecht, Ph.D.
Chief Executive Officer
February 7, 2014

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

EXHIBIT 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Ironwood Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael J. Higgins, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ MICHAEL J. HIGGINS

Michael J. Higgins
Chief Financial Officer
February 7, 2014

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.