IRONWOOD PHARMACEUTICALS INC

FORM 10-K
(Annual Report)

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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, 2010

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, 2010: $1,004,518,914

As of March 15, 2011, there were 48,612,174 shares of Class A common stock outstanding and 50,825,074 shares of Class B common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2011 Annual Meeting of Stockholders are incorporated by reference into Part III of this report.

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PART I

Item 1. *Business*

Our Company

We are an entrepreneurial pharmaceutical company that discovers, develops and intends to commercialize differentiated medicines that improve patients' lives. In order to be successful, 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. 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 deliver differentiated medicines to patients. To achieve our mission, we are building a team, a culture and processes centered on creating and marketing important new drugs. If we are successful getting medicines to patients, we hope to earn the right to build an enduring pharmaceutical company, an outstanding business that will thrive well beyond our lifetimes and generate substantial returns for our stockholders. Furthermore, if we are successful, we plan to reinvest a portion of our future cash flows into our research and development organization in order to accelerate and enhance our ability to bring new products to market.

We believe that linaclotide, our guanylate cyclase type-C, or GC-C, agonist being developed for the treatment of patients with irritable bowel syndrome with constipation, or IBS-C, or chronic constipation, or CC, could present patients and healthcare practitioners with a unique therapy for a major medical need not yet met by existing therapies. IBS-C and CC are gastrointestinal 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. Linaclotide was designed by Ironwood scientists to target the defining attributes of IBS-C: abdominal pain, discomfort, bloating and constipation. Linaclotide acts locally in the gut with no detectable systemic exposure in humans at therapeutic doses.

Linaclotide recently completed the clinical efficacy portion of its development program, achieving favorable efficacy and safety results in all four of its Phase 3 IBS-C and CC clinical trials. Across these four trials, linaclotide met 66 out of 66 U.S. and European Union, or E.U., primary and secondary endpoints. In the eight Phase 2 and Phase 3 clinical studies in almost 3,700 IBS-C and CC patients, linaclotide demonstrated rapid and sustained improvement of the pain and bloating as well as the constipation symptoms that define these chronic gastrointestinal disorders, with good tolerability and convenient once-daily oral dosing. Based on the results of our development program, we intend to submit a New Drug Application, or NDA, with the Food and Drug Administration, or FDA, in the third quarter of 2011, seeking approval to market linaclotide to IBS-C and CC patients age 18 and older in the U.S. Similarly, our European partner, Almirall S.A., or Almirall, intends to submit a Market Authorization Application, or MAA, with the European Medicines Agency, or EMA, in the second half of 2011, seeking approval to market linaclotide to IBS-C patients in the E.U. If linaclotide is approved for IBS-C and CC patients age 18 and older in the U.S., we may seek to expand linaclotide's market opportunity by exploring its utility in other gastrointestinal indications and in the pediatric population.

In each of the 12-week and 26-week Phase 3 studies in patients with IBS-C, linaclotide rapidly reduced abdominal pain, abdominal discomfort and bloating, and these reductions were sustained throughout the entire treatment period. In the 12-week trial, 50% of linaclotide-treated patients had at least a 30% reduction in abdominal pain for at least six of the 12 weeks, and in the 26-week trial, 49% of linaclotide-treated patients had at least a 30% reduction in abdominal pain for at least six of the first 12 weeks of the treatment period. In each trial, the abdominal pain reduction was observed within

the first week following initiation of therapy and was sustained throughout the treatment period. In the 26-week trial, linaclotide elicited a 40% mean decrease in abdominal pain by the sixth week, a 46% mean decrease by the twelfth week, and a 50% mean decrease at the twenty-sixth week.

As with abdominal pain, linaclotide-treated patients experienced a significant improvement in constipation symptoms during the first week of treatment in each of the Phase 3 IBS-C and CC clinical trials, and this improvement was sustained throughout the whole treatment period.

In the four Phase 3 studies, diarrhea was the most common adverse event (seen in 14% to 20% of linaclotide-treated patients), and the most common adverse event that led to study discontinuation (in 3% to 6% of linaclotide-treated patients). Diarrhea has generally been mild to moderate.

We have pursued a partnering strategy for commercializing linaclotide that has enabled us to retain significant control over linaclotide's development and commercialization, share the costs with high-quality collaborators whose capabilities complement ours, and retain approximately half of linaclotide's future long-term value in the major pharmaceutical markets, should linaclotide meet our sales expectations. As of December 31, 2010, licensing fees, milestone payments, related equity investments and development costs received from our linaclotide partners total approximately $307 million.

In September 2007, we entered into a partnership with Forest Laboratories, Inc., or Forest, to co-develop and co-market linaclotide in the U.S. Under the terms of the collaboration agreement, we and Forest are jointly and equally funding the development and commercialization of linaclotide in the U.S., with equal share of any profits. Forest also has exclusive rights to develop and commercialize linaclotide in Canada and Mexico, and will pay us royalties in the mid-teens on any net sales in these countries. In addition to having reimbursed us for half of linaclotide's development costs since September 2007, Forest has paid us $100 million in license fees and milestone payments to date and has purchased $25 million of our capital stock pursuant to the collaboration agreement. Remaining pre-commercial milestone payments could total up to $20 million upon NDA acceptance by the FDA and up to $85 million upon NDA approval. If linaclotide is successfully developed and 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 $125 million that has already been paid to us. Unless terminated by either us or Forest for material breach, violation of law, bankruptcy or certain adverse changes of control of the other party, or by Forest for convenience, the collaboration agreement will continue in full force and effect with respect to each of the U.S., Canada and Mexico as long as we and Forest are developing or commercializing a product under the agreement.

In April 2009, we entered into a license agreement with Almirall to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States countries and Turkey) for the treatment of IBS-C and other gastrointestinal conditions. Under the terms of the license agreement, Almirall has paid us $57 million in license fees and milestone payments and has purchased $15 million of our capital stock. Remaining pre-commercial milestone payments could total up to $20 million. Almirall is responsible for activities and expenses relating to regulatory approval and commercialization in the European market. If Almirall receives approval to market and sell linaclotide in Europe, we will receive gross royalties which escalate based on sales volume in the territory, beginning in the mid-twenties, less the transfer price paid for the active pharmaceutical ingredient, or API. Unless terminated by either us or Almirall for material breach, violation of law or bankruptcy, by Almirall for convenience, or by us in the event of an adverse change of control of Almirall, the license agreement will continue in full force and effect on a country-by-country basis until Almirall is no longer developing or commercializing linaclotide in such country.

In November 2009, we entered into a license agreement with Astellas Pharma Inc., or Astellas, to develop and commercialize linaclotide for the treatment of IBS-C and other gastrointestinal conditions

in Japan, South Korea, Taiwan, Thailand, the Philippines and Indonesia. Under the terms of the license agreement, Astellas paid us a $30 million up-front licensing fee. Remaining pre-commercial milestone payments could total up to $45 million. Astellas is responsible for activities and expenses relating to regulatory approval and commercialization in those markets. If Astellas receives approval to market and sell linaclotide, we will receive gross royalties which escalate based on sales volume in the territory, beginning in the low-twenties, less the transfer price paid for the API. Unless terminated in all or certain countries by either us or Astellas for material breach or bankruptcy, by Astellas for convenience, or by us in the event of an adverse change of control of Astellas, the license agreement will continue in full force and effect until the later of (a) the last-to-expire valid claim of our patent rights for linaclotide in the countries listed above has expired or (b) Astellas is no longer developing or commercializing linaclotide in all of the countries listed above.

We have retained all rights to linaclotide outside of the territories discussed above.

In addition to five years of exclusivity under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, that would be granted if linaclotide is approved by the FDA, linaclotide is covered by a U.S. composition of matter patent that expires in 2025, subject to possible patent term extension. 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.

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. Linaclotide is our only product candidate that has demonstrated clinical proof of concept. We have a pipeline of early stage, pre-proof of concept development candidates in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, and respiratory disease. We are also conducting early stage, preclinical research in these therapeutic areas, as well as in the area of cardiovascular disease. Finally, we are actively engaged in evaluating externally-discovered drug candidates at all stages of development. In evaluating potential assets, we apply the same criteria as those used for investments in internally-discovered assets.

We were incorporated in Delaware on January 5, 1998.

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 development model 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 development cycle 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 researchers. 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 applies only in the event of change of control votes) 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 and Astellas 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 make the program successful.

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 research for many years to come. Our singular passion is to create and develop novel drug candidates, seeking to integrate the most successful drugmaking practices of the past and the best of today's cutting-edge technologies and basic research 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 driving to 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.

4. We believe commercializing our drugs is a crucial element of our long-term success.

For the foreseeable future, we intend to play an active role in the commercialization of our products in the U.S., and to out-license commercialization rights for other territories. 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.

5. 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 from an accounting perspective. If and when we become profitable, we expect and accept uneven earnings growth. Our underlying product development model is risky and unpredictable, and we will not 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 be transparent about the key elements of our performance, including near-term operating plans and longer-term strategic goals.

Our Strategy

Our goal is to discover, develop and commercialize differentiated medicines that improve patients' lives, and to generate outstanding returns for our stockholders. Key elements of our strategy include:

- attract and incentivize a team with a singular passion for creating and commercializing medicines that can make a significant difference in patients' lives;
- successfully commercialize linaclotide in collaboration with Forest in the U.S.;
- support our international partners to commercialize linaclotide outside of the U.S.;
- harvest the maximum value of linaclotide outside of our partnered territories;
- if approved for IBS-C and CC, develop linaclotide for the treatment of other gastrointestinal disorders and for the pediatric population;
- invest in our pipeline of novel product candidates and evaluate candidates outside of the company for in-licensing or acquisition opportunities;
- maximize the commercial potential of our drugs and participate in an important way in the economics when they reach the market; and
- execute our strategy with our stockholders' long-term interests in mind by seeking to maximize long-term per share cash flows.

Linaclotide Overview

IBS-C and CC are functional gastrointestinal disorders that afflict millions of sufferers worldwide. IBS-C is characterized by frequent and recurrent abdominal pain and/or discomfort and constipation symptoms (*e.g.* infrequent bowel movements, hard/lumpy stools, straining during defecation). CC is primarily characterized by constipation symptoms, but a majority of these patients report experiencing bloating and abdominal discomfort as among their most bothersome symptoms. Available treatment options primarily improve constipation, leading healthcare providers to diagnose and manage IBS-C and CC 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

gastrointestinal symptoms, often delays diagnosis and may compromise treatment, possibly causing additional suffering and disruption to patients' daily activities.

IBS-C and CC are chronic conditions characterized by frequent and bothersome symptoms that dramatically affect patients' daily lives. We believe that gastroesophageal reflux disease, or GERD, serves as a reasonable analogue to illustrate the potential for a treatment that effectively relieves chronic gastrointestinal symptoms. Based on a study performed by M. Camilleri published in 2005 in *Clinical Gastroenterology and Hepatology* and 2007 U.S. census data, we estimate that in 2007, approximately 40 million people in the U.S. suffered from GERD. The typical GERD sufferer, who experiences frequent episodes of heartburn poorly controlled by over the counter products, will commonly seek medical care and is generally treated with a proton pump inhibitor, such as Prilosec (omeprazole), Nexium (esomeprazole magnesium), Prevacid (lansoprazole), or Protonix (pantoprazole). According to IMS Health, peak sales of the proton pump inhibitor class reached $12.8 billion in November 2007. The proton pump inhibitors generally provide relief of key heartburn symptoms within the first week of treatment and have a favorable safety and tolerability profile. Once GERD patients experience relief of heartburn, they tend to be highly adherent to therapy, taking a proton pump inhibitor for approximately 200 days a year, according to IMS Health. The relief of bothersome symptoms and the recurrence of symptoms following discontinuation, serve to reinforce patient adherence to chronic therapy for functional disorders, like GERD, IBS-C and CC.

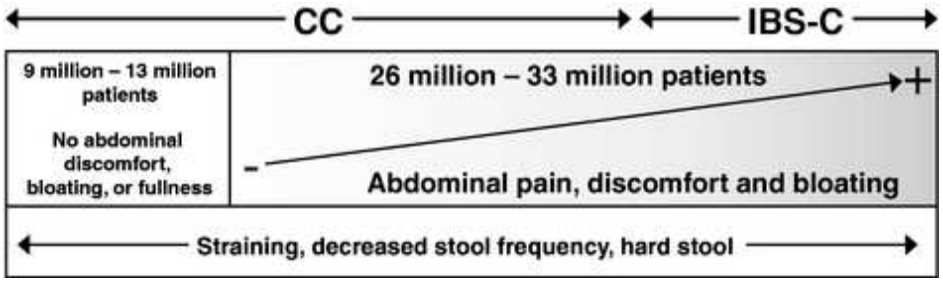
U.S. IBS-C and CC Opportunity

Based on the Talley and Higgins studies, studies performed by F.A. Luscombe (published in 2000 in *Quality of Life Research*) and J.F. Johanson (published in 2007 in *Alimentary Pharmacology and Therapeutics*), 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 and CC, of whom between 9 million to 15.5 million patients sought medical care. As a result of the less than optimal treatment options currently 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.

Irritable Bowel Syndrome with Constipation. Based on the Talley study and 2007 U.S. census data, we estimate that in 2007, approximately 12 million people or 5.2% of the U.S. adult population suffered from symptoms associated with IBS-C. As shown in a study conducted by the International Foundation of Functional Gastrointestinal Disorders, or IFFGD, in 2002, almost 35% of all IBS-C patients report suffering from some related symptoms daily. Based on this data and the Luscombe study, we estimate that up to 7 million of these patients sought medical attention for their symptoms. Based on the Talley, Luscombe and Johanson studies and 2007 U.S. census data, we estimate that between 5 million to 9 million sufferers have not consulted a physician and attempt to manage their symptoms with over the counter fiber and laxatives. Patients with IBS-C who seek medical care receive either a recommendation from their physician for an over the counter product or a prescription medication. As shown in a study conducted by the IFFGD in 2007, for all treated IBS-C patients, there continues to be a low rate of satisfaction with relief of their symptoms, with 92% of patients reporting that they are not fully satisfied with their treatments; and 77% of patients reporting that they were unsatisfied with overall care by their physician.

Chronic Constipation. Based on the Higgins study and 2007 U.S. census data, we estimate that in 2007, 23 million to 34 million people, or 10% to 15% of the U.S. adult population, were suffering from CC. Based on this data and the Johanson study, we estimate that of the total CC sufferers, only 6 million to 8.5 million patients suffering from CC sought medical care. Almost all of these patients, whether or not seeking medical care for their symptoms, took an over the counter or prescription treatment, or both. Similar to IBS-C, there continues to be a low rate of treatment satisfaction, with over 70% of those taking over the counter and prescription laxatives reporting that they are not fully satisfied with their treatment results as shown in the Johanson study.

As shown in the figure below, according to L.E. Brandt in a study published in 2005 in the *American Journal of Gastroenterology* , the symptoms underlying both disorders can be viewed on a continuum. During a consultation, patients will often discuss only the predominant symptom making it difficult for physicians to effectively diagnose and treat. For most patients, constipation is also accompanied by a set of symptoms broader than straining and infrequency of bowel movements. Given the limitations of available treatment options in addressing multiple symptoms, physicians tend to focus on the most easily treatable symptom, constipation. Our market research suggests that most physicians view abdominal pain and bloating as difficult to treat. We believe that linaclotide's profile could offer health care providers the opportunity to identify, diagnose, and treat the other important symptoms experienced by IBS-C and CC patients.



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

Burden of Illness. Both IBS-C and CC adversely affect the quality of life of patients, leading to increased absenteeism from work or school and increased costs to the healthcare system. According to both a study by A.P.S. Hungin published in 2005 in *Alimentary Pharmacology & Therapeutics* and the Johanson study, patients with IBS-C and CC reportedly suffer from their symptoms on average 166 and 97 days per year, respectively, and, according to the Drossman study, over one third have experienced their symptoms for more than ten years. In a typical month, IBS-C and CC patients will miss an average of one to three days of school or work, according to Johanson's study and a study by B. Cash published in 2005 in *The American Journal of Medical Care* , and their productivity will be disrupted an additional four to five days per month, according to the Cash study. When the level of suffering becomes acutely overwhelming for patients, they seek care at an ambulatory care facility. In 2004, CC was the second most common cause for ambulatory care visits after GERD, according to a 2008 article by J.E. Everhart published in *Functional Intestinal Disorders* . According to the Everhart article, CC accounted for 6.3 million ambulatory care visits (when considered as part of any listed diagnosis) and IBS accounted for 3 million ambulatory care visits. Estimates of the indirect and direct costs associated with these conditions range upwards of $25 billion, according to a study published in 2000 by M. Camilleri and D.E. Williams in *Pharmacoeconomics* .

Treatment Options for IBS-C and CC. 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 CC 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. Unfortunately, physicians have very limited treatment options beyond what is readily available to the patient alone. Physicians typically rely 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 CC, healthcare providers sometimes prescribe 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 and over the counter 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 the Brandt study, 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 Johanson study.

In 2002, the FDA approved Zelnorm, the first new drug for the treatment of IBS-C, and in 2004, Zelnorm was approved for the treatment of CC. 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 CC. 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 CC, according to IMS Health. Prior to its withdrawal, 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.

Currently, the only available prescription therapy for IBS-C and CC is Amitiza, which was approved for the treatment of CC in 2006, and for IBS-C in 2008. Amitiza sales have been modest in comparison to Zelnorm sales prior to its withdrawal from the market, according to IMS Health.

Although a significant unmet need exists for better treatments for IBS-C and CC, there are very few treatments in late-stage clinical development. The most recent entrant to the CC marketplace, solely in Europe, is Resolor (prucalopride). Resolor was approved in 2009 by the EMA and is indicated for the treatment of CC 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 is currently in Phase 3 trials being studied as a potential treatment for CC in males and for opioid induced constipation (OIC). Johnson & Johnson has U.S. rights to prucalopride. The U.S. patent covering the composition of matter expires in 2015.

The Linaclotide Opportunity. Linaclotide is a promising potential treatment for patients suffering from both abdominal and constipation symptoms related to IBS-C and CC. Based on the clinical profile we have observed to date, we believe linaclotide is well positioned to provide IBS-C and

CC patients with much needed reduction in abdominal and constipation symptoms, with a low incidence of adverse events, and a convenient once daily, oral dosing regimen.

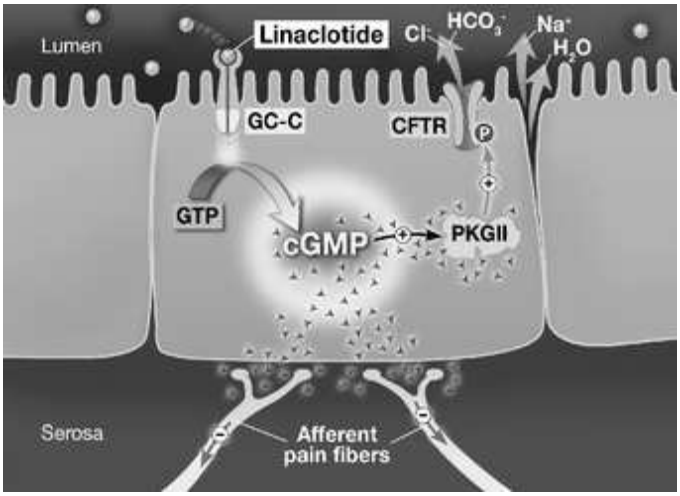
Annually, we estimate that over 30 million 30-day units of laxative and fiber medications are purchased in an effort to relieve chronic abdominal and constipation symptoms. Based on our analysis of data from IMS Health, The Nielsen Company and abstracts by P. Schoenfeld, et al. and W. Chey, et al. for the American College of Gastroenterology 2010 Annual Meeting and the 18th United European Gastroenterology Week, respectively, these 30 million units are comprised of 7-8 million laxative prescriptions for patients with constipation and abdominal symptoms and approximately 22 million over-the-counter (OTC) laxative and fiber units for chronic patients. Assuming a price comparable to those for branded prescription drugs for other gastrointestinal indications that are made available in Redbook and First Databank, the daily cost for linaclotide treatment per patient could range from $5.50 to $8.50 per day, with a prescription cost of $165 to $250 per month. Applying these assumptions to the potential market as a whole, these 30 million units could represent a potential U.S. commercial opportunity for a safe and effective IBS-C/CC drug in excess of $6 billion per year. Since many of these 30 million units are taken episodically or as rescue medications, there exists a potential upside in the market if the annual days of therapy increases, assuming that certain patients desire to manage and control their symptoms chronically. There is also the possibility that new patients could enter the marketplace as awareness of a new therapy increases.

Mechanism of Action

The underlying causes of the abdominal pain, discomfort and bloating suffered by patients with lower gastrointestinal disorders like IBS-C and CC are poorly understood. Further, because current therapeutic agents offer limited improvement in these symptoms, there has been limited medical research in this area. Since our clinical studies indicate that linaclotide provides rapid and sustained improvement of these symptoms, we have invested significant effort to define the mechanisms of linaclotide's physiological effects.

Linaclotide is a 14 amino acid peptide agonist of GC-C, a receptor found on the epithelial cells that line the intestine. Activation of GC-C leads to increases in intracellular and extracellular cyclic guanosine monophosphate, or cGMP, levels. cGMP is a well characterized "second messenger" that relays and amplifies signals received at receptors on the cell surface to target molecules in the cytosol and/or nucleus of a cell. We believe increased cGMP has dual effects on intestinal function. First, as the figure below shows, cGMP can exit the epithelial cells to block pain signaling by inhibiting the pain-sensing neurons that carry signals from the gastrointestinal tract to the central nervous system (afferent pain fibers). Second, cGMP can remain inside the epithelial cell to activate protein kinase GII, or PKGII, which activates the protein Cystic Fibrosis Transmembrane conductance Regulator, or CFTR, by phosphorylation, or P, to stimulate electrolyte (Na^+ = sodium, Cl^- = chloride, and

HCO_3^- = bicarbonate) and fluid (H_2O = water) secretion into the intestinal lumen. The resulting increase in intestinal fluid volume accelerates intestinal transit.



Our preclinical work supports the above model for the actions of linaclotide. Regarding the effect on pain sensation, we have found that increased extracellular cGMP inhibited noxious-stimulus-induced firing of afferent pain fibers. In addition, oral dosing with either linaclotide or directly with cGMP significantly reduced abdominal pain responses in a number of preclinical models. While much work remains to be done, we hypothesize that the reduction in abdominal pain, abdominal discomfort, and visceral hypersensitivity seen both preclinically and clinically is a result of increased extracellular cGMP, which may reduce firing of pain-sensing neurons and thus decrease sensitivity to otherwise painful stimuli.

Additionally, in other preclinical studies, linaclotide was shown to increase intracellular cGMP, leading to activation of channels in intestinal cell membranes that resulted in the secretion of ions and fluid out of intestinal cells and into the intestinal lumen. Increased fluid in the intestinal lumen causes accelerated intestinal transit.

Importantly, linaclotide's effects on pain sensation and gastrointestinal transit/secretion are dependent on the presence of the GC-C receptor; in preclinical experiments where the GC-C receptor was genetically deleted, the effects of linaclotide on pain sensation and secretion were eliminated.

The binding and activity of linaclotide at the GC-C receptor is highly specific. Linaclotide has no effect on the serotonin system, unlike Zelnorm, Resolor, cisapride (Propulsid, which was approved for heartburn caused by GERD), or alosetron (Lotronex, which was approved for irritable bowel syndrome with diarrhea), each of which work through serotonin receptors in the intestine. Zelnorm, Propulsid and Lotronex were all withdrawn from the market because of safety concerns.

Clinical

Linaclotide recently completed the efficacy portion of its clinical development program, and two long-term safety studies are still ongoing. The clinical development program consists of 13 studies in over 4,600 people: three in healthy volunteers, four in IBS-C patients, four in CC patients, and two long-term safety studies in IBS-C and CC patients.

Manufacturing and Supply

It is our goal to consistently and reliably produce and supply the highest quality drugs to our patients on a worldwide basis, with redundancy built into each critical step of the manufacturing process. We currently execute our global production and delivery of linaclotide through a combination

of independent third party organizations and our collaboration partners. We believe that we have sufficient in-house expertise to lead and manage our virtual global supply chain for linaclotide on an ongoing basis to meet worldwide patient demand, should it be approved by the regulatory authorities.

Pharmaceutical manufacturing consists of two phases—manufacturing of the active pharmaceutical ingredient, or API (sometimes referred to as drug substance), and manufacturing of the final drug product. We currently use contract manufacturers for the production of linaclotide API. Linaclotide is a 14 amino acid peptide, manufactured via solid phase synthesis using naturally occurring amino acids. We and Forest entered into a commercial supply agreement with PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB for the manufacture of the linaclotide API that will be used to obtain regulatory approval of linaclotide in the U.S., Canada and/or Mexico, and, pending any such approval, that will be incorporated into the finished product for commercialization in those countries. We continue to pursue additional commercial supply agreements with other 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 commercial needs.

Each of our collaboration partners, Forest, Almirall and Astellas, is responsible for linaclotide drug product manufacturing in its respective territory. In addition, we are pursuing arrangements with other manufacturers for the drug product manufacturing of linaclotide in the parts of the world outside of our partnered territories, and to further ensure continuity of drug product supply in partnered territories. Previous to linaclotide, there was little or no precedent for producing a convenient, room-temperature stable dosage form of an orally delivered peptide drug with a significant market opportunity. Our team developed a formulation with simple, safe excipients that was shown to be stable at room temperature for at least 24 months in various development batches. In addition, we have demonstrated stability in these development batches under accelerated conditions of 40°C with 75% relative humidity for six months, which, based on industry precedent, is predictive of stability of greater than 18 months at room temperature conditions. We optimized our formulation following the achievement of development batch stability, and prepared scale up batches and Phase 3 clinical trial material for stability testing. These scale up batches and Phase 3 clinical trial material batches have shown acceptable room temperature stability at the six, 12 and 18 month time points. Our partners, Forest and Almirall, have prepared pre-registration and registration batches to be utilized for regulatory submissions in their respective territories. We, together with Forest, are on track to submit an NDA in the third quarter of 2011. Almirall is on track to submit an EMA in the second half of 2011. We and our partners will continue to monitor those batches going forward.

We believe our efforts to date have led to a formulation that is both cost effective and able to meet the stability requirements for pharmaceutical products. Our work in this area has created an opportunity to seek additional intellectual property protections around the linaclotide program. In conjunction with Forest, we have filed patent applications worldwide to cover the room temperature stable linaclotide formulation as well as related formulations. If these claims are allowed, they would expire in 2029 in the U.S. These patent rights would be subject to any potential patent term adjustments or extensions and/or supplemental protection certificates extending such term extensions in countries where such extensions may become available.

Sales and Marketing

For the foreseeable future, we intend to develop and commercialize our drugs in the U.S. alone or with partners, while out-licensing commercialization rights for other territories. In executing our strategy, our goal is to retain significant control over the development process and commercial execution for our products, while participating in a meaningful way in the economics of all drugs that we bring to the market.

We plan to develop our commercial organization around linaclotide, with the intent to leverage this organization for future products. To deliver on our strategy, we intend to create a high-quality commercial organization dedicated to bringing innovative, highly-valued healthcare solutions to our customers, including patients, payors, and healthcare providers.

Maximizing the Value of Linaclotide in the U.S.

Our commercial strategy for linaclotide, if approved, will be to establish linaclotide as the prescription product of choice for both IBS-C and CC. We, together with our U.S. commercialization partner Forest, plan to build awareness that patients suffer from multiple, highly bothersome symptoms of IBS-C and CC, and that these symptoms can dramatically impair sufferers' quality of life.

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. We have strong alignment with Forest and a shared vision for linaclotide. The combined marketing team possesses a deep understanding of gastroenterology and primary care customers, and this knowledge will be utilized 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 and CC.

Maximizing the Value of Linaclotide Outside the U.S.

We have out-licensed commercialization rights for territories outside of the U.S. to Almirall in Europe and Astellas in Japan, South Korea, Taiwan, Thailand, the Philippines and Indonesia.

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 plans to coordinate sales and marketing efforts from its central office in an effort to ensure consistency of the overall brand strategy and objectively assess performance. Almirall's knowledge of the local markets should help 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 gastrointestinal franchise in Japan make them an ideal partner for Ironwood.

We have retained all rights to linaclotide outside of the territories discussed above.

Pipeline Strategy

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 preclinical 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, 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 are actively seeking to identify attractive external opportunities. We utilize the same critical filters for investment when evaluating external programs as we do with our own, internally-derived candidates.

Pipeline

We aim to create differentiated, first-in-class/best-in-class medicines that provide relief and clear therapeutic benefits to patients suffering from chronic diseases. To support this vision, we have ongoing efforts to identify product candidates that strengthen our pipeline, including treatments for gastrointestinal disorders, pain and inflammation, respiratory disease, and cardiovascular disease. Linaclotide is our only product candidate that has demonstrated clinical proof of concept. We have a pipeline of early stage, pre-proof of concept development candidates in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, and respiratory disease. We are also conducting early stage, preclinical research in these therapeutic areas, as well as in the area of cardiovascular disease.

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 and GC-C Patent Portfolio

Our linaclotide patent portfolio is currently composed of five issued U.S. patents, two granted European patents (each of which has been validated in 31 European countries and in Hong Kong), a granted Japanese patent, eight 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 gastrointestinal disorders and processes for making the molecule. If claims in our pending patent application covering the room temperature stable formulation are allowed, they would expire in August 2029. The granted European patent, which will expire in 2024, contains claims directed to the linaclotide molecule, pharmaceutical compositions thereof and uses of linaclotide to prepare medicaments for treating gastrointestinal disorders. The pending provisional, U.S. non-provisional, foreign and PCT applications contain claims 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 patent applications, if issued, will expire between 2024 and 2031.

In addition to the patents and patent applications related to linaclotide, we currently have one issued U.S. patent and a number of pending provisional, U.S. non-provisional, foreign and PCT applications directed to other GC-C agonist molecules, pharmaceutical compositions thereof, methods

of using these molecules to treat various diseases and disorders and processes of synthesizing the molecules. The issued U.S. patent will expire in 2024. The patent applications, if issued, will expire between 2024 and 2029.

Additional Intellectual Property

Our pipeline patent portfolio is currently composed of three issued U.S. patents; a granted European patent (which has been validated in 31 European countries and in Hong Kong); six 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. One of the issued U.S. patents expires in 2022, and the other two patents expire in 2024. The European patent and the other foreign issued patents expire in 2024. The pending patent applications, if issued, will expire between 2024 and 2031.

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.

The patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. We expect to apply for patent term extensions for some of our current patents, depending upon the length of clinical trials and other factors involved in the submission of an 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, 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 criminal prosecution.

FDA Approval Process

We believe that our product candidates, including linaclotide, 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:

- preclinical 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 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; and
- FDA review and approval of the NDA.

Preclinical 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 pre-clinical tests must comply with federal regulations and requirements including good laboratory practices. We must submit the results of the preclinical 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 trials. In such a case, we must work with the FDA to resolve any outstanding concerns before clinical trials 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 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 may impose other conditions.

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 1, 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 2 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 3 trials; and
- identify possible adverse effects and safety risks.

Phase 3 trials generally further evaluate clinical efficacy and test for safety within an expanded patient population. The conduct of the 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 preclinical 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 FDA may "refuse to file" the NDA if it

does not contain all pertinent information and data. In that case, the applicant may resubmit the NDA when it contains the missing information and data. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of new drug applications. Most such applications for non-priority drug products are reviewed within 10 months. The review process, however, may be extended by FDA requests for additional information, preclinical 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 preclinical studies and initial clinical trials of our product candidates, including linaclotide, 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 and Astellas, to obtain, or any delay in obtaining, regulatory approvals or in complying with requirements could adversely affect the commercialization of product candidates 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 generic drugs is "abbreviated" because it need not include preclinical 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 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 patent challenges). 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 protects against FDA approval of ANDAs and 505(b)(2) applications for generic drugs that include the innovation that required clinical data; it does not prohibit the FDA from accepting or approving ANDAs or 505(b)(2) NDAs for generic drugs that do not include the 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 30 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 one-time 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 restoration 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 4 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, 2010, we had 217 employees. Approximately 68 were scientists engaged in discovery research, 85 were in our drug development organization, 8 were in our commercial team, and 56 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.

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 largely dependent on the success of linaclotide, which may never receive regulatory approval or be successfully commercialized.

Our lead product candidate, linaclotide, recently completed the clinical efficacy portion of its development program. Our other drug candidates are in earlier stages of development. Our business depends entirely on the successful development and commercialization of our product candidates. We currently generate no revenue from sales, and we may never be able to develop marketable drugs. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of pharmaceutical products is subject to extensive regulation by the FDA and foreign regulatory authorities, and regulations differ from jurisdiction to jurisdiction. We are not permitted to market any of our product candidates in the U.S. until we receive approval of an NDA from the FDA, or in any foreign jurisdictions until we receive the requisite approvals from such jurisdictions. We have not yet submitted an NDA or foreign equivalent in any jurisdiction. Obtaining regulatory approval is a lengthy, expensive and uncertain process. The FDA and foreign regulatory authorities also have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Potential risks include those that the regulatory authorities:

- may not deem linaclotide or another product candidate safe and effective;
- may not find the data from preclinical studies and clinical trials sufficient to support approval;
- may not approve of manufacturing processes and facilities;
- may not approve linaclotide for both IBS-C and CC indications;
- may require significant warnings or restrictions on use to the product label for linaclotide or another product candidate; or
- may change their approval policies or adopt new regulations.

Linaclotide is our GC-C agonist that is currently in Phase 3 clinical development for the treatment of IBS-C and CC. In September and November 2010, we announced the positive top-line results from each of the two Phase 3 clinical trials assessing the safety and efficacy of linaclotide in patients with IBS-C, and in November 2009, we announced that we achieved positive results in each of our Phase 3 CC trials. Even though linaclotide met the endpoints of the CC trials and the top-line results indicate that it met the endpoints of the IBS-C trials, it may not be approved for either or both indications or for any other indication for which we seek approval from the FDA.

Further, the FDA and any foreign regulatory authority may disagree with our trial design or our interpretation of data from clinical trials, or they may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. The FDA and any foreign regulatory authority might also approve linaclotide for fewer or more limited indications than we

request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA and any foreign regulatory authority may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of linaclotide. Any failure to obtain regulatory approval of linaclotide would significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

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

Undesirable side effects caused by linaclotide could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential products liability claims. Any serious adverse events deemed to be caused by linaclotide could have a material adverse effect upon the linaclotide program and our business as a whole. The most common adverse event to date in the clinical studies evaluating the safety and efficacy of linaclotide has been diarrhea. For the most part, the diarrhea has been considered mild or moderate by the patients. In the four Phase 3 clinical trials, our top-line results indicate that diarrhea was seen in 14% to 20% of linaclotide-treated patients, and was the most common adverse event that led to study discontinuation in 3% to 6% of linaclotide-treated patients. In our clinical development program, there have been no serious adverse events in any patients receiving linaclotide treatment that were deemed by a study investigator or us to be "definitely related" or "probably related" to linaclotide treatment, nor have there been any deaths in any patients receiving linaclotide treatment that were deemed by a study investigator or us to be related to linaclotide treatment.

If linaclotide receives marketing approval, and we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of linaclotide;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of linaclotide and could substantially increase commercialization costs.

If we or our collaboration partners and other third parties upon whom we rely to produce linaclotide are unable to satisfy FDA quality standards and related regulatory requirements, experience manufacturing difficulties, or are unable to manufacture sufficient quantities of our product candidates, our development and commercialization efforts may be materially harmed.

We do not currently possess internal manufacturing capacity. We currently utilize the services of contract manufacturers to manufacture our clinical supplies. With respect to the manufacturing of linaclotide, we (along with our U.S. collaboration partner, Forest) entered into a commercial supply agreement with PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB for the manufacture of the linaclotide API that will be used to obtain regulatory approval of linaclotide in the U.S., Canada and/or Mexico, and, pending any such approval, that will be incorporated into the finished product for commercialization in those countries. In addition, we have established development

agreements with multiple peptide manufacturers and continue to pursue commercial supply agreements with these manufacturers for the linaclotide API. We may not be able to enter into agreements with such other manufacturers on commercially reasonable terms, or at all. If we enter into a commercial supply agreement with another manufacturer but then change or add manufacturers, the regulatory authorities in each territory must approve these manufacturers' facilities and processes prior to use, which would require new testing and compliance inspections, and the new manufacturers would have to be educated in or independently develop the processes necessary for the production of linaclotide. While we believe we will have arrangements to produce a sufficient amount of API, if we lose a manufacturer, it would take us a substantial amount of time to identify and develop a relationship with an alternative manufacturer.

These third party manufacturers acquire the raw materials for the API from a limited number of sources. Any curtailment in the availability of these raw materials could result in production or other delays with consequent adverse effects on us. In addition, because regulatory authorities must generally approve raw material sources for pharmaceutical products, changes in raw material suppliers may result in production delays or higher raw material costs.

Upon production of our API, each of our collaboration partners, Forest, Almirall and Astellas, is responsible for completing the manufacturing process of linaclotide in its respective territory, which consists of finishing and packaging linaclotide into capsules. In addition, we are pursuing arrangements with additional manufacturers to complete the manufacturing process of linaclotide in the parts of the world outside of our partnered territories, and for the purpose of introducing redundancy into our supply chain in case of a manufacturing shortage or supply interruption. We will be dependent upon the success of our partners, and these other manufacturers, provided that we are successful in developing supply arrangements with the other manufacturers, in producing drug product for commercial sale. No party has experience producing finished drug product for linaclotide at commercial scale, and such efforts may fail. Traditionally, peptide manufacturing is costly and time consuming, resulting in low yields and poor stability. We cannot give any assurances that we will overcome these issues when scaling up manufacturing for linaclotide.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, shortages of qualified personnel, as well as compliance with federal, state and foreign regulations, and the challenges associated with complex supply chain management. We, together with our partners Forest and Almirall, are currently evaluating the stability of different batch sizes of linaclotide at various points in time. If we are unable to demonstrate stability in accordance with commercial requirements, or if our manufacturers were to encounter difficulties or otherwise fail to comply with their obligations to us, our ability to obtain FDA or MAA approval and market linaclotide would be jeopardized. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of our clinical trials, increase the costs associated with conducting our clinical trials and, depending upon the period of delay, require us to commence new trials at significant additional expense or to terminate a trial.

Each of the linaclotide manufacturers would need to comply with GMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. 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. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the quality of linaclotide is compromised due to a

manufacturers' or collaboration partners' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize linaclotide, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of linaclotide or our other product candidates, entail higher costs or result in our being unable to effectively commercialize linaclotide or our other product candidates. Furthermore, if our manufacturers or collaboration partners fail to deliver the required commercial quantities on a timely basis and at commercially reasonable prices, we may be unable to meet demand for any approved products and would lose potential revenues.

Because we work with partners to develop, manufacture and promote linaclotide, we are dependent upon third parties in our efforts to obtain regulatory approval for, and to commercialize, linaclotide.

We co-develop and plan to co-promote linaclotide in the U.S. with Forest. Forest plays a significant role in the conduct of the clinical trials for linaclotide and the subsequent collection and analysis of data. Each of Almirall, our European partner, and Astellas, our partner in certain Asian countries, is responsible for obtaining regulatory approval of linaclotide in its respective territory. In addition, each of our partners is responsible for completing the manufacturing process of linaclotide upon production of the API, which consists of finishing and packaging linaclotide into capsules. Employees of our partners are not our employees, and we have limited ability to control the amount or timing of resources that they 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 approval of regulatory applications for linaclotide as well as the commercialization and manufacturing of linaclotide. A material breach by any of our partners of our collaboration agreement with such partner could also delay regulatory approval and commercialization of linaclotide. In addition, the execution of our clinical development program for linaclotide, and the compilation and analysis of the data produced from the clinical trials, requires coordination among various parties. Further, each of our partners is responsible for reporting adverse event information to us. These functions may not be carried out effectively and efficiently if we fail to communicate and coordinate with our partners, and vice versa. 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.

Even if linaclotide receives regulatory approval, it may still face future development and regulatory difficulties.

We anticipate submitting an NDA for linaclotide with the FDA in the third quarter of 2011. However, even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Linaclotide and our other product candidates would also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market information. In addition, 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 the facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;

- suspend 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 if linaclotide receives regulatory approval in the U.S., we or our collaborators may never receive approval to commercialize linaclotide outside of the U.S.

We have out-licensed the European rights to develop and commercialize linaclotide to Almirall, and we have out-licensed the same rights in certain Asian countries to Astellas. In the future, we may seek to commercialize linaclotide in foreign countries outside of Europe and those Asian countries with other parties or by ourselves. In order to market any products outside of the U.S., we must establish and 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. Almirall anticipates submitting an MAA with the EMA in the second half of 2011. The time required to obtain approval in other jurisdictions, including the E.U., might differ from that required to obtain FDA approval. The regulatory approval process in other jurisdictions may include all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. 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. Failure to obtain regulatory approvals in other jurisdictions or any delay or setback in obtaining such approvals could have the same adverse effects detailed above regarding FDA approval in the U.S. As described above, such effects include the risks that linaclotide may not be approved for all indications requested, which could limit the uses of linaclotide and have an adverse effect on its commercial potential or require costly post-marketing studies.

Linaclotide may not be widely adopted by patients, payors or healthcare providers, which would adversely impact our potential profitability and future business prospects.

The commercial success of linaclotide depends upon its level of market adoption by patients, payors and healthcare providers. If linaclotide does not achieve an adequate level of market adoption for any reason, our potential profitability and our future business prospects will be severely adversely impacted. The degree of market acceptance of linaclotide depends on a number of factors, including:

- our ability to demonstrate to the medical community, particularly general practitioners, internists and gastrointestinal specialists who may purchase or prescribe linaclotide, the clinical efficacy and safety of linaclotide as the prescription product of choice for patients who suffer from IBS-C or CC;
- the effectiveness of our sales and marketing organizations and our distribution network;
- the ability of physicians and other providers to be adequately reimbursed for linaclotide in a timely manner from government and private payors; and
- the actual or perceived safety profile of linaclotide, particularly if unanticipated adverse events related to linaclotide treatment arise and create safety concerns among potential patients or prescribers.

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

If approved and commercialized, linaclotide will compete globally with certain prescription therapies and over the counter products for the treatment of IBS-C and CC, or certain associated symptoms. The availability of prescription competitors and over the counter products for gastrointestinal 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 clinical benefits in our clinical trials. 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. Currently, there are a few 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 CC. If our potential competitors are successful in completing drug development for their drug candidates and obtain approval from the FDA, they could limit the demand for linaclotide.

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 have limited sales and marketing experience and resources, and we may not be able to effectively market and sell linaclotide.

With linaclotide, we are developing a product candidate for large markets traditionally served by general practitioners and internists, as well as gastrointestinal specialists. Traditional pharmaceutical companies employ groups of sales representatives to call on these large generalist physician populations. In order to adequately address these physician groups, we must optimize our co-development and co-promotion relationship in the U.S., Canada and Mexico with Forest, our license and commercialization relationship in Europe with Almirall, and our license and commercialization relationship in certain Asian countries with Astellas. Likewise, we must either establish sales and marketing collaborations or co-promotion arrangements or expend significant resources to develop our own sales and marketing presence outside of North America, Europe, and those Asian countries. We currently possess limited resources and may not be successful in establishing additional collaborations or co-promotion arrangements on acceptable terms, if at all. We also face competition in our search for collaborators, co-promoters and sales force personnel.

If any of our partners undergoes a change in control or management, this may adversely affect our collaborative relationship.

We work jointly and collaboratively with Forest, Almirall and Astellas on many decisions related to the development, manufacturing and commercialization of linaclotide. In doing so, we have established relationships with several key members of our partners' management teams in functional areas such as development, quality, regulatory and commercial. The success of our collaboration is highly dependent on the resources, efforts and skills of our partners and their key employees. If a partner undergoes a change of control or a change of management, we will need to reestablish many of these relationships and we will need to regain alignment of our development and commercialization strategy for linaclotide. Further, any change of control or management may result in a reprioritization of linaclotide within such partner's profile, and such a change may adversely affect the timeline and likelihood of achieving regulatory approval and, ultimately, the commercialization of linaclotide, or such partner may

fail to maintain the financial resources necessary to continue financing its portion of the development, manufacturing or commercialization costs.

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

Our ability to commercialize linaclotide successfully will depend in part on the coverage and reimbursement levels set by governmental authorities, private health insurers and other third-party payors. As a threshold for coverage and reimbursement, third-party payors generally require that drug products have been approved for marketing by the FDA. Third-party payors also are increasingly challenging the effectiveness of and prices charged for medical products and services. We may not obtain adequate third-party coverage or reimbursement for linaclotide or we may be required to sell linaclotide at a discount.

We expect that private insurers will consider the efficacy, cost effectiveness and safety of linaclotide in determining whether to approve reimbursement for linaclotide and at what level. Obtaining these approvals can be a time consuming and expensive process. Our business would be materially adversely affected if we do not receive approval for reimbursement of linaclotide from private insurers on a timely or satisfactory basis. Our business could also be adversely affected if private insurers, including managed care organizations, the Medicare program or other reimbursing bodies or payors limit the indications for which linaclotide will be reimbursed to a smaller set than we believe it is effective in treating.

In some foreign countries, particularly Canada and the countries of Europe, the pricing of prescription pharmaceuticals is subject to strict 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 may be required to conduct a clinical trial that compares the cost-effectiveness of our products, including linaclotide, to other available therapies. Further, several European countries have implemented government measures to either freeze or reduce pricing of pharmaceutical products. 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 unsatisfactory levels, our business could be materially harmed.

We expect to experience pricing pressures in connection with the sale of linaclotide and our future products due to the potential healthcare reforms discussed below, as well as the trend toward programs aimed at reducing health care costs, the increasing influence of health maintenance organizations and additional legislative proposals.

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

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

- federal healthcare program anti-kickback laws, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which 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 payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts; and

- the recently-enacted federal Physician Payments Sunshine Act, and similar state laws in certain states, that require pharmaceutical and medical device companies to monitor and report payments, gifts 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 governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

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

The U.S. government and other governments have shown significant interest in pursuing healthcare reform, as evidenced by the passing of the Patient Protection and Affordable Healthcare Act and the Health Care and Education Reconciliation Act. This healthcare reform law increases the number of individuals who receive health insurance coverage and closes a gap in drug coverage under Medicare Part D as established under the Medicare Prescription Drug Improvement Act of 2003; each of these reforms could potentially increase our future revenue from linaclotide or any other product candidates that are approved for sale. The law, however, also implements cost containment measures that could adversely affect our future revenue. These measures include increased drug rebates under Medicaid for brand name prescription drugs and extension of these rebates to Medicaid managed care. The legislation also extends 340B discounted pricing on outpatient drugs to children's hospitals, critical access hospitals, and rural health centers; this expansion reduces the amount of reimbursement received for drugs purchased by these new 340B-covered entities.

Additional provisions of the health care reform law, which become effective in 2011, may negatively affect our future revenue and prospects for profitability. Along with other pharmaceutical manufacturers and importers of brand name prescription drugs, we would be assessed a fee based on

our proportionate share of sales of brand name prescription drugs to certain government programs, including Medicare and Medicaid. As part of the health care reform law's provisions closing a funding gap that currently exists in the Medicare Part D prescription drug program (commonly known as the "donut hole"), we will also be required to provide a 50% discount on brand name prescription drugs sold to beneficiaries who fall within the donut hole.

In the aftermath of the healthcare reform law, private health insurers and managed care plans are likely to continue challenging the prices charged for medical products and services. These cost-control initiatives could decrease the price we might establish for linaclotide, which would result in lower product revenue or royalties payable to us.

In addition, in some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the health care system in ways that could affect our ability to sell our products profitably. These proposed reforms could result in reduced reimbursement rates for linaclotide and our other potential products, which would adversely affect our business strategy, operations and financial results.

The Food and Drug Administration Amendments Act of 2007 gives 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. The FDA's exercise of this authority could result in delays or increased costs during product development, clinical trials and regulatory review, increased costs to assure compliance with post-approval regulatory requirements, and potential restrictions on the sale and/or distribution of approved products.

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 develop and market additional products and product candidates. We are pursuing various therapeutic opportunities through our pipeline. We may spend several years 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 end up being successful. 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 product candidates on terms that we find acceptable, or at all.

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

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt, 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
- signing-up 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; and
- 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 requires 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 and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the greater-Boston area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our objectives.

We are highly dependent on the 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 of research and development and our chief scientific officer; 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 and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

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

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. If we cannot successfully

defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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

We currently have product liability insurance coverage for our clinical trials that is subject to industry-standard terms, conditions and exclusions. Our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain marketing approval for any of our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

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 will depend 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.

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 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 that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates 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 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 our product candidates may infringe.

We may be exposed to, or threatened with, future litigation by third parties alleging that our product candidates infringe their intellectual property rights. If 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 the applicable product candidate unless we obtain a license to the patent. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us 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, time consuming and unsuccessful.

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide 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 application at risk of not issuing.

Interference proceedings brought by the U.S. Patent and Trademark Office 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. 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, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceeding or developments.

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 linaclotide, with the goal of supporting regulatory approval for this product candidate. We have financed our operations primarily through the issuance of equity, including our initial public offering, and our collaboration and license arrangements, and we have incurred losses in each year since our inception in 1998. We incurred net losses attributable to Ironwood Pharmaceuticals, Inc. of approximately $53.0 million, approximately $71.2 million and approximately $53.9 million in the years ended December 31, 2010, 2009 and 2008, respectively. As of December 31, 2010, we had an accumulated deficit of approximately $367.5 million. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our expenses to increase in connection with our efforts to commercialize linaclotide and our research and development of our

other product candidates. As a result, we expect to continue to incur significant and increasing 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 would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing product candidates, conducting clinical trials, establishing manufacturing relationships and marketing drugs are expensive and uncertain. We believe that our cash on hand as of the date of this Annual Report on Form 10-K and additional cash milestone payments we may receive from our current and future collaborators give us substantial strategic optionality and will enable us to operate the company in a productive way through at least 2014. However, unforeseen circumstances may arise, our strategic imperatives could change, or opportunities to create or acquire new development programs may emerge, which could require us 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 rate of progress and cost of our clinical trials and other product development programs for linaclotide and our other product candidates;
- the costs associated with launching and commercializing linaclotide, should it be approved by FDA;
- if linaclotide receives regulatory approval, the level of underlying demand for that product;
- the costs and timing of in-licensing additional product candidates or acquiring other complementary companies;
- the timing of any regulatory approvals of our product candidates;
- the costs of establishing sales, marketing and distribution capabilities; and
- the status, terms and timing of any collaboration, licensing, co-promotion or other arrangements.

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 or eliminate one or more of our development programs or our commercialization efforts.

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 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;
- the costs associated with launching and commercializing linaclotide and any of our product candidates, if we receive regulatory approval of such candidate;
- if linaclotide receives regulatory approval, the level of underlying demand for that product and wholesalers' buying patterns;
- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;

- regulatory developments affecting our product candidates; and
- any intellectual property infringement 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.

Risks Relating to Securities Markets and Investment in Our Stock

The concentration of our capital stock ownership with our pre-IPO investors (and their affiliates), founders, directors, executives and employees will limit your ability to influence certain corporate matters.

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 such term is used in Regulation 13D of the Securities Exchange Act of 1934, as amended, or 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.

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 employees, will continue to be able to control the corporate matters listed above if any such matter is submitted to our stockholders for approval even if they come to own less than 50% of the outstanding shares of our common stock. As of March 15, 2011, the holders of our Class A common stock own 48.9% and the holders of our Class B common stock own 51.1% 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 8.7% and holders of our Class B common stock have 91.3% of the total votes in each of the matters identified in the list above. This concentrated control with our Class B common stock holders 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.

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, our pre-IPO investors (and each of their affiliates), founders, directors, executives and employees, each of whom hold shares of our Class B common stock, have significant influence over certain matters requiring stockholder approval, including significant corporate transactions, such as a merger. 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 Class B common stock are required to amend our by-laws, 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.

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:

- FDA or international regulatory actions, including actions on regulatory applications for any of our product candidates;

- the commercial performance of any of our product candidates that receive marketing approval;

- announcements of the introduction of new products by us or our competitors;

- market conditions in the pharmaceutical and biotechnology sectors;

- announcements concerning product development results, including clinical trial results, or intellectual property rights of others;

- litigation or public concern about the safety of our potential products;

- 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;
- any third-party coverage and reimbursement policies for linaclotide;
- 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections titled "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forward-looking statements. Forward-looking statements convey our current expectations or forecasts of future events. 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 progress of, timing of and amount of expenses associated with our research, development and commercialization activities;
- the timing, conduct and success of our clinical studies for our product candidates;
- our ability to obtain U.S. and foreign regulatory approval for our product candidates and the ability of our product candidates to meet existing or future regulatory standards;
- our goal to execute on our owner-related business principles;
- our expectations regarding federal, state and foreign regulatory requirements;
- the therapeutic benefits and effectiveness of our product candidates;
- the safety profile and related adverse events of our product candidates;
- our ability to manufacture sufficient amounts of linaclotide for commercialization activities with target characteristics;
- our plans with respect to collaborations and licenses related to the development, manufacture or sale of our product candidates;
- our expectations as to future financial performance, expense levels and liquidity sources;
- the timing of commercializing our product candidates;

- the accuracy of our estimates of the size and characteristics of the markets that may be addressed by our product candidates;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with our product candidates;
- anticipated 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 SEC after the date of this Annual Report on Form 10-K.

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

None.

Item 2. ***Properties***

Our corporate headquarters and operations are located in Cambridge, Massachusetts, where, as of December 31, 2010, we lease and occupy approximately 170,679 rentable square feet of office and laboratory space at 301 Binney Street. In February 2011, we amended our lease at 301 Binney Street to lease an additional 23,307 rentable square feet of office space that we do not yet occupy. The term of our lease at 301 Binney Street expires on January 31, 2016, with an option to extend the term of the lease for two additional five year periods. We believe that our facilities are suitable and adequate for our needs for the foreseeable future.

Item 3. ***Legal Proceedings***

None.

Item 4. ***Reserved***

Executive Officers of the Registrant

The following table sets forth the name, age and position of each of our executive officers as of March 15, 2011:

Name	Age	Position
Peter M. Hecht, Ph.D.	47	Chief Executive Officer, Director
Michael J. Higgins	48	Senior Vice President, Chief Operating Officer and Chief Financial Officer
Mark G. Currie, Ph.D.	56	Senior Vice President, R&D and Chief Scientific Officer
Thomas A. McCourt	53	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 serves on the board of directors of Whitehead Institute. He also serves on the Leadership Council for The David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology. 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 has served as our senior vice president, chief operating officer and chief financial officer since joining Ironwood 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 of research and development and chief scientific officer, and has led our R&D efforts since joining us in 2002. Prior to joining Ironwood, he 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, he 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 CC 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. Mr. McCourt has a degree in pharmacy from the University of Wisconsin.

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 only been publicly traded since February 3, 2010; therefore, the following table shows the high and low sales price for our Class A common stock as reported by NASDAQ for each quarter in the year ended December 31, 2010.

	Class A Common Stock 2010	
	High	Low
First Quarter	$ 14.91	$ 11.20
Second Quarter	$ 15.03	$ 9.73
Third Quarter	$ 13.14	$ 8.90
Fourth Quarter	$ 11.49	$ 10.00

As of March 15, 2011, there were 42 stockholders of record of our Class A common stock and 199 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.

We did not purchase any of our equity securities during the period covered by this report. The following sets forth information regarding all unregistered securities issued during the last fiscal year:

1. From January 1, 2010 through December 31, 2010, we issued options to purchase 1,541,000 shares of our Class A common stock to our employees, consultants and directors with an exercise price of $11.25 per share.

2. From January 1, 2010 through December 31, 2010, we issued 58,551 shares of our Class B common stock upon the exercise of stock options to our employees, consultants and directors.

These issuances of restricted securities were deemed to be exempt from registration under the Securities Act in reliance upon Rule 701 promulgated under Section 3(b) of the Securities Act of 1933, as amended, or the Securities Act, as transactions pursuant to a written compensation benefit plan and contracts relating to compensation as provided under Rule 701.

In February 2010, we completed our IPO of our Class A common stock pursuant to a registration statement on Form S-1, as amended (File No. 333-163275) that was declared effective on February 2, 2010. There has been no material change in our planned use of proceeds from the IPO from that described in the final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on February 4, 2010. As of December 31, 2010, approximately $72.3 million of the net proceeds remained available and were invested in liquid, short-term, interest-bearing funds, pending their use to fund our operations. Since our IPO, we estimate that we have used the proceeds in the following way:

- approximately $28.0 million to fund the development and commercialization of linaclotide;
- approximately $18.3 million to fund both research and development of early stage product candidates and preclinical research in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, respiratory disease, and cardiovascular disease; and
- approximately $84.6 million for general corporate purposes.

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.

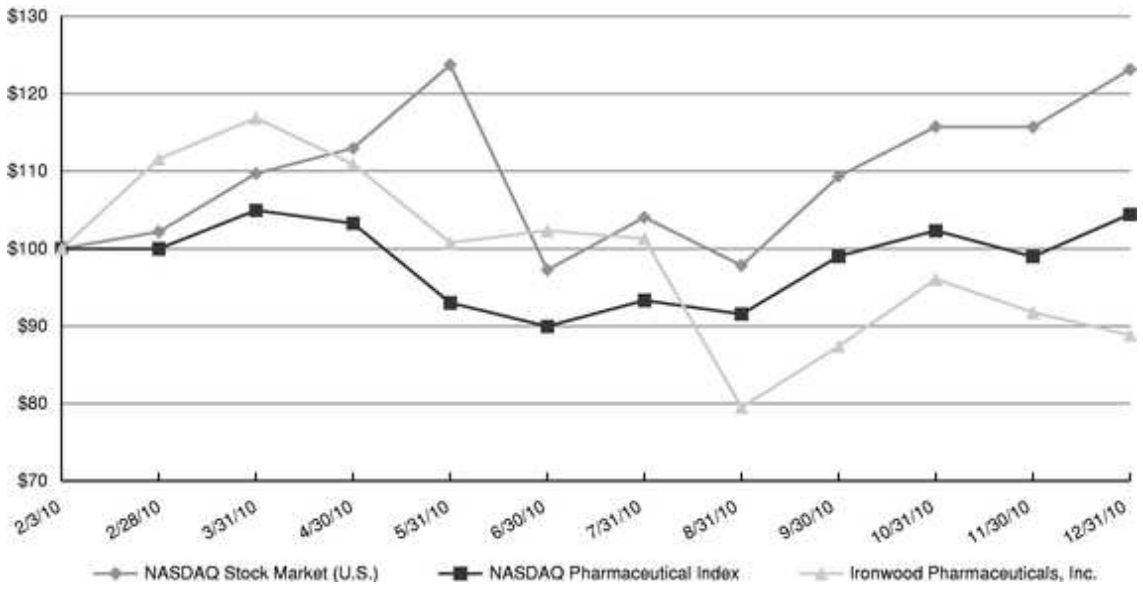
The information required to be disclosed by Item 201(d) of Regulation S-K, "Securities Authorized for Issuance Under Equity Compensation Plans," is referenced under Item 12 of Part III of this Annual Report on Form 10-K.

Corporate Performance Graph

The following performance graph 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 or the Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our Class A common stock to the NASDAQ Stock Market (U.S.) and to the NASDAQ Pharmaceutical Index from February 3, 2010 (the first date that shares of our Class A common stock were publicly traded) through December 31, 2010. 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 foregoing indices, and it assumes reinvestment of dividends, if any.

COMPARISON OF 10-MONTH 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, 2010, 2009 and 2008 and the consolidated balance sheet data as of December 31, 2010 and 2009 from our audited financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2007 and 2006 and consolidated balance sheet data as of December 31, 2008, 2007 and 2006 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,				
	2010	2009	2008	2007	2006
	(in thousands, except share and per share data)				
Consolidated Statement of Operations Data:					
Collaborative arrangements revenue	$ 43,857	$ 34,321	$ 18,383	$ 4,608	$ —
Operating expenses:					
Research and development [1]	77,454	76,100	51,421	50,424	29,559
General and administrative [1]	27,169	19,037	15,269	8,872	7,158
Total operating expenses	104,623	95,137	66,690	59,296	36,717
Loss from operations	(60,766)	(60,816)	(48,307)	(54,688)	(36,717)
Other income (expense):					
Interest expense	(196)	(318)	(291)	(232)	(198)
Interest and investment income	614	240	2,088	3,872	2,276
Remeasurement of forward purchase contracts	—	600	(900)	600	—
Other income	993	—	—	—	—
Other income (expense), net	1,411	522	897	4,240	2,078
Net loss from continuing operations before income tax benefit	(59,355)	(60,294)	(47,410)	(50,448)	(34,639)
Income tax benefit	(2,944)	(296)	—	—	—
Net loss from continuing operations	(56,411)	(59,998)	(47,410)	(50,448)	(34,639)
Net income (loss) from discontinued operations [1]	4,551	(13,314)	(7,621)	(2,712)	(2,640)
Net loss	(51,860)	(73,312)	(55,031)	(53,160)	(37,279)
Net (income) loss from discontinued operations attributable to noncontrolling interest	(1,121)	2,127	1,157	408	99
Net loss attributable to Ironwood Pharmaceuticals, Inc.	$ (52,981)	$ (71,185)	$ (53,874)	$ (52,752)	$ (37,180)
Net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted:					
Continuing operations	$ (0.63)	$ (8.43)	$ (6.88)	$ (7.57)	$ (5.40)
Discontinued operations	0.04	(1.57)	(0.94)	(0.34)	(0.39)
Net loss per share	$ (0.59)	$ (10.00)	$ (7.82)	$ (7.91)	$ (5.79)
Weighted average number of common shares used in net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	89,653,364	7,116,774	6,889,817	6,666,601	6,417,499

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

Research and development	$ 4,112	$ 2,372	$ 1,627	$ 673	$ 316
General and administrative	3,384	2,723	991	359	633
Discontinued operations	59	149	176	122	—

	December 31,				
	2010	2009	2008	2007	2006
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents and available-for-sale securities	$ 248,027	$ 122,306	$ 88,375	$ 87,860	$ 47,421
Working capital of continuing operations (excluding deferred revenue)	234,699	107,485	86,022	101,036	36,029
Assets of discontinued operations	—	2,346	3,817	4,949	7,843
Total assets	301,365	162,451	138,371	135,635	57,520
Deferred revenue, including current portion	102,433	126,002	66,008	74,392	—
Long-term debt, including current portion	—	1,763	1,815	2,752	2,243
Capital lease obligations, including current portion	590	255	306	—	—
Liabilities of discontinued operations	—	2,301	1,327	786	1,008
Total liabilities	141,814	162,441	95,382	90,207	9,900
Convertible preferred stock	—	298,350	273,400	223,802	173,851
Noncontrolling interest	—	3,212	5,339	6,495	6,903
Total stockholders' equity (deficit)	159,551	(298,340)	(230,411)	(178,374)	(126,231)

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 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 that discovers, develops and intends to commercialize differentiated medicines that improve patients' lives. To achieve this, we are building a team, a culture and processes centered on creating and marketing important new drugs. We believe that linaclotide, our GC-C agonist being developed for the treatment of patients with IBS-C or CC, could present patients and healthcare practitioners with a unique therapy for a major medical need not yet met by existing therapies. Linaclotide is our only product candidate that has demonstrated clinical proof of concept. In addition to linaclotide, we have a pipeline of early stage, pre-proof of concept development candidates in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, and respiratory disease. We are also conducting early stage, preclinical research in these therapeutic areas, as well as in the area of cardiovascular disease. We have pursued a partnering strategy for commercializing linaclotide that has enabled us to retain significant control over linaclotide's development and commercialization, share the costs with high-quality collaborators whose capabilities complement ours, and retain approximately half of linaclotide's future long-term value in the major pharmaceutical markets, should linaclotide meet our sales expectations.

We were incorporated in Delaware as Microbia, Inc. (which was the name of our formerly majority-owned subsidiary), on January 5, 1998. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc.

Prior to September 2010, we held a majority ownership interest in Microbia, Inc. (formerly known as Microbia Precision Engineering), a subsidiary formed in September 2006. Microbia, Inc., or Microbia, engaged in a specialty biochemicals business based on a proprietary strain-development platform. On September 21, 2010, we sold our interest in Microbia to DSM Holding Company USA, Inc., or DSM, in exchange for cash proceeds of $9.5 million, the payment of approximately

$1.1 million of Microbia debt and interest by DSM and future contingent consideration based on the sale of products incorporating Microbia's technology.

We currently operate in one reportable business segment—human therapeutics. Our human therapeutics segment consists of the development and commercialization of our product candidates, including linaclotide. Prior to the sale of our interest in Microbia, we also operated in the biomanufacturing segment. Our biomanufacturing segment, which comprised a much smaller part of our business, consisted of our majority ownership interest in Microbia. Our human therapeutics segment represented 100% and 99% of our total assets at December 31, 2010 and 2009, respectively, while our biomanufacturing segment represented approximately 1% of our total assets at December 31, 2009. For the years ended December 31, 2010, 2009 and 2008, results of operations of our biomanufacturing segment are included in net income (loss) from discontinued operations in our financial statements.

To date, we have dedicated substantially all of our activities to the research and development of our product candidates. We have not generated any revenue to date from product sales and have incurred significant operating losses since our inception in 1998. We incurred net losses attributable to Ironwood Pharmaceuticals, Inc. of approximately $53.0 million, $71.2 million and $53.9 million in the years ended December 31, 2010, 2009 and 2008, respectively. As of December 31, 2010, we had an accumulated deficit of approximately $367.5 million and we expect to incur losses for the foreseeable future.

Financial Overview

Revenue. Revenue to date from our human therapeutics segment is generated primarily through our collaboration agreement with Forest and our license agreements with Almirall and Astellas. The terms of these agreements include payment to us of one or more of the following: nonrefundable, up-front license fees; milestone payments; and royalties on product sales. Revenue from our human therapeutics segment is shown in our consolidated statements of operations as collaborative arrangements revenue. Revenue from our biomanufacturing segment was generated by our former subsidiary, Microbia, which had entered into research and development service agreements with various third parties. These agreements generally provided for fees for research and development services rendered. As a result of the sale of our interest in Microbia, revenue from our biomanufacturing segment is included in net income (loss) from discontinued operations. We expect our revenue to fluctuate for the foreseeable future as our collaborative arrangements revenue is principally based on the achievement of clinical and commercial milestones.

Research and development expense. Research and development expense consists of expenses incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of compensation, benefits and other employee related expenses, research and development related facility costs and third-party contract costs relating to research, formulation, manufacturing, preclinical study and clinical trial activities. The costs of revenue related to the Microbia services contracts and costs associated with Microbia's research and development activities are included in net income (loss) from discontinued operations. We charge all research and development expenses to operations as incurred. Under our Forest collaboration agreement we are reimbursed for certain research and development expenses and we net these reimbursements against our research and development expenses as incurred.

Our lead product candidate is linaclotide and it represents the largest portion of our research and development expense for our product candidates. Linaclotide is a first-in-class compound currently in Phase 3 clinical development for the treatment of IBS-C and CC and is our only product candidate that has demonstrated clinical proof of concept. In September and November 2010, we announced the positive top-line results from each of the two Phase 3 clinical trials assessing the safety and efficacy of linaclotide in patients with IBS-C, and in November 2009, we announced that we achieved positive results in each of our Phase 3 CC trials. We have a pipeline of early stage, pre-proof of concept development candidates in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, and respiratory disease. We are also conducting early stage, preclinical research in these therapeutic areas, as well as in the area of cardiovascular disease.

The following table sets forth our research and development expenses related to our product pipeline for the years ended December 31, 2010, 2009 and 2008. These expenses relate primarily to external costs associated with manufacturing, preclinical studies and clinical trial costs. Costs related to facilities, depreciation, share-based compensation and research and development support services are not directly charged to programs.

	Years Ended December 31,		
	2010	2009 (unaudited)	2008
		(in thousands)	
Demonstrated clinical proof of concept	$ 26,684	$ 41,052	$ 13,588
Early stage	13,067	5,742	10,917
Early stage, preclinical	6,134	5,701	3,724

We began tracking program expenses for linaclotide in 2004, and research and development program expenses from inception to December 31, 2010 were approximately $123.4 million. The expenses for linaclotide include both reimbursements to us by Forest as well as our portion of costs incurred by Forest for linaclotide and invoiced to us under the cost-sharing provisions of our collaboration agreement.

The lengthy process of securing FDA 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. Accordingly, 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 or our other product candidates prior to their regulatory approval, if such approval is ever granted. 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, or 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. In evaluating potential assets, we apply the same criteria as those used for investments in internally-discovered assets.

The majority of our external costs are spent on linaclotide, as costs associated with later stage clinical trials are, in most cases, more significant than those incurred in earlier stages of our pipeline. We expect external costs related to the linaclotide program to begin decreasing provided that no other clinical trials are necessary to obtain regulatory approval in the U.S. If our other product candidates are successful in early stage clinical trials, we would expect external costs to increase as the programs progress through later stage clinical trials. The remainder of our research and development expense is not tracked by project as it consists primarily of our internal costs, and it benefits multiple projects that are in earlier stages of development and which typically share resources.

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 preclinical and clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of any 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 scientific and clinical data of each product candidate, as well as ongoing assessments of such product candidate's commercial potential.

We expect our research and development costs to continue to be substantial for the foreseeable future and to increase with respect to our product candidates other than linaclotide as we advance those product candidates through preclinical studies and clinical trials. Additionally, our research and development costs will increase as we will fund full-time equivalents for Protagonist's drug discovery activities under the terms of our collaboration agreement.

General and administrative expense. 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 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 a result of our IPO in February 2010, we have experienced and will likely continue to experience increases in general and administrative expense relating to operating as a public company. These increases include legal fees, accounting fees, costs associated with implementing and complying with the requirements of the Sarbanes-Oxley Act of 2002 and the Dodd-Frank Wall Street Reform and Protection Act of 2010 and fees for investor relations services. We also anticipate substantial increases in expenses related to developing the organization necessary to commercialize linaclotide.

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., or GAAP. The preparation of these financial statements requires us to make certain

estimates and assumptions that affect the reported amounts of assets and liabilities and the reported amounts of revenues and expenses during the reported periods. These estimates and assumptions, including those related to revenue recognition, available-for-sale securities, impairments of long-lived assets, income taxes including the valuation allowance for deferred tax assets, research and development expenses, contingencies, 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. Prior to our IPO, we also evaluated our estimates and judgments regarding the fair value assigned to our common stock. These critical estimates and assumptions are based on our historical experience, our observance of trends in the industry, and various other factors that are believed to be reasonable under the circumstances and form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. 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.

As a result of the sale of our interest in Microbia, we have presented the assets, liabilities, operations, and cash flows of Microbia as discontinued operations for all periods presented prior to the sale.

Revenue Recognition

Our revenue is generated primarily through collaborative research and development and license agreements. The terms of these agreements typically include payment to us of one or more of the following: nonrefundable, up-front license fees; milestone payments; the sale of drug substance to our collaborators; and royalties on product sales. In addition, prior to September 2010, we generated services revenue through agreements that generally provided for fees for research and development services rendered.

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. We evaluate revenue from agreements that have multiple elements and 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;
- there is objective and reliable evidence of fair value of the undelivered items; 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.

The determination that multiple elements in an arrangement meet the criteria for separate units of accounting requires us to exercise our judgment.

The determination of whether we should recognize revenue on a gross or net basis involves judgment based on the relevant facts and circumstances, which relate primarily to whether we act as a principal or agent in the process of generating revenues from our collaboration and licensing arrangements.

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, including the $70.0 million up-front license fee under the Forest collaboration agreement entered into in September 2007 and the $40.0 million up-front license fee, of which $38.0 million was received net of foreign withholding taxes, under the Almirall license agreement entered into in April 2009, on a straight-line basis over the contracted or estimated period of performance due to our continued involvement in research and development. 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. To date, we have had no material changes to our estimated periods of continuing involvement under existing collaboration and license agreements. In the case where we cannot reliably estimate the period of performance due to our continued involvement in research and development, we defer the commencement of revenue recognition of the up-front license fee until the earlier of either (i) the expected performance period of our joint steering committee obligations can be reasonably and reliably estimated or (ii) we are no longer contractually obligated to perform all joint steering committee duties. As a result, at December 31, 2009, we deferred the entire $30.0 million up-front licensing fee received from Astellas in November 2009. We began recognizing revenue from this up-front payment from Astellas in March 2010, when an estimate of the development period could be derived.

Milestones

At the inception of each agreement that includes contingent milestone payments, we evaluate whether the contingencies underlying each milestone are substantive and at risk to both parties, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. If we do not consider a milestone to be substantive and at risk to both parties, the revenues from the related milestone payment cannot be recognized when the milestone is achieved, but must be recognized on a straight-line basis over the remaining performance period. All of the milestones that have been achieved to date under our Forest collaboration agreement and our Almirall license agreement have been considered substantive. As of December 31, 2010, we had not achieved any milestones under our Astellas license agreement.

In those circumstances where a substantive milestone is achieved, collection of the related receivable is reasonably assured and we have remaining obligations to perform under the collaboration arrangement, we recognize as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that has elapsed as of the date the milestone is achieved, with the balance being deferred and recognized over the remaining period of performance.

Payments received or reasonably assured after performance obligations are fully met are recognized as earned. Because the recognition of a substantive milestone under a collaboration agreement typically requires the completion of a number of activities conducted over a significant period of time, the expenses related to achieving the milestone often are incurred prior to the period in which the milestone payment is recognized. When we do achieve milestones that we consider substantive under any of our collaborations, we may experience significant fluctuations in our

collaborative revenues from quarter to quarter and year to year depending on the timing of achieving such substantive milestones.

Services Revenue

Prior to September 2010, services revenue was recognized when there was persuasive evidence that an arrangement existed, services had been rendered or delivery had occurred, the price was fixed or determinable, and collection was reasonably assured. Revenue from research and development services rendered was recognized as services were performed. As a result of the sale of our interest in Microbia in September 2010, services revenue is included in net income (loss) from discontinued operations.

Research and Development Expense

All research and development expenses are expensed as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including compensation, benefits and other employee costs; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; contractual services, including clinical trial and related clinical manufacturing expenses; and other external expenses. In addition, research and development expense includes reimbursements from Forest for services performed pursuant to our collaboration agreement. Clinical trial expenses include expenses associated with 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. Under our Forest collaboration agreement, we are reimbursed for certain research and development expenses and we net these reimbursements against our research and development expenses as incurred. 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

Prior to January 1, 2006, we accounted for employee share-based awards, including stock options, to employees using the intrinsic value method. Under the intrinsic value method, compensation expense was measured on the date of award as the difference, if any, between the deemed fair value of our common stock and the option exercise price, multiplied by the number of options granted. The option exercise prices and fair value of our common stock were determined by our management and board of directors based on a review of various objective and subjective factors. No compensation expense was recorded for stock options issued to employees prior to January 1, 2006 for awards with fixed amounts and with fixed exercise prices at least equal to the fair value of our common stock at the date of grant.

Effective January 1, 2006, we recognize compensation expense for all share-based awards granted, modified, repurchased or cancelled on or after January 1, 2006, based on the grant date fair value. These costs are recognized on a straight-line basis over the requisite service period for all time-based vested awards. We continue to account for share-based awards granted prior to January 1, 2006 under the intrinsic value method.

We record 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 as of the respective vesting date. Further, we expense the fair value of non-employee stock options over the vesting term of the underlying stock options.

For employee share-based awards subsequent to January 1, 2006, we estimate the fair value of the share-based awards, including stock options, using the Black-Scholes option-pricing model. Determining

the fair value of share-based awards requires the use of highly subjective assumptions, including the expected term of the award and expected stock price volatility. The weighted average assumptions used in calculating the fair value of share-based awards granted in 2010, 2009 and 2008 are set forth below:

	Years Ended December 31,		
	2010	2009	2008
Volatility	57.4%	62.3%	64.0%
Dividend yield	—%	—%	—%
Expected life of options (in years)	6.5	6.5	6.5
Risk-free interest rate	2.9%	2.7%	3.1%

The assumptions used in determining the fair value of share-based awards represent management's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change, and we use different assumptions, our share-based compensation could be materially different in the future. 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. Because we do not have a sufficient history to estimate the expected term, we use the simplified method for estimating the expected term. The simplified method is based on the average of the vesting tranches and the contractual life of each grant. Because there was no public market for our common stock prior to our initial public offering, we lacked company-specific historical and implied volatility information. Therefore, we estimate our expected stock volatility based on that of publicly-traded peer companies, and we expect to continue to use this methodology until such time as we have adequate historical data regarding the volatility of our publicly-traded stock price. For purposes of identifying publicly-traded peer companies, we selected publicly-traded companies that are in the biopharmaceutical industry, have products or product candidates in similar therapeutic areas (gastrointestinal dysfunction and pain management) and stages of preclinical and clinical development as us, have sufficient trading history to derive a historic volatility rate and have similar vesting terms as our granted options. We have not paid and do not anticipate paying cash dividends on our shares of common stock; therefore, the expected dividend yield is assumed to be zero. We also recognize compensation expense for only the portion of options that are expected to vest. Accordingly, we have estimated expected forfeitures of stock options based on our historical forfeiture rate, adjusted for known trends, and used these rates in developing a future forfeiture rate. Our forfeiture rates were 5.5%, 5.8% and 4.4% as of December 31, 2010, 2009 and 2008, respectively. If our actual forfeiture rate varies from our historical rates and estimates, additional adjustments to compensation expense may be required in future periods.

We have historically granted stock options at exercise prices not less than the fair value of our common stock as determined by our board of directors, with input from management. Due to the absence of an active market for our common stock, prior to our initial public offering on February 2, 2010, our board of directors has historically determined, with input from management, the estimated fair value of our common stock on the date of grant based on a number of objective and subjective factors, including:

- the prices at which we sold shares of convertible preferred stock;
- the superior rights and preferences of securities senior to our common stock at the time of each grant;
- the likelihood of achieving a liquidity event such as an initial public offering or sale of our company;
- our historical operating and financial performance and the status of our research and product development efforts;
- achievement of enterprise milestones, including our entering into collaboration and license agreements; and
- external market conditions affecting the biotechnology industry sector.

In connection with the preparation of the consolidated financial statements for the years ended December 31, 2009 and 2008, our board of directors also considered valuations provided by management in determining the fair value of our common stock. Such valuations were prepared as of March 31, June 30, October 28 and December 31, 2008, and March 31, June 30, September 30, November 2 and December 31, 2009, and valued our common stock at $4.33, $4.67, $4.98, $4.89, $5.00, $5.48, $7.36, $11.75 and $12.05 per share, respectively. The valuations have been used to estimate the fair value of our common stock as of each option grant date and in calculating share-based compensation expense. Our board of directors has consistently used the most recent quarterly valuation provided by management for determining the fair value of our common stock unless a specific event occurred that necessitated an interim valuation.

The valuations were prepared consistent with the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation* , or the Practice Aid. We used the guideline company method and the similar transaction method of the market approach, which compare our company to similar publicly-traded companies or transactions, and an income approach, which looks at projected future cash flows, to value our company from among the alternatives discussed in the Practice Aid. In addition, as we had several series of convertible preferred stock outstanding prior to our initial public offering in February 2010, it was also necessary to allocate our company's value to the various classes of stock, including stock options. As provided in the Practice Aid, there are several approaches for allocating enterprise value of a privately-held company among the securities held in a complex capital structure. The possible methodologies include the probability-weighted expected return method, the option-pricing method and the current value method.

We used the probability-weighted expected return method described in the Practice Aid to allocate the enterprise values to the common stock. Under this method, the value of our common stock is estimated based upon an analysis of future values for our company assuming various future outcomes, the timing of which is based on the plans of our board of directors and management. Under this approach, share value is based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the rights of each share class. We estimated the fair value of our common stock using a probability-weighted analysis of the present value of the returns afforded to our stockholders under each of four possible future scenarios. Three of the scenarios assumed a stockholder exit, either through an IPO or a sale of our company. The fourth scenario assumed a sale of our company at a value that is less than the cumulative amounts invested by our preferred stockholders.

For the March 31, 2008 valuation, we utilized a one product IPO scenario reflecting only linaclotide advancing in the clinic at the time of an IPO. Beginning with the October 28, 2008 valuation, we included two separate IPO scenarios to better reflect our company's risk profile at that time. The linaclotide program was by then advancing in two indications, CC and IBS-C. We believed that the IBS-C indication had a significantly higher market value and higher clinical risk for Ironwood. To better reflect the potential liquidity outcomes for linaclotide, the first IPO scenario included an assumption of successful Phase 3 clinical trials for both the CC and IBS-C indications at the time of an IPO, and the second IPO scenario reflected successful Phase 3 clinical trials in only the CC indication at the time of the IPO. For both IPO scenarios and the sale scenario, the estimated future values of our common stock were calculated using assumptions including: the expected pre-money or sale valuations based on the market approach, and the income approach using the discounted cash flow method, and the expected dates of the future expected IPO or sale. For the sale at an assumed price less than the liquidation preference scenario, the estimated future and present values of our common stock were calculated using assumptions including the estimated aggregate enterprise value that could be attained through such a sale and the estimated expected date of the future sale. The present values of our common stock under each scenario were then calculated using a risk-adjusted discount rate. Finally, the calculated present values for our common stock were probability-weighted based on our

estimate of the relative occurrence of each scenario to derive the concluded value of our common stock.

There are significant judgments and estimates inherent in the determination of these valuations. These judgments and estimates included assumptions regarding our future performance, the time to completing an IPO or other liquidity event, and the timing of and probability of launching our product candidate as well as determinations of the appropriate valuation methods. If we had made different assumptions, our share-based compensation expense, net loss and net loss per share could have been significantly different.

We have also granted performance-based stock options with terms that allow the recipients to vest in a specific number of shares based upon the achievement of performance-based milestones as specified in the grants. Share-based compensation expense associated with these performance-based stock options is recognized if the performance condition is considered probable of achievement using management's best estimates of the time to vesting for the achievement of the performance-based milestones. If the actual achievement of the performance-based milestones varies from our estimates, share-based compensation expense could be materially different than what is recorded in the period. The cumulative effect on current and prior periods of a change in the estimated time to vesting for performance-based stock options will be recognized as compensation cost in the period of the revision, and recorded as a change in estimate.

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.

The total estimated compensation cost related to non-vested stock options and stock awards, with time-based vesting, not yet recognized was approximately $18.6 million, $9.4 million and $6.4 million as of December 31, 2010, 2009 and 2008, respectively. The weighted-average period over which this expense is expected to be recognized is approximately 3.36 years. At December 31, 2010, approximately $3.9 million of additional share-based compensation related to options subject to performance-based milestone vesting was not yet recognized. See Notes 2 and 16 to our consolidated financial statements located in this Annual Report on Form 10-K for further discussion of share-based compensation.

Fair Value of Financial Instruments

In September 2007, we entered into a collaboration agreement with Forest, which included a contingent equity investment in the form of a forward purchase contract, which required Forest to purchase 2,083,333 shares of our Series G convertible preferred stock at a price of $12.00 per share if we achieved a specific clinical milestone. This preferred stock, which was issued to Forest in September 2009, had rights and conditions substantially identical to our outstanding preferred stock prior to the issuance. These shares of convertible preferred stock converted into 2,083,333 shares of our Class B common stock at the time of our IPO in February 2010.

In April 2009, we entered into a license agreement with Almirall, which also included a contingent equity investment in the form of a forward purchase contract, which required Almirall to purchase 681,819 shares of our Series I convertible preferred stock, if a specific clinical milestone was met, at a price of $22.00 per share. The milestone in this agreement was a different milestone from the one contained in the Forest collaboration agreement. This preferred stock, which was issued to Almirall and

for which we received $15.0 million of cash proceeds on November 13, 2009, had rights and conditions substantially identical to our outstanding preferred stock. These shares of convertible preferred stock converted into 681,819 shares of our Class B common stock at the time of our IPO in February 2010.

We evaluated both of these financial instruments and determined that because we may have been required to settle these instruments by transferring assets to Forest and Almirall due to "deemed liquidation" provisions of the preferred stock, these instruments should have been considered assets or liabilities. Each contingent equity investment was assessed at fair market value at its inception. A significant input in the valuation of the forward purchase contracts was the fair value of our convertible preferred shares which were estimated using the probability-weighted expected return method. Under the probability-weighted expected return method, the value of our convertible preferred shares was calculated based on an analysis of potential future values of our company assuming various future liquidity events, the timing and amount of which were based on estimates from our company's management. The resulting preferred share value was based on the probability-weighted present value of the expected future returns, considering each of the possible outcomes as well as the rights of each preferred share class. At each measurement date, assumptions used in the probability-weighted expected return model, including future values, liquidity dates and scenario weightings, were consistent with the assumptions used in our common stock valuations at such time, as described above. The calculated discount or premium from the pre-determined price paid by Forest and Almirall for their shares in excess of the estimated fair value of our convertible preferred stock at the expected time of meeting the respective milestone was then discounted using a company risk-adjusted rate consistent with the common stock valuations being performed at the time to arrive at the present value of the respective forward purchase contract.

At the inception of the Forest collaboration agreement, the fair value of our convertible preferred stock to be issued upon the achievement of the milestone was equal to the sum of the probability-weighted present values for the four identified possible exit scenarios—initial public offering (either one-product IPO or two-product IPO or later a one-indication IPO and two-indication IPO), sale and sale at an assumed price below the liquidation preference, all with June 30, 2009 as the expected milestone achievement date. The probability weight assigned to the two-product IPO scenario was 20% and the probability weight assigned to the one-product IPO scenario was 70%. The probability weight assigned to the sale scenario was 5% and the probability weight assigned to the sale at an assumed price less than the liquidation preference scenario was 5%. The resulting enterprise values for each scenario were discounted to an estimated investment date of October 31, 2008, using a risk-adjusted discount rate of 20%. Based on this calculation, the fair value of the convertible preferred stock to be issued upon achievement of the Forest milestone was valued at $5.32 per share. The resulting difference of $6.68 per share between the fair value of $5.32 and the purchase price of $12.00 per share represented the estimated premium Forest would pay above the fair value of the convertible preferred stock. This per share premium was then adjusted by the probability of achieving the milestone, which was estimated at 80%, based on clinical risk, resulting in a probability adjusted premium of $5.34 per share. The resulting total premium was then discounted as of September 12, 2007 using a company risk-adjusted discount rate of 20%. As a result, the Forest contingent equity investment was valued at the inception of the agreement to be $9.0 million, which represents the fair value of the premium that Forest would pay for shares of our stock should the milestone be achieved.

The fair value of our convertible preferred stock to be issued upon the achievement of the Almirall milestone at the inception of the license agreement in April 2009 was equal to the sum of the probability-weighted present values for the four identified possible exit scenarios—one-indication IPO, two-indication IPO, sale and sale at an assumed price less than the liquidation preference, all with September 30, 2010 as the expected event date. The resulting enterprise values for each scenario were discounted as of the investment date which was estimated to be October 15, 2009. Based on this calculation, the fair value of the convertible preferred stock to be issued upon achievement of the

Almirall milestone was estimated at $9.23 per share. The resulting difference of $12.77 per share between the estimated fair value of $9.23 and the purchase price of $22.00 per share is the estimated premium Almirall will pay above the fair value of the convertible preferred stock. This per share premium was then adjusted by the probability of achieving the milestone, which was estimated at 75%, resulting in a probability adjusted premium of $9.58 per share. The resulting total premium was then discounted as of April 30, 2009 at 20%. As a result, the Almirall contingent equity investment was valued at the inception of the agreement to be $6.0 million, which represents the fair value of the premium that Almirall would pay for shares of our stock should the milestone be achieved.

In addition to valuing these instruments at their inception, we were also required to remeasure the fair value of our contingent equity investments at each reporting period, using current assumptions, with changes in value recorded as other income or expense. At December 31, 2008, we remeasured the fair value of the Forest contingent equity investment using valuation methodologies consistent with those used at inception, updated for current assumptions. Based on these calculations, the fair value of the convertible preferred stock to be issued upon achievement of the Forest milestone was estimated at $7.16 per share. The resulting difference of $4.84 per share was then adjusted by an updated probability of achieving the milestone, which was now estimated at 90%, resulting in a probability adjusted premium of $4.35 per share. The resulting total premium was then discounted as of December 31, 2008 using a risk-adjusted discount rate of 19%. As a result, the Forest contingent equity investment was valued at December 31, 2008 to be $8.7 million.

On July 22, 2009, we achieved the Forest milestone, thus triggering the Forest equity investment. As a result, we remeasured the fair value of the equity investment as of July 22, 2009 using valuation methodologies consistent with those used at December 31, 2008, updated for current assumptions including a change to the investment date to July 22, 2009. Based on these calculations, the fair value of the convertible preferred stock to be issued upon achievement of the Forest milestone was calculated at $7.76 per share. The resulting difference of $4.24 per share was not adjusted by a probability discount as the milestone was achieved. The resulting total premium was then discounted as of July 22, 2009 using a risk-adjusted discount rate of 20%. As a result, the Forest contingent equity investment was valued at July 22, 2009 to be $8.8 million and at that time we reclassified the forward purchase contract as a reduction to convertible preferred stock. On September 1, 2009, we received from Forest $25.0 million for the 2,083,333 shares of Series G convertible preferred stock.

On November 2, 2009, we achieved the Almirall milestone, thus triggering the Almirall equity investment. As a result, we remeasured the fair value of the equity investment as of November 2, 2009 using valuation methodologies consistent with those used at April 30, 2009, updated for current assumptions including a change to the investment date to November 2, 2009. Based on these calculations, the fair value of the convertible preferred stock to be issued upon achievement of the Almirall milestone was estimated at $12.41 per share. The resulting difference of $9.59 per share was not adjusted by a probability discount as the milestone was achieved. The resulting total premium was then discounted as of November 2, 2009 using a risk-adjusted discount rate of 15%. As a result, the Almirall contingent equity investment was valued at November 2, 2009 to be $6.5 million and at that time we reclassified the forward purchase contract as a reduction to convertible preferred stock. On November 13, 2009, we received from Almirall $15.0 million for the 681,819 shares of Series I convertible preferred stock.

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,		
	2010	2009	2008
	(in thousands)		
Collaborative arrangements revenue	$ 43,857	$ 34,321	$ 18,383
Operating expenses:			
Research and development	77,454	76,100	51,421
General and administrative	27,169	19,037	15,269
Total operating expenses	104,623	95,137	66,690
Loss from operations	(60,766)	(60,816)	(48,307)
Other income (expense):			
Interest expense	(196)	(318)	(291)
Interest and investment income	614	240	2,088
Remeasurement of forward purchase contracts	—	600	(900)
Other income	993	—	—
Other income (expense), net	1,411	522	897
Net loss from continuing operations before income tax benefit	(59,355)	(60,294)	(47,410)
Income tax benefit	(2,944)	(296)	—
Net loss from continuing operations	(56,411)	(59,998)	(47,410)
Net income (loss) from discontinued operations	4,551	(13,314)	(7,621)
Net loss	(51,860)	(73,312)	(55,031)
Net (income) loss from discontinued operations attributable to noncontrolling interest	(1,121)	2,127	1,157
Net loss attributable to Ironwood Pharmaceuticals, Inc.	$ (52,981)	$ (71,185)	$ (53,874)

Year Ended December 31, 2010 Compared to Year Ended December 31, 2009

Revenue

	Years Ended December 31,		Change	
	2010	2009	$	%
	(dollars in thousands)			
Collaborative arrangements revenue	$ 43,857	$ 34,321	$ 9,536	27.8%

Collaborative Arrangements. The increase in revenue from collaborative arrangements for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily due to increases in revenue from the Almirall license agreement, which we entered into in April 2009, and the Astellas license agreement, which we entered into in November 2009, offset by decreases in revenue from the Forest collaboration. In the year ended December 31, 2010, we recognized approximately $10.6 million of revenue, compared with approximately $7.0 million of revenue in 2009, related to the $38.0 million up-front license payment received in May 2009 from Almirall and the amortization of the deferred revenue resulting from recording the initial $6.0 million valuation of the Almirall forward purchase contract. Additionally in 2010, we recognized approximately $7.6 million of revenue associated

with the $19.0 million milestone payment, net of taxes, received in December 2010 under the Almirall license agreement. In the year ended December 31, 2010, we recognized approximately $2.6 million of revenue related to the $30.0 million up-front license payment received in November 2009 from Astellas, compared with none in 2009, as the development period and related amortization did not commence until March 2010. Additionally, in the year ended December 31, 2010 we recognized approximately $1.3 million from shipments of clinical trial materials to both Almirall and Astellas compared to approximately $0.3 million in 2009. This was offset by a decrease in revenue recognized in relation to the Forest collaboration primarily due to the achievement of a $20.0 million milestone in July 2009. During the year ended December 31, 2010, we recognized approximately $4.0 million related to this milestone compared to approximately $9.2 million during 2009, of which approximately $7.5 million was recognized upon achievement, resulting in a decrease of approximately $5.2 million from 2010 to 2009.

Operating Expenses

	Years Ended December 31,		Change	
	2010	2009	$	%
	(dollars in thousands)			
Operating expenses:				
Research and development	$ 77,454	$ 76,100	$ 1,354	1.8%
General and administrative	27,169	19,037	8,132	42.7%
Total operating expenses	$ 104,623	$ 95,137	$ 9,486	10.0%

Research and Development Expense. The increase in research and development expense of approximately $1.4 million for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily due to an increase of approximately $4.3 million in compensation, benefits, and employee related expenses associated mainly with increased headcount, an increase of approximately $1.8 million due to the implementation in the first quarter of 2010 of our employee incentive plan, an increase of approximately $1.7 million in share-based compensation expense primarily related to our annual stock option grant made in February 2010, an increase of approximately $2.9 million in research and development related facilities and other research and development support costs largely due to increased rent and depreciation expense associated with the additional space we leased at our 301 Binney Street facility in February 2010 and an increase of approximately $0.8 million in internal research costs, such as laboratory supplies, to support the development of our pipeline, offset by a decrease of approximately $10.2 million in support of linaclotide, primarily resulting from lower clinical trial, collaboration and manufacturing expenses as we completed the efficacy portion of linaclotide's development program.

General and Administrative Expense. The increase in general and administrative expense of approximately $8.1 million for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily due to an increase of approximately $2.3 million in compensation, benefits and other employee related expenses associated with increased headcount, an increase of approximately $0.7 million in share-based compensation expense primarily related to our annual stock option grant made in February 2010, an increase of approximately $0.8 million due to the implementation in the first quarter of 2010 of our employee incentive plan, an increase of approximately $1.2 million in general and administrative related facilities costs primarily due to increased rent expense associated with the additional space we leased at our 301 Binney Street facility in February 2010, an increase of approximately $0.8 million in expenses due to being a public company, such as audit and tax fees, filing fees, and directors' and officers' insurance and an increase in external consulting costs of approximately $2.2 million primarily associated with preparing to commercialize linaclotide and public company requirements, such as investor relations, Sarbanes-Oxley compliance and stock administration offset by an increase of approximately $0.8 million in the reimbursement from Forest on our collaborative commercial activities.

Other Income (Expense), Net

	Years Ended December 31,		Change	
	2010	2009	$	%
	(dollars in thousands)			
Other income (expense):				
Interest expense	$ (196)	$ (318)	$ 122	38.4%
Interest and investment income	614	240	374	155.8%
Remeasurement of forward purchase contracts	—	600	(600)	(100.0)%
Other income	993	—	993	100.0%
Total other income (expense), net	$ 1,411	$ 522	$ 889	170.3%

Interest Expense. The decrease in interest expense of approximately $0.1 million for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily the result of a reduction in long-term debt, partially offset by early payment fees incurred in connection with the repayment of the long-term debt in September 2010.

Interest and Investment Income. The increase in interest and investment income of approximately $0.4 million for the year ended December 31, 2010 compared to the year ended December 31, 2009 was due to higher average cash, cash equivalents and investment balances, partially offset by lower prevailing interest rates during the period.

Remeasurement of Forward Purchase Contracts. The decrease in the remeasurement of forward purchase contracts of approximately $0.6 million for the year ended December 31, 2010 compared to the year ended December 31, 2009 resulted from the final settlement of the Forest forward purchase contract in July 2009 and the Almirall forward purchase contract in November 2009. The Forest forward purchase contract was remeasured in July 2009 when Forest made its equity investment and the Almirall forward purchase contract was remeasured at November 2, 2009 when Almirall made its equity investment, resulting in total respective gains on remeasurement of $0.1 million and $0.5 million for the year ended December 31, 2009. As a result of the final settlements of both forward purchase contracts, there were no corresponding remeasurements during 2010.

Other Income. The increase in other income for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily due to approximately $978,000 in grants awarded to us under the Qualifying Therapeutic Discovery Project Program in 2010. There was no corresponding award in 2009.

Income Tax Benefit. The approximately $2.6 million increase in income tax benefit for the year ended December 31, 2010 compared to the year ended December 31, 2009 was related to intra-period income tax allocation requirements for which we recorded a benefit for income taxes from continuing operations of approximately $2.9 million, offset by an identical income tax provision from discontinued operations for the year ended December 31, 2010. The intra-period income tax allocation considers discontinued operations for purposes of determining the amount of tax benefit that results from our loss from continuing operations.

Net Income (Loss) From Discontinued Operations. The approximately $17.9 million increase in net income (loss) from discontinued operations for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily the result of the approximately $12.2 million gain recognized on the sale of Microbia in September 2010 and lower operating expenses of Microbia resulting from reduced headcount and rent expense associated with Microbia's November 2009 restructuring activities, partially offset by the tax provision related to the intra-period tax allocation.

Net (Income) Loss From Discontinued Operations Attributable to Noncontrolling Interest. The approximately $3.2 million increase in net income from discontinued operations attributable to noncontrolling interest for the year ended December 31, 2010 compared to the year ended December 31, 2009 was primarily due to an increase in net income for Microbia due to a gain recognized on the settlement of intercompany balances immediately prior to the sale of Microbia in September 2010 and lower operating expenses of Microbia resulting from reduced headcount and rent expense associated with Microbia's November 2009 restructuring activities.

Year Ended December 31, 2009 Compared to Year Ended December 31, 2008

Revenue

	Years Ended December 31,		Change	
	2009	2008	$	%
	(dollars in thousands)			
Collaborative arrangements revenue	$ 34,321	$ 18,383	$ 15,938	86.7%

Collaborative Arrangements. The increase in revenue from collaborative arrangements of approximately $15.9 million for the year ended December 31, 2009 compared to the year ended December 31, 2008 was primarily due to increases in revenue from the Forest collaboration and the Almirall license agreement. During the year ended December 31, 2009, we recognized approximately $9.2 million of revenue related to a $20.0 million Forest milestone payment we received in July 2009, and a total of approximately $7.0 million of revenue related to the $38.0 million up-front license payment received from Almirall in May 2009 and the amortization of the deferred revenue resulting from recording the initial $6.0 million valuation of the Almirall forward purchase contract. Additionally, in 2009, we recognized approximately $0.3 million in revenue related to the initial sale of development material to Almirall. These increases were partially offset by an incremental approximately $0.6 million of revenue recognized in the year ended December 31, 2008 related to the initial recognition upon achievement of a clinical milestone in September 2008 under the Forest collaboration.

Operating Expenses

	Years Ended December 31,		Change	
	2009	2008	$	%
	(dollars in thousands)			
Operating expenses:				
Research and development	$ 76,100	$ 51,421	$ 24,679	48.0%
General and administrative	19,037	15,269	3,768	24.7%
Total operating expenses	$ 95,137	$ 66,690	$ 28,447	42.7%

Research and Development Expense. The increase in research and development expense of approximately $24.7 million for the year ended December 31, 2009 compared to the year ended December 31, 2008 was primarily due to an increase of approximately $21.4 million in expenses primarily associated with the Phase 3 clinical trials for linaclotide and an increase of approximately $3.3 million in spending for compensation, benefits and other employee related expenses resulting from an increase in headcount to support our linaclotide program.

General and Administrative Expense. The increase in general and administrative expense of approximately $3.8 million for the year ended December 31, 2009 compared to the year ended December 31, 2008 was primarily due to increased compensation, benefits and other employee related expenses of approximately $2.9 million related to an increase in headcount to support our overall growth, increased general and administrative related facilities costs of approximately $0.8 million

associated with new office space and increased legal costs of approximately $0.7 million primarily associated with intellectual property and other corporate legal matters, partially offset by approximately $0.6 million decrease in professional fees primarily associated with marketing related activities.

Other Income (Expense), Net

	Years Ended December 31,		Change	
	2009	2008	$	%
	(dollars in thousands)			
Other income (expense):				
Interest expense	$ (318)	$ (291)	$ (27)	(9.3)%
Interest and investment income	240	2,088	(1,848)	(88.5)%
Remeasurement of forward purchase contracts	600	(900)	1,500	166.7%
Total other income (expense), net	$ 522	$ 897	$ (375)	(41.8)%

Interest Expense. The increase in interest expense for the year ended December 31, 2009 compared to the year ended December 31, 2008 was a result of additional borrowings in 2009 under our debt facility as well as two new capital leases that we entered into in 2008.

Interest and Investment Income. The decrease in interest and investment income for the year ended December 31, 2009 compared to the year ended December 31, 2008 was due to lower average cash balances and lower prevailing interest rates during the period.

Remeasurement of Forward Purchase Contracts. The increase in the fair value of the forward purchase contracts for the year ended December 31, 2009 compared to the year ended December 31, 2008 resulted from changes in the fair value of the Forest and Almirall forward purchase contracts at the time of remeasurement. The valuation of the Forest forward purchase contract for the year ended December 31, 2009 increased $0.1 million as compared to a decrease of $0.9 million for the year ended December 31, 2008. The large decrease in the valuation of the Forest forward purchase contract was primarily a result of an increase in the fair value of our convertible preferred stock at the time of remeasurement. This increase was driven by higher estimated enterprise values and a lower risk-adjusted interest rate assumption used in our valuation. As a result, at December 31, 2008, the valuation of the Forest forward purchase contract decreased. The Almirall forward purchase contract valuation increased $0.5 million in the year ended December 31, 2009 without a corresponding change in the year ended December 31, 2008 as we entered into the license agreement with Almirall in April 2009.

Income Tax Benefit. The approximately $0.3 million increase in income tax benefit for the year ended December 31, 2009 was related to a refundable federal research and development tax credit. We received approximately $0.2 million of this refund in October 2009 and we received approximately $0.1 million in October 2010.

Net Loss Attributable to Discontinued Operations. The approximately $5.7 million increase in net loss attributable to discontinued operations for the year ended December 31, 2009 compared to the year ended December 31, 2008 was due to a larger net loss associated with our former subsidiary, Microbia. Revenue associated with this segment declined approximately $2.1 million during 2009 primarily due to the winding down of service contracts, while expenses increased approximately $2.3 million. In November 2009 Microbia implemented a strategic restructuring plan and recorded approximately $0.3 million of expense related primarily to a workforce reduction and approximately $0.9 million related to impairments of long-lived assets.

Net Loss Attributable to Noncontrolling Interest. The approximately $1.0 million increase in net loss attributable to noncontrolling interest was due to the larger net loss for Microbia as a result of lower

revenue and increased expenses, including its restructuring expense, during the year ended December 31, 2009 compared to the year ended December 31, 2008.

Liquidity and Capital Resources

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

	Years Ended December 31,		
	2010	2009	2008
	(in thousands)		
Net cash (used in) provided by:			
Operating activities	$ (67,899)	$ (3,445)	$ (25,511)
Investing activities	(213,042)	17,758	(15,073)
Financing activities	202,956	41,663	48,563
Net increase in cash and cash equivalents	$ (77,985)	$ 55,976	$ 7,979

We have incurred losses since our inception on January 5, 1998 and, as of December 31, 2010, we had a cumulative deficit of approximately $367.5 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 IPO, payments received under collaborative arrangements, including reimbursement of certain expenses, debt financings and interest earned on investments. At December 31, 2010, we had approximately $248.0 million of unrestricted cash, cash equivalents and available-for-sale securities. Our cash equivalents include amounts held in money market funds, stated at cost plus accrued interest, which approximates fair market value and amounts held in certain 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 A+ rated so as to primarily achieve liquidity and capital preservation.

Cash Flows From Operating Activities

Net cash used in operating activities totaled approximately $67.9 million for the year ended December 31, 2010. The primary uses of cash were our net loss from continuing operations of approximately $56.4 million, approximately $6.0 million used in operating activities from discontinued operations and a decrease of approximately $21.3 million in working capital 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 $15.8 million.

Net cash used in operating activities totaled approximately $3.4 million for the year ended December 31, 2009. The primary uses of cash were our net loss from continuing operations of approximately $60.0 million and approximately $11.5 million included in net cash used in operating activities from discontinued operations, offset by approximately $9.6 million in non-cash items and an increase of approximately $58.5 million in working capital. The increase in working capital was due primarily to an increase in deferred revenue resulting from the $38.0 million up-front cash payment associated with the Almirall license agreement, the $30.0 million up-front payment associated with the Astellas license and the $20.0 million milestone payment related to the Forest collaboration agreement, partially offset by reductions in deferred revenue as revenue was recognized from our Forest collaboration and our Almirall license agreement.

Net cash used in operating activities totaled approximately $25.5 million for the year ended December 31, 2008. The primary uses of cash were our net loss from continuing operations of approximately $47.4 million and approximately $4.0 million included in net cash used in operating activities from discontinued operations, offset by approximately $5.8 million in non-cash items and approximately $20.1 million increase in working capital. The increase in working capital was due primarily to a decrease in accounts receivable as we collected the up-front payment associated with the Forest collaboration of $20.0 million in 2008, an increase in deferred revenue resulting from the receipt of the $10.0 million milestone payment in our Forest collaboration partially offset by revenue recognized, as well as an increase in deferred rent primarily as a result of having received approximately $6.6 million in cash reimbursements for tenant improvements.

Cash Flows From Investing Activities

Cash used in investing activities for the year ended December 31, 2010 totaled approximately $213.0 million and resulted primarily from the purchase of approximately $441.8 million of securities related to the investment of the net proceeds of our IPO and the purchase of approximately $17.2 million of property and equipment, primarily leasehold improvements, associated with the expansion of our 301 Binney Street facility. These uses of cash were partially offset by the sale and maturity of approximately $236.5 million in investments and $9.5 million in proceeds received from DSM for the sale of our interest in Microbia.

Cash provided by investing activities for the year ended December 31, 2009 totaled approximately $17.8 million and resulted primarily from the sales and maturities of securities of approximately $48.5 million, partially offset by the purchase of approximately $26.7 million of securities, the purchase of approximately $4.0 million of property and equipment of which approximately $0.5 million is included in net cash provided by (used in) investing activities from discontinued operations.

Cash used by investing activities for the year ended December 31, 2008 totaled approximately $15.1 million and resulted primarily from the purchase of approximately $82.6 million of securities, the purchase of approximately $22.9 million of property and equipment of which approximately $1.5 million is included in net cash provided by (used in) investing activities from discontinued operations, partially offset by the sales and maturities of securities of approximately $90.5 million. The property and equipment purchased in 2008 primarily related to the leasehold improvements for our new facility at 301 Binney Street and the purchase of laboratory equipment for the facility.

Cash Flows From Financing Activities

Cash provided by financing activities for the year ended December 31, 2010 totaled approximately $203.0 million and resulted primarily from the net proceeds of our IPO of approximately $203.2 million and approximately $2.0 million in cash provided by stock option exercises, partially offset by approximately $2.2 million in cash used for payments of the long term debt, of which approximately $0.3 million was repayment of debt from discontinued operations.

Cash provided by financing activities for year ended December 31, 2009 totaled approximately $41.7 million, primarily resulting from approximately $40.3 million in proceeds from the sale of preferred stock and approximately $1.1 million received from net borrowings under our debt facility, of which approximately $1.3 million is included in net cash (used in) provided by financing activities from discontinued operations. We received a total of $25.0 million of proceeds from the sale of 2,083,333 shares of our Series G convertible preferred stock to Forest, $15.0 million of proceeds from the sale of 681,819 shares of our Series I convertible preferred stock to Almirall and approximately $0.2 million of proceeds from the sale of 20,833 shares of series H convertible preferred stock.

Cash provided by financing activities for the year ended December 31, 2008 totaled approximately $48.6 million primarily resulting from approximately $49.6 million in proceeds from the sale of 4,141,586 shares of our Series H convertible preferred stock offset by approximately $1.0 million in payments made under our debt facility.

Funding Requirements

To date, we have not commercialized any products and have not achieved profitability. We anticipate that we will continue to incur substantial net losses for the next several years as we further develop and prepare for the potential commercial launch of linaclotide, continue to invest in our pipeline, develop the organization required to sell our product candidates and operate as a publicly traded company.

We have generated revenue from services, up-front license fees and milestones, but have not generated any product revenue since our inception and do not expect to generate any product revenue from our collaborative arrangements or the sale of products unless we receive regulatory approval for commercial sale of linaclotide. We believe that our cash on hand as of the date of this Annual Report on Form 10-K and additional cash milestone payments we may receive from our current and future collaborators give us substantial strategic optionality and will enable us to operate the company in a productive way, through at least 2014. 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, 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 and our other product candidates for all of the indications 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 time and costs involved in obtaining regulatory approvals for our product candidates;
- the rate of progress and cost of our commercialization activities;
- the success of our research and development efforts;
- the expenses we incur in marketing and selling our product candidates;
- the revenue generated by sales of our product candidates;
- the emergence of competing or complementary technological 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.

Contractual Commitments and Obligations

Under our collaborative agreement with Forest, we share equally with Forest all development and commercialization costs related to linaclotide in the U.S. The actual amounts that we pay Forest or that Forest pays 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 FDA, the reimbursement and competitive landscape around linaclotide and our other product candidates, and other factors described under the heading "Risk Factors."

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 cancellation penalties. These items are not included in the table below.

In June 2010, we entered into a commercial supply agreement with a contract manufacturing organization for the purchase of a portion of the linaclotide API that will be used to seek regulatory approval of linaclotide in the U.S., Canada and/or Mexico, and, depending on such approval, that would be used for commercial sales in such countries. The commercial supply agreement contains minimum purchase requirements that commence with the commercial launch of linaclotide and that are dependent upon forecasted commercial requirements. Since, at this time, linaclotide has not yet been approved for commercialization and future commercial demand for linaclotide is unknown, the table below does not include an estimate of our future minimum purchase requirements under the commercial supply agreement.

In connection with our collaboration agreement with Protagonist entered into in February 2011, we are obligated to make an up-front payment to Protagonist. We will also fund full-time equivalents for Protagonist's drug discovery activities. Due to the uncertainties involved in the discovery phase of a product candidate, we are unable to determine the duration and costs required to complete Protagonist's drug discovery activities and as a result, we have not included these amounts in the table below. Pending the achievement of certain development and commercialization milestones, we will make certain milestone and royalty payments. As these payments are contingent upon the occurrence of certain future events and, given the nature of these events, it is unclear when, if ever, we may be required to pay such amounts and as a result, these contingent payments have not been included in the table below.

The following table summarizes our contractual obligations at December 31, 2010 (excluding interest):

	Payments Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Capital lease obligations	$ 590	$ 197	$ 359	$ 34	$ —
Operating lease obligations	48,535	8,671	29,725	10,139	—
Total contractual obligations	$ 49,125	$ 8,868	$ 30,084	$ 10,173	$ —

Our commitment for capital lease obligations relates to leased computer and office equipment.

Our commitments for operating leases relate to our lease of office and laboratory space in Cambridge, Massachusetts. In February 2011, we entered into a fourth amendment to our lease for 301 Binney Street. Under the amended lease, we leased an additional 23,307 square feet of the 301 Binney Street building. Rent for the additional space commences no later than February 2012 and base rent will be $42.50 per rentable square foot per year, and will increase annually by $0.50 per rentable square foot. The landlord will provide us with a finish work allowance of $40.00 per rentable square foot of additional space rented pursuant to this amendment. The amendment does not change the January 31, 2016 expiration date of the original lease.

Related Party Transactions

We have and currently obtain legal services from a law firm that is an investor of ours. We paid approximately $0.3 million, $0.1 million and $0.1 million in legal fees to this investor during the years ended December 31, 2010, 2009 and 2008, respectively.

In September 2009, Forest became a related party when we sold to them 2,083,333 shares of our convertible preferred stock at a price of $12.00 per share for cash proceeds of $25.0 million. Forest accounted for approximately 50%, 79% and 100% of our revenue from continuing operations for the years ended December 31, 2010, 2009 and 2008, respectively.

In November 2009, Almirall became a related party when we sold to them 681,819 shares of our convertible preferred stock at a price of $22.00 per share for cash proceeds of $15.0 million. Almirall accounted for approximately 43% and 21% of our revenue from continuing operations for the years ended December 31, 2010 and 2009, respectively.

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

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies that are adopted by us as of the specified effective date. Unless otherwise discussed, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our consolidated financial position or results of operations upon adoption.

Recently Issued Accounting Standards

In October 2009, the FASB issued Accounting Standards Update No. 2009-13, *Multiple-Deliverable Revenue Arrangements* , or ASU 2009-13. ASU 2009-13 amends existing revenue recognition accounting pronouncements that are currently within the scope of FASB Accounting Standards Codification Subtopic 605-25 (previously included within EITF 00-21, *Revenue Arrangements with Multiple Deliverables* ("EITF 00-21"). The consensus to ASU 2009-13 provides accounting principles and application guidance on whether multiple deliverables exist, how the arrangement should be separated, and the consideration allocated. This guidance eliminates the requirement to establish the fair value of undelivered products and services and instead provides for separate revenue recognition based upon management's estimate of the selling price for an undelivered item when there is no other means to determine the fair value of that undelivered item. EITF 00-21 previously required that the fair value of the undelivered item be the price of the item either sold in a separate transaction between unrelated third parties or the price charged for each item when the item is sold separately by the vendor. Under EITF 00-21, if the fair value of all of the elements in the arrangement was not determinable, then revenue was deferred until all of the items were delivered or fair value was determined. This new approach is effective prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010 and allows for retrospective application. As this guidance is applicable to future transactions, we do not expect the implementation to have a material impact on our consolidated financial position or results of operations.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition—Milestone Method* , or ASU 2010-017. ASU 2010-017 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. Under this guidance management may recognize revenue contingent upon the achievement of a milestone in its entirety, in the period in which the milestone is

achieved, only if the milestone meets all the criteria within the guidance to be considered substantive. This ASU is effective on a prospective basis for research and development milestones achieved in fiscal years, beginning on or after June 15, 2010. Early adoption is permitted; however, adoption of this guidance as of a date other than January 1, 2011 requires application of this guidance retrospectively effective as of January 1, 2010 and disclosure of the effect of this guidance as applied to all previously reported interim periods in the fiscal year of adoption. As we plan to implement ASU No. 2010-17 prospectively, the effect of this guidance will be limited to future transactions.

In December 2010, the FASB issued ASU No. 2010-027, *Fees Paid to the Federal Government by Pharmaceutical Manufacturers* , or ASU 2010-027, which provides guidance on how to recognize and classify the fees mandated by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act, together the Acts. The Acts impose an annual fee for each calendar year beginning on or after January 1, 2011. The liability for the fee should be estimated and recorded in full upon the first qualifying sale with a corresponding deferred cost that is amortized to expense using a straight-line method of allocation over the calendar year that it is payable. As we do not currently have a commercial product, the effect of this guidance will be limited to future transactions.

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 deposits, 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.

Recently, there has been concern in the credit markets regarding the value of a variety of mortgage-backed and auction rate securities and the resulting effect on various securities markets. We do not currently have any auction rate securities. We do not believe our cash, cash equivalents and available-for-sale investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and available-for-sale 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 current instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits.

Our capital lease obligations bear interest at a fixed rate and therefore have minimal exposure to changes in interest rates.

Foreign Currency Risk

We have no operations outside the U.S. and do not have any foreign currency or other derivative financial instruments.

Effects of Inflation

We do not believe that inflation and changing prices over the years ended December 31, 2010, 2009 and 2008 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-48, respectively, 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 Securities Exchange Act of 1934, or 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. Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2010.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our independent registered public accounting firm pursuant to an exemption under Section 989G of the Dodd-Frank Wall Street Reform and Consumer Protection Act.

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, 2010 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, 2010 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

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

On March 28, 2011, we, along with our collaboration partner Forest, entered into a commercial supply agreement with Roche Colorado Corporation, or RCC. Pursuant to the terms of this supply agreement and subject to certain conditions and limits, RCC agrees to manufacture and supply to us and Forest, and we and Forest agree to purchase from RCC, a portion of the linaclotide API that will be used to support regulatory approval of linaclotide in the U.S. and/or Canada, and, subject to obtaining such approval, that will be incorporated into finished product that will be sold commercially in such country. The purchase price for the linaclotide API under the supply agreement is a fixed price for the initial firm order and thereafter will be a volume-based price.

The initial term of the supply agreement ends on March 28, 2016. The initial term is subject to three automatic one-year renewals unless a party to the supply agreement provides written notice of non-renewal to the other at least one year prior to the expiration of the initial term or any such renewal period. Either party may terminate the supply agreement following an uncured material breach by the other party.

We and Forest are party to a collaboration agreement pursuant to which we co-develop and plan to co-promote linaclotide in the U.S. for the treatment of IBS-C and CC. Pursuant to the terms of the collaboration agreement, Forest is responsible, among other things, for completing the manufacturing process of linaclotide for use in the U.S., Canada and Mexico, which consists of finishing and packaging linaclotide into capsules.

The foregoing summary of the supply agreement is qualified in its entirety by reference to the supply agreement, which will be filed as an exhibit to our Quarterly Report on Form 10-Q for the quarter ending March 31, 2011.

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 ethics and business conduct, 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 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 2011 Annual Meeting of Stockholders.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference from our proxy statement for our 2011 Annual Meeting of Stockholders.

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

The information required by this item is incorporated by reference from our proxy statement for our 2011 Annual Meeting of Stockholders.

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 2011 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 2011 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 as 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
10.1#	1998 Amended and Restated Stock Option 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 2002 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.3#	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
10.4#	2010 Employee, Director and Consultant Equity Incentive Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 20, 2010
10.4.1#	Form agreement under the 2010 Employee, Director and Consultant Equity Incentive Plan	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
10.5#	2010 Employee Stock Purchase Plan	Registration Statement on Form S-8 (File No. 333-165230)	March 5, 2010

Number	Description	Incorporated by reference herein	
		Form	Date
10.6#	Change of Control Severance Benefit Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.7#	Director Compensation Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.8#	Form of Indemnification Agreement with directors and officers	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.9#	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
10.10+	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
10.11+	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
10.12+	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
10.13+	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	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
10.14.1	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
10.14.2*	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		
10.14.3*	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		
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		

* 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 with the SEC pursuant to the confidential treatment request.

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

(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 30th day of March 2011.

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)*	March 30, 2011
/s/ MICHAEL J. HIGGINS Michael J. Higgins	Chief Operating Officer & Chief Financial Officer *(Principal Financial Officer & Principal Accounting Officer)*	March 30, 2011
/s/ BRYAN E. ROBERTS Bryan E. Roberts	Chairman of the Board	March 30, 2011
/s/ GEORGE CONRADES George Conrades	Director	March 30, 2011
/s/ JOSEPH C. COOK, JR. Joseph C. Cook, Jr.	Director	March 30, 2011
/s/ DAVID EBERSMAN David Ebersman	Director	March 30, 2011
/s/ MARSHA H. FANUCCI Marsha H. Fanucci	Director	March 30, 2011

Signature	Title	Date
/s/ TERRANCE G. MCGUIRE Terrance G. McGuire	Director	March 30, 2011
/s/ GINA BORNINO MILLER Gina Bornino Miller	Director	March 30, 2011
/s/ DAVID E. SHAW David E. Shaw	Director	March 30, 2011
/s/ CHRISTOPHER T. WALSH Christopher T. Walsh	Director	March 30, 2011

Index to Consolidated Financial Statements of
Ironwood Pharmaceuticals, Inc.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited the accompanying consolidated balance sheets of Ironwood Pharmaceuticals, Inc. as of December 31, 2010 and 2009, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2010. 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and 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, 2010 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2010, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 30, 2011

Ironwood Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2010	December 31, 2009
Assets		
Current assets:		
Cash and cash equivalents	$ 44,321	$ 122,306
Available-for-sale securities	203,706	—
Accounts receivable	19	7
Related party accounts receivable, net	2,876	5,212
Prepaid expenses and other assets	5,320	2,673
Restricted cash	2,833	—
Current assets of discontinued operations	—	1,250
Total current assets	259,075	131,448
Restricted cash	7,647	8,132
Property and equipment, net	34,369	21,754
Other assets	274	21
Long-term assets of discontinued operations	—	1,096
Total assets	$ 301,365	$ 162,451
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 4,302	$ 4,754
Accrued research and development costs	8,140	12,401
Accrued expenses	8,938	4,299
Current portion of long-term debt	—	936
Current portion of capital lease obligations	197	143
Current portion of deferred rent	2,799	180
Current portion of deferred revenue	40,050	32,360
Current liabilities of discontinued operations	—	1,364
Total current liabilities	64,426	56,437
Long-term debt, net of current portion	—	827
Capital lease obligations, net of current portion	393	112
Deferred rent, net of current portion	14,612	10,486
Deferred revenue, net of current portion	62,383	93,642
Long-term liabilities of discontinued operations	—	937
Commitments and contingencies (Note 12 and Note 13)		
Convertible preferred stock, $0.001 par value, no shares authorized and issued and outstanding at December 31, 2010 and 74,942,226 shares authorized and 69,904,843 shares issued and outstanding at December 31, 2009; liquidation value of $415,237 at December 31 2009 (Note 14)	—	298,350
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value, 75,000,000 shares authorized, no shares issued and outstanding at December 31, 2010 and no shares authorized, issued and outstanding at December 31, 2009	—	—
Class A common stock, $0.001 par value, 500,000,000 shares authorized and 48,202,089 shares issued and outstanding at December 31, 2010 and 98,530,700 shares authorized and no shares issued and outstanding at December 31, 2009	48	—
Class B common stock, $0.001 par value, 100,000,000 shares authorized and 50,970,247 shares issued and outstanding at December 31, 2010 and 98,530,700 shares authorized and 7,854,602 shares issued and outstanding at December 31, 2009	51	8
Additional paid-in capital	526,991	12,999
Accumulated deficit	(367,540)	(314,559)
Accumulated other comprehensive income	1	—
Total Ironwood Pharmaceuticals, Inc. stockholders' equity (deficit)	159,551	(301,552)
Noncontrolling interest	—	3,212
Total stockholders' equity (deficit)	159,551	(298,340)
Total liabilities and stockholders' equity (deficit)	$ 301,365	$ 162,451

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

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Operations

(In thousands, except share and per share amounts)

	Years Ended December 31,		
	2010	2009	2008
Collaborative arrangements revenue	$ 43,857	$ 34,321	$ 18,383
Operating expenses:			
Research and development	77,454	76,100	51,421
General and administrative	27,169	19,037	15,269
Total operating expenses	104,623	95,137	66,690
Loss from operations	(60,766)	(60,816)	(48,307)
Other income (expense):			
Interest expense	(196)	(318)	(291)
Interest and investment income	614	240	2,088
Remeasurement of forward purchase contracts	—	600	(900)
Other income	993	—	—
Other income (expense), net	1,411	522	897
Net loss from continuing operations before income tax benefit	(59,355)	(60,294)	(47,410)
Income tax benefit	(2,944)	(296)	—
Net loss from continuing operations	(56,411)	(59,998)	(47,410)
Net income (loss) from discontinued operations, net of tax provision of $2,944 in the year ended December 31, 2010	4,551	(13,314)	(7,621)
Net loss	(51,860)	(73,312)	(55,031)
Net (income) loss from discontinued operations attributable to noncontrolling interest	(1,121)	2,127	1,157
Net loss attributable to Ironwood Pharmaceuticals, Inc.	$ (52,981)	$ (71,185)	$ (53,874)
Net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted:			
Continuing operations	$ (0.63)	$ (8.43)	$ (6.88)
Discontinued operations	0.04	(1.57)	(0.94)
Net loss per share	$ (0.59)	$ (10.00)	$ (7.82)
Weighted average number of common shares used in net income (loss) per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	89,653,364	7,116,774	6,889,817

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

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands, except share amounts)

	Convertible preferred stock (Note 14)		Class A common stock		Class B common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive income (loss)	Noncontrolling interest	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
Balance at December 31, 2007	62,977,272	$223,802	—	$ —	6,948,730	$ 7	$ 4,621	$ (189,500)	$ 3	$ 6,495	$ (178,374)
Issuance of common stock upon exercise of stock options	—	—	—	—	129,448	—	179	—	—	—	179
Proceeds from sale of noncontrollin interest in subsidiary	—	—	—	—	—	—	—	—	—	1	1
Issuance of Series H Convertible preferred stock	4,141,586	49,598	—	—	—	—	—	—	—	—	—
Share-based compensatior expense related to issuance of stock options to non-employees	—	—	—	—	—	—	300	—	—	—	300
Issuance of common stock award	—	—	—	—	5,000	—	25	—	—	—	25
Share-based compensatior expense related to issuance of stock options to employees	—	—	—	—	—	—	2,293	—	—	—	2,293
Share-based compensatior expense from discontinued operations	—	—	—	—	—	—	176	—	—	—	176
Comprehensive income (loss):											
Unrealized gain on short-term investments	—	—	—	—	—	—	—	—	20	—	20
Net loss	—	—	—	—	—	—	—	(53,874)	—	(1,157)	(55,031)
Total comprehensiv loss											(55,011)
Balance at December 31, 2008	67,118,858	273,400	—	—	7,083,178	7	7,594	(243,374)	23	5,339	(230,411)
Issuance of common stock upon exercise of stock options	—	—	—	—	255,875	—	272	—	—	—	272
Issuance of restricted common stock awards	—	—	—	—	515,549	1	—	—	—	—	1
Issuance of Series G Convertible preferred stock	2,083,333	25,000	—	—	—	—	—	—	—	—	—
Settlement of forward											

purchase contract in connection with issuance of Series G Convertible preferred stock	—	(8,800)	—	—	—	—	—	—	—	—	—
Issuance of Series H Convertible preferred stock	20,833	250	—	—	—	—	—	—	—	—	—
Issuance of Series I Convertible preferred stock	681,819	15,000	—	—	—	—	—	—	—	—	—
Settlement of forward purchase contract in connection with issuance of Series I Convertible preferred stock	—	(6,500)	—	—	—	—	—	—	—	—	—
Share-based compensation expense related to issuance of stock options to non-employees	—	—	—	—	—	—	301	—	—	—	301
Share-based compensation expense related to issuance of stock options to employees	—	—	—	—	—	—	4,794	—	—	—	4,794
Share-based compensation expense from discontinued operations	—	—	—	—	—	—	149	—	—	—	149
Restricted common stock shares subject to repurchase	—	—	—	—	—	—	(111)	—	—	—	(111)
Comprehensive income (loss):											
Unrealized loss on short-term investments	—	—	—	—	—	—	—	—	(23)	—	(23)
Net loss	—	—	—	—	—	—	—	(71,185)	—	(2,127)	(73,312)
Total comprehensiv loss											(73,335)

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

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) (Continued)

(In thousands, except share amounts)

	Convertible preferred stock (Note 14)		Class A common stock		Class B common stock		Additional		Accumulated other		Total stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	paid-in capital	Accumulated deficit	comprehensive income (loss)	Noncontrolling interest	equity (deficit)
Balance at December 31, 2009	69,904,843	$ 298,350	—	$ —	7,854,602	$ 8	$ 12,999	$ (314,559)	$ —	$ 3,212	$ (298,340)
Issuance of common stock upon exercise of stock options and employee stock purchase plan	—	—	30,438	—	1,746,184	2	2,021	—	—	—	2,023
Issuance of common stock awards	—	—	22,825	—	—	—	259	—	—	—	259
Cancellation of restricted common stock awards	—	—	—	—	(40,000)	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock upon initial public offering	(69,904,843)	(298,350)	—	—	70,391,620	70	298,280	—	—	—	298,350
Issuance of shares upon initial public offering, net of offering costs of approximatel $12.4 million	—	—	19,166,667	19	—	—	203,148	—	—	—	203,167
Conversion of Class B common stock to Class A common stock	—	—	28,982,159	29	(28,982,159)	(29)	—	—	—	—	—
Share-based compensatior expense related to issuance of stock options to non-employees	—	—	—	—	—	—	123	—	—	—	123
Share-based compensatior expense related to issuance of stock options to employees and employee purchase plan	—	—	—	—	—	—	7,114	—	—	—	7,114
Share-based compensatior expense from discontinued operations	—	—	—	—	—	—	59	—	—	—	59
Restricted common stock no longer subject to											

repurchase	—	—	—	—	—	—	55	—	—	—	55
Decrease in noncontrollin interest in subsidiary	—	—	—	—	—	—	2,933	—	—	(4,333)	(1,400)
Comprehensive income (loss):											
Unrealized gain on short-term investments	—	—	—	—	—	—	—	—	1	—	1
Net loss	—	—	—	—	—	—	—	(52,981)	—	1,121	(51,860)
Total comprehensi loss											(51,859)
Balance at December 31, 2010	—	$ —	48,202,089	$ 48	50,970,247	$ 51	$ 526,991	$ (367,540)	$ 1	$ —	$ 159,551

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,		
	2010	2009	2008
Cash flows from operating activities:			
Net loss	$ (51,860)	$ (73,312)	$ (55,031)
Income (loss) from discontinued operations	4,551	(13,314)	(7,621)
Loss from continuing operations	(56,411)	(59,998)	(47,410)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	6,161	4,763	2,620
Loss (gain) on disposal of property and equipment	474	80	(1)
Remeasurement of forward purchase contracts	—	(600)	900
Share-based compensation expense	7,496	5,095	2,618
Accretion of discount/premium on investment securities	1,619	239	(367)
Changes in assets and liabilities:			
Accounts receivable	2,324	(648)	20,116
Restricted cash	(2,348)	(446)	(4,726)
Prepaid expenses and other current assets	(2,647)	(464)	(504)
Other assets	(253)	50	(46)
Accounts payable and accrued expenses	2,740	1,732	(97)
Accrued research and development costs	(4,261)	2,990	4,373
Deferred revenue	(23,569)	53,993	(8,383)
Deferred rent	6,745	1,279	9,370
Net cash (used in) provided by operating activities from continuing operations	(61,930)	8,065	(21,537)
Net cash used in operating activities from discontinued operations	(5,969)	(11,510)	(3,974)
Total net cash used in operating activities	(67,899)	(3,445)	(25,511)
Cash flows from investing activities:			
Purchases of available-for-sale securities	(441,799)	(26,673)	(82,613)
Sales and maturities of available-for-sale securities	236,475	48,455	90,465
Purchases of property and equipment	(17,220)	(3,524)	(21,465)
Proceeds from sale of property and equipment	1	21	5
Proceeds from sale of subsidiary	9,500	—	—
Net cash (used in) provided by investing activities from continuing operations	(213,043)	18,279	(13,608)
Net cash provided by (used in) investing activities from discontinued operations	1	(521)	(1,465)
Total net cash (used in) provided by investing activities	(213,042)	17,758	(15,073)
Cash flows from financing activities:			
Proceeds from issuance of preferred stock, net of issuance costs	—	40,250	49,598
Proceeds from initial public offering	203,167	—	—
Proceeds from exercise of stock options, stock purchase plan and issuance of restricted stock	2,023	272	179
Proceeds from borrowings	—	1,079	—
Payments on borrowings	(1,957)	(1,250)	(1,004)
Net cash provided by financing activities from continuing operations	203,233	40,351	48,773
Net cash (used in) provided by financing activities from discontinued operations	(277)	1,312	(210)
Total net cash provided by financing activities	202,956	41,663	48,563
Net (decrease) increase in cash and cash equivalents	(77,985)	55,976	7,979
Cash and cash equivalents, beginning of period	122,306	66,330	58,351
Cash and cash equivalents, end of period	$ 44,321	$ 122,306	$ 66,330
Supplemental cash flow disclosures:			
Cash paid for interest (includes cash paid by Microbia)	$ 325	$ 412	$ 333
Cash paid for income taxes	$ —	$ (153)	$ —
Settlement of forward purchase contracts	$ —	$ (15,300)	$ —
Purchases under capital leases	$ 529	$ 67	$ 373
Debt and interest paid by purchaser of subsidiary	$ 1,075	$ —	$ —

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

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

1. Nature of Business

Ironwood Pharmaceuticals, Inc. (the "Company") is an entrepreneurial pharmaceutical company that discovers, develops and intends to commercialize differentiated medicines that improve patients' lives. Linaclotide, the Company's guanylate cyclase type-C ("GC-C") agonist being developed for the treatment of patients with irritable bowel syndrome with constipation ("IBS-C") or chronic constipation ("CC") is currently in Phase 3 clinical development. The Company also has a pipeline focused on both research and development of early stage product candidates and preclinical research in multiple therapeutic areas, including gastrointestinal disease, pain and inflammation, respiratory disease, and cardiovascular disease.

Prior to September 2010, the Company held a majority ownership interest in Microbia, Inc. (formerly known as Microbia Precision Engineering), a subsidiary formed in September 2006. Microbia, Inc. ("Microbia") engaged in a specialty biochemicals business based on a proprietary strain-development platform. On September 21, 2010, the Company sold its interest in Microbia to DSM Holding Company USA, Inc. ("DSM") in exchange for cash proceeds of $9.5 million, the payment of approximately $1.1 million of Microbia debt and interest by DSM and future contingent consideration based on the sale of products incorporating Microbia's technology.

The Company was incorporated in Delaware on January 5, 1998. On April 7, 2008, the Company changed its name from Microbia, Inc. to Ironwood Pharmaceuticals, Inc. The Company currently operates in one reportable business segment, human therapeutics. Prior to September 21, 2010, the Company operated in two reportable business segments, human therapeutics and biomanufacturing (Note 20).

The Company has generated an accumulated deficit as of December 31, 2010 of approximately $367.5 million since inception. In February 2010, the Company completed its initial public offering of Class A common stock and raised a total of approximately $203.2 million in net proceeds (Note 3).

2. Summary of Significant Accounting Policies

Principles of Consolidation

During 2006, the Company formed Microbia as a 100% wholly owned subsidiary of the Company. In September 2006, Microbia sold additional equity interests to a third party, which reduced the Company's ownership interest in Microbia to 85% (Note 22). The accompanying consolidated financial statements of Ironwood Pharmaceuticals, Inc. include the assets, liabilities, revenue, and expenses of Microbia, over which the Company exercised control until September 21, 2010, when the Company sold its interest in Microbia to DSM. The Company recorded noncontrolling interest in its consolidated statements of operations for the ownership interest of the minority owners of Microbia. All intercompany transactions and balances are eliminated in consolidation.

Sale of Subsidiary and Discontinued Operations

As a result of the sale of its interest in Microbia, the Company ceased to have any financial interest in Microbia. The Company maintains no further investment in Microbia and has recorded a gain on the sale of Microbia in its statements of operations based on current accounting guidance as the difference between the sum of the fair value of the consideration received, the carrying value of the noncontrolling interest in the subsidiary at the date of sale, the fair value of the retained noncontrolling interest (which was zero) and the carrying amount of Microbia's assets and liabilities. The consideration

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

received includes $9.5 million in cash as well as DSM's payment of Microbia's approximately $1.1 million in debt and interest immediately prior to the sale. The gain on the sale of Microbia is included in income from discontinued operations in the Company's consolidated statements of operations.

The calculation of the gain on the sale of Microbia is calculated as follows (in thousands):

Consideration received	$ 10,575
Carrying value of noncontrolling interest	1,400
	11,975
Net liabilities of Microbia	187
Gain on sale of Microbia	$ 12,162

The net liabilities of Microbia on September 21, 2010, prior to the sale, consisted of the following (in thousands):

Assets	
Prepaid expenses and other assets	$ 52
Restricted cash	30
Property and equipment, net	648
Total assets	730
Liabilities	
Accounts payable	193
Accrued expenses	724
Total liabilities	917
Net liabilities	$ 187

Additionally, in accordance with the applicable accounting standards, the operations and cash flows of Microbia have been eliminated from the ongoing operations. The agreement includes future contingent consideration in the form of a royalty on future sales of products incorporating Microbia's technology through the earlier of a) 2024, b) the invalidity of any Microbia patent, or c) the maximum agreed upon amount is reached. The cash flows from the future contingent consideration are indirect cash flows, as the Company has no continuing involvement with Microbia after the sale, and as such, they represent a passive royalty interest and therefore the cash flows are considered to be eliminated from the ongoing operations. As a result, Microbia meets the requirements for presentation as discontinued operations and the Company has classified the assets, liabilities, operations, and cash flows of Microbia as discontinued operations for all periods presented prior to the sale. The Company has elected as its accounting policy to account for the future contingent consideration, if any, as a gain contingency as the proceeds have not been received and the receipt of royalty income is uncertain. As a result, proceeds will only be recorded in future earnings as they are earned. As of December 31, 2010, no amounts have been recorded for the contingent consideration in the Company's financial statements.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

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, impairment of long-lived assets, income taxes including the valuation allowance for deferred tax assets, valuation of forward purchase contracts, research and development, 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 an original maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents primarily consist of money market funds and certain 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 $39.2 million and $120.6 million at December 31, 2010 and 2009, respectively.

Restricted Cash

The Company is contingently liable under unused letters of credit with a bank, related to the Company's facility lease agreements and credit card arrangements, in the amount of approximately $10.5 million and $8.4 million as of December 31, 2010 and 2009, respectively. As a result, the Company has restricted cash of approximately $10.5 million and $8.4 million as of December 31, 2010 and 2009, respectively, securing these letters of credit. At December 31, 2009, approximately $0.3 million was related to Microbia commitments and is included in long-term assets of discontinued operations. The cash will be restricted until the termination of the leases and credit card arrangements. In January 2011, approximately $2.8 million of restricted cash was released due to the expiration of the 320 Bent Street facility lease in December 2010. As of December 31, 2010, the $2.8 million is shown as a current asset on the Company's consolidated balance sheets.

Available-for-Sale Securities

The Company classifies all short-term investments with an original maturity when purchased of greater than three months as available-for-sale. Available-for-sale securities are carried 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 amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, and declines in value judged to be other than temporary on available-for-sale securities, are included in interest and investment income.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest and investment income. 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, 2010, 2009 and 2008.

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, 2010 and 2009.

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 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 A+ rated, thereby reducing credit risk concentration.

Accounts receivable primarily consist of amounts due under the collaboration agreement with Forest and license agreements with Almirall, S.A. ("Almirall") and Astellas Pharma Inc. ("Astellas") (Note 5) for which the Company does not obtain collateral. Effective September 1, 2009, Forest became a related party when the Company sold to Forest 2,083,333 shares of the Company's Series G convertible preferred stock and effective November 2, 2009, Almirall became a related party when the Company sold to them 681,819 shares of its Series I convertible preferred stock.

Forest accounted for approximately 50%, 79% and 100% of the Company's revenue from continuing operations for the years ended December 31, 2010, 2009 and 2008, respectively. Almirall accounted for approximately 43%, 21% and 0% of the Company's revenue from continuing operations for the years ended December 31, 2010, 2009 and 2008, respectively. Astellas accounted for approximately 7% of the Company's revenue from continuing operations for the year ended December 31, 2010. Tate & Lyle Investments, Ltd. ("T&L") accounted for approximately 98%, 100% and 57% of the Company's revenue from discontinued operations for the years ended December 31, 2010, 2009 and 2008, respectively. For the years ended December 31, 2010, 2009 and 2008, no additional customers accounted for more than 10% of the Company's revenue from continuing operations and for the year ended December 31, 2008 one additional customer accounted for approximately 30% of revenue from discontinued operations.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

At December 31, 2010 and 2009, accounts receivable from Forest, net of any payables due Forest, accounted for approximately 89% and 94%, respectively, of the Company's total accounts receivable. At December 31, 2010 and 2009, Almirall accounted for approximately 10% and 6%, respectively, of the Company's total accounts receivable.

Revenue Recognition

The Company's revenue is generated primarily through collaborative research and development and licensing agreements. The terms of these agreements typically include payment to the Company of one or more of the following: nonrefundable, up-front license fees; milestone payments; sale of drug substance to its collaborators; and royalties on product sales. In addition, prior to September 2010, the Company generated services revenue through agreements that generally provided for fees for research and development services rendered.

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 and determinable, and collection is reasonably assured. The Company evaluates revenue from agreements that have multiple elements and accounts for the components as separate elements when the following criteria are met:

- the delivered items have value to the customer on a stand-alone basis;
- there is objective and reliable evidence of fair value of the undelivered items; 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 the Company's control.

Collaborative Arrangements Revenue

Up-front License Fees

The Company recognizes revenues from nonrefundable, up-front license fees for which the separation criteria were not met due to continuing involvement in the performance of research and development services on a straight-line basis over the contracted or estimated period of performance, which is typically the research or development term.

Milestones

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

In those circumstances where a substantive milestone is achieved, collection of the related receivable is reasonably assured and the Company has remaining obligations to perform under the collaboration arrangement, the Company recognizes as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that has elapsed as of the date the milestone is achieved, with the balance being deferred and recognized on a straight-line basis over the remaining period of performance.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Payments received or reasonably assured after performance obligations are fully satisfied are recognized as earned. For certain of the Company's arrangements, particularly the Company's license agreement with Almirall, it is required that taxes be withheld on payments made to the Company. The Company has adopted a policy to recognize revenue net of these tax withholdings.

The Company receives research and development funding under the Forest collaboration agreement and considers the factors or indicators within this arrangement to determine whether reporting such funding on a gross or net basis is appropriate. 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.

Active Pharmaceutical Ingredient Shipments

The Company produces clinical materials for its collaborators and is reimbursed for its costs to produce the active pharmaceutical ingredient ("API"). The Company recognizes revenue on clinical materials when the materials have 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.

Services Revenue

The Company recognized services revenue when there was persuasive evidence that an arrangement existed, services had been rendered or delivery had occurred, the price was fixed and determinable, and collection was reasonably assured. Revenue from research and development services rendered was recognized as services were performed. As a result of the sale of the Company's interest in Microbia in September 2010, services revenue is included in net income (loss) from discontinued operations.

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 and benefits; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; contractual services, including clinical trial and related clinical manufacturing expenses; and other outside expenses. As a result of the sale of the Company's interest in Microbia in September 2010, costs of revenue related to the Microbia services contracts and costs associated with Microbia's research and development activities are included in net income (loss) from discontinued operations.

The Company has entered into a collaboration agreement in which it shares research and development expenses with a collaborator. The Company records the expenses for such work as research and development expense. Because the collaboration arrangement is a cost-sharing arrangement, the Company records the payments by the collaborator for their share of the development effort as a reduction of research and development expense.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Share-Based Compensation

Share-based compensation is recognized as an expense in the financial statements based on the grant date fair value. Compensation expense recognized relates to stock awards, restricted stock and stock options granted, modified, repurchased or cancelled on or after January 1, 2006. Stock options granted to employees prior to that time continue to be accounted for using the intrinsic value method. Under the intrinsic value method, compensation associated with share-based awards to employees was determined as the difference, if any, between the fair value of the underlying common stock on the date compensation was measured, generally the grant date, and the price an employee must pay to exercise the award. 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, expected term and the fair value of the underlying common stock, among others.

The Company records the expense for stock option grants subject to performance-based milestone vesting 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 are remeasured at each reporting period and expensed over the vesting term of the underlying stock options.

Accounting for Sabbatical Leave

The Company accrues an employee's right to a compensated absence under a sabbatical, or other similar benefit arrangement that requires the completion of a minimum service period and the benefit increases with additional years of service, accumulates, and for arrangements in which the individual continues to be a compensated employee and is not required to perform duties for the entity during the absence. Therefore, the compensation cost associated with a sabbatical or other similar benefit arrangement should be accrued over the requisite service period. During the years ended December 31, 2010, 2009 and 2008, the Company recorded expense for sabbatical costs of approximately $0.3 million, $0.1 million and $0.2 million, respectively. These values exclude any amounts recorded for sabbatical costs from discontinued operations.

Noncontrolling Interest

Noncontrolling interest represents the noncontrolling stockholder's proportionate share of equity and net income or net loss of the Company's former consolidated subsidiary, Microbia. On September 21, 2010, the Company sold its interest in Microbia, resulting in the deconsolidation of its former subsidiary bringing the noncontrolling interest balance to zero. Immediately prior to the sale, the Company converted certain intercompany debt and payables into preferred stock of Microbia, which resulted in an approximately $2.9 million decrease in the noncontrolling interest. The noncontrolling stockholder's proportionate share of the equity in Microbia of approximately $3.2 million as of December 31, 2009 is reflected as noncontrolling interest in the Company's consolidated balance sheets as a component of stockholders' equity (deficit).

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

The proportionate share of the net loss attributable to noncontrolling interest is reflected in the accompanying consolidated statements of operations. The following table is a roll-forward of the noncontrolling interest (in thousands):

Balance at December 31, 2007	$ 6,495
Proceeds from sale of noncontrolling interest in subsidiary	1
Net loss from discontinued operations attributable to noncontrolling interest	(1,157)
Balance at December 31, 2008	5,339
Net loss from discontinued operations attributable to noncontrolling interest	(2,127)
Balance at December 31, 2009	3,212
Net income from discontinued operations attributable to noncontrolling interest	1,121
Change in noncontrolling interest due to additional investment by Company in subsidiary	(2,933)
Sale of subsidiary	(1,400)
Balance at December 31, 2010	$ —

Net Loss Per Share

The Company calculates basic and diluted net loss per common share by dividing the net loss by the weighted average number of common shares outstanding during the period. The Company has excluded unvested restricted stock and shares that are subject to repurchase by the Company from the weighted average number of common shares outstanding. The Company's potentially dilutive shares, which include convertible preferred stock, outstanding common stock options and unvested shares of restricted stock, have not been included in the computation of diluted net loss per share for all periods as the result would be antidilutive. The loss attributable to the noncontrolling interest is included in the net income (loss) per share from discontinued operations.

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)
Laboratory equipment	5
Computer and office equipment	3
Furniture and fixtures	7
Software	3

Included in property and equipment is the cost of internally developed software. Costs incurred during the application development stage are capitalized and amortized over the estimated useful life

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

of the software. Leasehold improvements are amortized over the shorter of the estimated useful life of the asset or the lease term. 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.

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 indicators of impairment at December 31, 2010. At December 31, 2009, the Company concluded that impairments of certain long-lived assets existed at its former subsidiary, Microbia, resulting from its restructuring in the fourth quarter of 2009 (Note 22). Such long-lived assets were written down to their estimated fair value, which resulted in a charge of approximately $0.9 million. This charge is shown as part of net income (loss) from discontinued operations. There were no indicators of impairment at December 31, 2008.

Comprehensive Income (Loss)

All components of comprehensive income (loss) are required to be disclosed in the consolidated financial statements. 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 in deciding how to allocate resources and in assessing performance.

Prior to the sale of its interest in Microbia in September 2010, the Company had two reportable business segments: human therapeutics and biomanufacturing (Note 20). Revenue from the Company's human therapeutics segment is shown in the consolidated statements of operations as collaborative

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

arrangements revenue. Revenue from the Company's biomanufacturing segment is presented as a component of the net income (loss) from discontinued operations.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that are adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its consolidated financial position or results of operations upon adoption.

Recently Issued Accounting Standards

In October 2009, the FASB issued ASU No. 2009-13, *Multiple-Deliverable Revenue Arrangements* ("ASU 2009-13"). ASU 2009-13, amends existing revenue recognition accounting pronouncements that are currently within the scope of FASB Accounting Standards Codification ("ASC") Subtopic 605-25 (previously included within EITF 00-21, *Revenue Arrangements with Multiple Deliverables* ("EITF 00-21"). The consensus to ASU 2009-13 provides accounting principles and application guidance on whether multiple deliverables exist, how the arrangement should be separated, and the consideration allocated. This guidance eliminates the requirement to establish the fair value of undelivered products and services and instead provides for separate revenue recognition based upon management's estimate of the selling price for an undelivered item when there is no other means to determine the fair value of that undelivered item. EITF 00-21 previously required that the fair value of the undelivered item be the price of the item either sold in a separate transaction between unrelated third parties or the price charged for each item when the item is sold separately by the vendor. Under EITF 00-21, if the fair value of all of the elements in the arrangement was not determinable, then revenue was deferred until all of the items were delivered or fair value was determined. This new approach is effective prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010 and allows for retrospective application. As this guidance is applicable to future transactions, the Company does not expect the implementation to have a material impact on its consolidated financial position or results of operations.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition—Milestone Method* ("ASU 2010-017"). ASU 2010-017 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. Under this guidance management may recognize revenue contingent upon the achievement of a milestone in its entirety, in the period in which the milestone is achieved, only if the milestone meets all the criteria within the guidance to be considered substantive. This ASU is effective on a prospective basis for research and development milestones achieved in fiscal years, beginning on or after June 15, 2010. Early adoption is permitted; however, adoption of this guidance as of a date other than January 1, 2011 requires the application of this guidance retrospectively effective as of January 1, 2010 and disclosure of the effect of this guidance as applied to all previously reported interim periods in the fiscal year of adoption. As the Company plans to implement ASU No. 2010-17 prospectively, the effect of this guidance will be limited to future transactions.

In December 2010, the FASB issued ASU No. 2010-027, *Fees Paid to the Federal Government by Pharmaceutical Manufacturers* ("ASU 2010-027") which provides guidance on how to recognize and

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

classify the fees mandated by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act (together, the "Acts"). The Acts impose an annual fee for each calendar year beginning on or after January 1, 2011 payable by branded prescription drug manufacturers and importers on branded prescription drugs. The liability for the fee should be estimated and recorded in full upon the first qualifying sale with a corresponding deferred cost that is amortized to expense using a straight-line method of allocation over the calendar year that it is payable. ASU 2010-027 is effective for calendar years beginning on or after December 31, 2010, when the fee initially becomes effective. As the Company does not currently have a commercial product, the effect of this guidance will be limited to future transactions.

Reclassification *s*

Amounts associated with the Company's former subsidiary, Microbia, have been presented as discontinued operations for all periods in the consolidated financial statements.

3. Initial Public Offering

In February 2010, the Company completed its initial public offering of Class A common stock pursuant to a registration statement that was declared effective on February 2, 2010. The Company sold 19,166,667 shares of its Class A common stock, which included 2,500,000 shares of the Company's Class A common stock sold pursuant to an over-allotment option granted to the underwriters, at a price to the public of $11.25 per share. As a result of the initial public offering, the Company raised a total of $215.6 million in gross proceeds, and approximately $203.2 million in net proceeds after deducting underwriting discounts and commissions of $10.5 million and offering expenses of approximately $1.9 million. Costs directly associated with the Company's initial public offering were capitalized and recorded as deferred offering costs prior to the closing of the initial public offering. These costs have been recorded as a reduction of the proceeds received in arriving at the amount to be recorded in additional paid-in capital.

Upon the closing of the initial public offering, 69,904,843 shares outstanding of the Company's convertible preferred stock automatically converted into 70,391,620 shares of its Class B common stock.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

4. Net Loss Per Share

Basic and diluted net loss per share is calculated as follows (in thousands, except share and per share amounts):

	Years Ended December 31,		
	2010	2009	2008
Numerator:			
Net loss from continuing operations.	$ (56,411)	$ (59,998)	$ (47,410)
Net income (loss) from discontinued operations	4,551	(13,314)	(7,621)
Less: net (income) loss from discontinued operations attributable to noncontrolling interest	(1,121)	2,127	1,157
Net income (loss) from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	3,430	(11,187)	(6,464)
Net loss attributable to Ironwood Pharmaceuticals, Inc.	$ (52,981)	$ (71,185)	$ (53,874)
Denominator:			
Weighted average number of common shares used in net loss per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	89,653,364	7,116,774	6,889,817
Net loss per share associated with continuing operations	$ (0.63)	$ (8.43)	$ (6.88)
Net income (loss) per share from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	0.04	(1.57)	(0.94)
Net loss per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	$ (0.59)	$ (10.00)	$ (7.82)

The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding as of December 31, 2010, 2009 and 2008, as they would be anti-dilutive:

	Years Ended December 31,		
	2010	2009	2008
Convertible preferred stock	—	69,904,843	67,118,858
Options to purchase common stock	14,603,229	13,691,579	11,505,866
Shares subject to repurchase	284,960	434,156	65,990
	14,888,189	84,030,578	78,690,714

5. Collaboration and License Agreements

Forest Laboratories, Inc.

In September 2007, the Company entered into a collaboration agreement with Forest to jointly develop and commercialize linaclotide, a drug candidate for the treatment of IBS-C, CC and other lower gastrointestinal conditions, in North America. Under the terms of this collaboration agreement, the Company shares equally with Forest all development costs, as well as potential future profits and losses from the development and sale of linaclotide in the U.S. The Company will receive royalties

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

5. Collaboration and License Agreements (Continued)

from Forest for sales in Canada and Mexico. The Company retained the rights to commercialize linaclotide outside of North America. Forest made non-refundable, up-front payments totaling $70.0 million to the Company in order to obtain rights to linaclotide in North America. These payments were made in two tranches, one of $50.0 million paid in September 2007, and the second of $20.0 million, which was paid in January 2008. Because of the Company's continuing involvement in the development program, the Company is recognizing the up-front license fee as revenue on a straight-line basis over five years, which is the Company's estimate of the period over which linaclotide will be 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 clinical and commercial milestones. These payments, including the up-front license fee, could total up to $330.0 million, of which $125.0 million has already been received, if certain development and sales milestones are achieved for linaclotide. In September 2008, the Company achieved a clinical milestone which triggered a $10.0 million milestone payment from Forest. The Company recognized revenue of approximately $2.1 million upon achievement of the milestone. This amount represents the portion of the milestone payment equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved. The remainder of the balance was deferred, and is being recognized on a straight-line basis over the remaining development period. At December 31, 2010, approximately $23.9 million and $3.4 million of the up-front license fee and milestone payment, respectively, remain deferred and are being recognized on a straight-line basis over the remaining estimated development period.

The collaboration agreement included a contingent equity investment, in the form of a forward purchase contract, which required Forest to purchase 2,083,333 shares of the Company's convertible preferred stock, when a specific clinical milestone was met, at a price of $12.00 per share. The Company evaluated this financial instrument and determined that because the Company may be required to settle the instrument by transferring assets to Forest due to "deemed liquidation" provisions of the preferred stock, it should be considered an asset or liability, which is required to be carried at fair value. The changes in fair value are recorded as other income or expense. The contingent equity investment was valued at inception at its estimated fair value. A significant input in the valuation of the forward purchase contract was the fair value of the Company's convertible preferred shares which were estimated using the probability-weighted expected return method under the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation* (the "Practice Aid"). Under the probability-weighted expected return method, the value of the Company's convertible preferred shares was estimated based on an analysis of potential future values of the Company assuming various future liquidity events, the timing and amount of which was based on estimates from the Company. The resulting share value was based on the probability-weighted present value of the expected future returns, considering each of the possible outcomes as well as the rights of each share class. The calculated discount or premium from the pre-determined price paid by Forest for their shares in excess of the estimated fair value of the Company's convertible preferred stock at the expected time of meeting the milestone was discounted to arrive at the present value of the forward purchase contract.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

5. Collaboration and License Agreements (Continued)

After applying the methodology discussed above, the Company valued the contingent equity investment in September 2007 at $9.0 million, which represented the value of the premium that Forest will pay for shares of the Company's stock should the milestone be achieved. The $9.0 million was recorded as an asset and incremental deferred revenue at the inception of the arrangement. The $9.0 million of incremental deferred revenue, together with the $70.0 million non-refundable up-front payments, are being recognized as revenue on a straight-line basis over the period of the Company's continuing involvement, which was estimated to be five years from the inception of the arrangement. At December 31, 2010, approximately $3.1 million of the incremental deferred revenue associated with the contingent equity investment remains deferred and is being recognized on a straight-line basis over the remaining estimated development period.

In addition, the Company was required to remeasure the fair value of the contingent equity investment at each reporting period using valuation methodologies consistent with the Practice Aid and using current assumptions. The resulting changes in value were then recorded as other income or expense. At December 31, 2008, the Company remeasured the fair value of the contingent equity investment using current assumptions and as a result, the contingent equity investment was valued at December 31, 2008 at $8.7 million. During the year ended December 31, 2008, the Company recognized approximately $0.9 million of other expense in relation to the remeasurement of the Forest forward purchase contract.

On July 22, 2009, the Company achieved the clinical milestone in the Forest collaboration agreement, thus triggering the equity investment. As a result, the Company remeasured the fair value of the contingent equity investment as of July 22, 2009 using assumptions as of that date. The resulting final fair value of the contingent equity investment was $8.8 million. The increase of approximately $0.1 million in the fair value of the contingent equity investment from December 31, 2008 was recorded to other income (expense) at that time and the Company reclassified the forward purchase contract as a reduction to convertible preferred stock. The Company issued the 2,083,333 shares to Forest on September 1, 2009. Additionally, the achievement of the clinical milestone triggered a $20.0 million milestone payment from Forest that was received on August 20, 2009, of which approximately $7.5 million was recognized upon achievement of the milestone. This amount represents the portion of the milestone payment equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved. The remainder of the balance was deferred, and is being recognized on a straight-line basis over the remaining development period. At December 31, 2010, approximately $6.8 million of the milestone payment remains deferred.

The Company recognized approximately $21.8 million, $27.0 million and $18.4 million in revenue associated with the Forest collaboration agreement during the years ended December 31, 2010, 2009 and 2008, respectively.

Further, because the Company shares development costs equally with Forest, payments from Forest with respect to research and development costs incurred by the Company are recorded as a reduction to expense, and not as revenue. As a result of the cost-sharing arrangements under the collaboration, the Company offset approximately $15.5 million, $15.1 million and $11.8 million during the years ended December 31, 2010, 2009 and 2008, respectively, against research and development expense.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

5. Collaboration and License Agreements (Continued)

Almirall, S.A.

In April 2009, the Company entered into a license agreement with Almirall for European rights to develop and commercialize linaclotide for the treatment of IBS-C, CC and other lower gastrointestinal 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. The license agreement requires the Company to participate on a joint development committee over linaclotide's development period. The Company will receive escalating royalties from the sales of linaclotide in the European territory. In May 2009, the Company received a $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 on a net basis. Because of the Company's continuing involvement in the development program, the Company is recognizing the up-front license fee as revenue on a straight-line basis over fifty months, which is the Company's estimate of the period over which linaclotide will be developed under the license agreement for the European territory. At December 31, 2010, approximately $22.8 million of the up-front license fee remains deferred. The license agreement also includes contingent milestone payments, as well as a contingent equity investment based on the achievement of specific clinical and sales milestones. These payments could total up to $55.0 million, before foreign tax withholdings, including the contingent equity investment discussed below, of which $34.0 million, net of foreign withholding taxes, has already been received, if certain development and sales milestones are achieved for linaclotide.

The license agreement included a contingent equity investment, in the form of a forward purchase contract, which required Almirall to purchase 681,819 shares of the Company's convertible preferred stock when a specific clinical milestone was met, at a price of $22.00 per share. The Company evaluated this financial instrument and determined that because the Company may be required to settle the instrument by transferring assets to Almirall, it should be considered an asset or liability. The contingent equity investment was valued at inception at its fair value. The valuation was prepared using the same methodology that the Company used to value the Forest contingent equity investment. After applying this methodology, the Company valued the contingent equity investment at April 30, 2009 at $6.0 million, which represented the value of the premium that Almirall would pay for shares of the Company's stock should the milestone be achieved. The $6.0 million was recorded as an asset and incremental deferred revenue at the inception of the arrangement. The $6.0 million of incremental deferred revenue, is being recognized as revenue on a straight-line basis over the period of the Company's continuing involvement, which is estimated to be fifty months. At December 31, 2010 approximately $3.6 million of the incremental deferred revenue remains deferred.

On November 2, 2009, the Company achieved the clinical milestone in the Almirall license agreement, thus triggering the equity investment. As a result, the Company remeasured the fair value of the contingent equity investment as of November 2, 2009 using assumptions as of that date. The resulting final fair value of the contingent equity investment was $6.5 million. The increase of approximately $0.5 million in the fair value of the contingent equity investment from April 30, 2009 was recorded to other income (expense) at that time and the Company 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 681,819 shares of convertible preferred stock.

In November 2010, the Company achieved a clinical milestone which resulted in a $19.0 million payment, representing the $20.0 million milestone, net of foreign withholding taxes. The Company

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

5. Collaboration and License Agreements (Continued)

recognized revenue of approximately $7.2 million upon achievement of the milestone. This amount represents the portion of the milestone payment equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved. The remainder of the balance was deferred, and is being recognized on a straight-line basis over the remaining development period. At December 31, 2010, approximately $11.4 million of the milestone payment remains deferred.

The Company recognized approximately $18.9 million and $7.4 million in total revenue from the Almirall license agreement during the years ended December 31, 2010 and 2009, respectively, including approximately $0.7 million and $0.3 million, respectively, from the sale of clinical materials to Almirall.

Astellas Pharma Inc.

On November 9, 2009, the Company entered into a license agreement with Astellas. Astellas has the right to develop and commercialize linaclotide for the treatment of IBS-C, CC and other gastrointestinal conditions in Japan, South Korea, Taiwan, Thailand, Philippines, and Indonesia. Under the terms of the agreement, Astellas paid the Company an up-front licensing fee of $30.0 million on November 16, 2009. The license agreement requires the Company to participate on a joint development committee over linaclotide's development period. The agreement includes additional development milestone payments that could total up to $45.0 million. In addition, the Company will receive escalating royalties on linaclotide sales should Astellas receive approval to market and sell linaclotide in the Asian market. Astellas will be responsible for activities relating to regulatory approval and commercialization. Because of the Company's continuing involvement in the development program, the Company is recognizing the up-front license fee as revenue on a straight-line basis over 115 months, which is the Company's estimate of the period over which linaclotide will be developed under the license agreement for the Asian market. At December 31, 2010, approximately $27.4 million of the up-front license fee remains deferred. During the year ended December 31, 2010, the Company recognized approximately $3.2 million, in revenue from the Astellas license agreement, including approximately $0.6 million from the sale of clinical materials to Astellas. The Company did not recognize any revenue associated with the Astellas agreement in 2009 because the expected performance period of the Company's significant continuing obligations could not be reasonably and reliably estimated until the first quarter of 2010.

6. 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, 2010 and 2009 and indicates 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 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 applied other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare evaluations. In addition, model processes were used to

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

6. Fair Value of Financial Instruments (Continued)

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, 2010	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds (included in cash and cash equivalents)	$ 36,228	$ 36,228	$ —	$ —
U.S. government-sponsored securities (included in cash and cash equivalents)	2,998	—	2,998	—
U.S. Treasury securities	116,219	116,219	—	—
U.S. government-sponsored securities	87,487	—	87,487	—
Total	$ 242,932	$ 152,447	$ 90,485	$ —

		Fair Value Measurements at Reporting Date Using		
Description	December 31, 2009	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds (included in cash and cash equivalents)	$ 102,583	$ 102,583	$ —	$ —
U.S. government-sponsored entities (included in cash and cash equivalents)	18,049	—	18,049	—
Total	$ 120,632	$ 102,583	$ 18,049	$ —

During the years ended December 31, 2009 and 2008, the Company held forward purchase contracts associated with the Company's collaboration agreement with Forest and license agreement with Almirall, as described in Note 5. The agreements required Forest and Almirall to purchase shares of the Company's convertible preferred stock at a pre-determined price upon meeting specific development milestones. The values of the forward purchase contracts represented the estimated probability weighted value of the premium above fair value that Forest and Almirall paid for the convertible preferred shares should the milestones be achieved. The Company estimated the fair value of the convertible preferred stock using methods consistent with the Practice Aid as discussed in Note 5. The Company remeasured the fair value of the forward purchase contracts at each reporting period using current assumptions, with changes in value recorded as other income or expense.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

6. Fair Value of Financial Instruments (Continued)

The following table is a roll-forward of the fair value the forward purchase contracts, where fair value is determined by Level 3 inputs (in thousands):

Balance at December 31, 2008	$ 8,700
Issuance of Almirall forward purchase contract	6,000
Increase in fair value of forward purchase contracts upon remeasurement included in other income (expense)	600
Settlement of forward purchase contracts	(15,300)
Balance at December 31, 2009	$ —

Cash equivalents, accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses and the current portion of capital lease obligations at December 31, 2010 and December 31, 2009, and the current portion of long-term debt at December 31, 2009 are carried at amounts that approximate fair value due to their short-term maturities.

Capital lease obligations at December 31, 2010 and December 31, 2009 and long-term debt at December 31, 2009, approximate fair value as they bear interest at a rate approximating a market interest rate.

As a result of the strategic restructuring plan implemented by Microbia in November 2009 (Note 22), the Company identified certain assets as impaired and at December 31, 2009 had classified these assets measured at fair value on a nonrecurring basis as follows (in thousands):

		Fair Value Measurements at Reporting Date Using			
Description	December 31, 2009	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total Gains (Losses)
Long-lived assets held and used	$ 657	$ —	$ 657	$ —	$ (890)

The long-lived assets held and used have been classified as Level 2. These assets were initially valued at cost and when identified as impaired, valued at estimated selling price. The Company used observable inputs such as selling prices of similar equipment in similar condition. The impaired assets are associated with the biomanufacturing segment and are included in long-term assets of discontinued operations on the consolidated balance sheets and the loss associated with the restructuring and impairment is shown as part of net income (loss) from discontinued operations on the consolidated statements of operations. The assets held at fair value were included in the sale of the Company's interest in Microbia to DSM and thus were not re-evaluated for impairment at December 31, 2010.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

7. Available-for-Sale Investments

The following is a summary of available-for-sale securities at December 31, 2010 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
December 31, 2010:				
U.S. government-sponsored entities	$ 87,503	$ 3	$ (19)	$ 87,487
U.S. Treasury securities	116,200	24	(5)	116,219
Total	$ 203,703	$ 27	$ (24)	$ 203,706

The Company did not have any available-for-sale securities at December 31, 2009.

The contractual maturities of all securities held at December 31, 2010 are one year or less. There were thirty-one investments classified as available-for-sale securities in an unrealized loss position at December 31, 2010, none of which had been in an unrealized loss position for more than twelve months. The aggregate fair value of these securities was approximately $94.7 million. 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 an 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 did not hold any securities with an other-than-temporary impairment at December 31, 2010.

The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. Gross realized gains and losses on the sales of investments have not been material to the Company's consolidated results of operations.

8. Property and Equipment

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

	December 31,	
	2010	2009
Laboratory equipment	$ 11,375	$ 9,679
Computer and office equipment	3,198	2,662
Furniture and fixtures	1,481	972
Software	3,299	1,790
Construction in process	2,701	1,861
Leasehold improvements	29,248	17,184
	51,302	34,148
Less accumulated depreciation and amortization	(16,933)	(12,394)
	$ 34,369	$ 21,754

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

8. Property and Equipment (Continued)

In both the years ended December 31, 2010 and December 31, 2009, the Company entered into capital leases for certain computer and office equipment. As of December 31, 2010 and December 31, 2009, the Company had approximately $1.0 million and $0.4 million of assets under capital lease with accumulated amortization balances of approximately $0.4 million and $0.2 million, respectively.

Depreciation and amortization expense of property and equipment associated with continuing operations, including equipment recorded under capital leases, was approximately $6.2 million, $4.8 million and $2.6 million for the years ended December 31, 2010, 2009 and 2008, respectively. Approximately $0.1 million, $0.5 million and $0.2 million in depreciation and amortization expense associated with property and equipment of Microbia, included in net income (loss) from discontinued operations, was recorded in the years ended December 31, 2010, 2009 and 2008, respectively. In the year ended December 31, 2009, the Company recorded a charge for impairment of long-lived assets of approximately $0.9 million, which was required to adjust certain assets at Microbia to their fair value at the time Microbia implemented its strategic restructuring plan. This amount is included in net income (loss) from discontinued operations for the year ended December 31, 2009.

9. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2010	2009
Salaries and benefits	$ 5,063	$ 1,875
Professional fees	836	697
Other	3,039	1,727
	$ 8,938	$ 4,299

This table does not reflect accruals from discontinued operations. At December 31, 2009, current liabilities from discontinued operations contained approximately $0.6 million in accrued expenses, primarily for salary and benefits.

10. Patent Costs

The Company incurred and recorded as operating expense legal and other fees related to patents of approximately $1.9 million, $1.6 million and $1.3 million for the years ended December 31, 2010, 2009 and 2008, respectively. These costs were charged to general and administrative expenses as incurred. Additionally, patent costs of approximately $0.1 million, $0.2 million and $0.2 million related to Microbia are included in net income (loss) from discontinued operations for the years ended December 31, 2010, 2009 and 2008, respectively.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

11. Debt

At December 31, 2009, the Company had outstanding borrowings under a master loan and security agreement with a financing company to finance the purchase of laboratory and other equipment of approximately $3.1 million, of which approximately $1.3 million is included in liabilities of discontinued operations. The borrowings had maturity dates ranging from 2010 to 2013 with a weighted average interest rate of 12.2%. In September 2010, the Company repaid all outstanding principal and interest under this agreement. The Company incurred pre-payment fees of approximately $67,000 in conjunction with the repayment of debt of which approximately $31,000 is included in net income (loss) from discontinued operations and the remainder is included in interest expense in the statements of operations.

12. Commitments and Contingencies

The Company leases various facilities and equipment under leases that expire at varying dates through 2016. Certain of these leases contain renewal options, and require the Company to pay operating costs, including property taxes, insurance, and maintenance.

In January 2007, the Company entered into a lease agreement for 113,646 rentable square feet of office and lab space at 301 Binney Street, Cambridge, Massachusetts. The initial term of the lease is eight years expiring in January 2016, and the Company has the right to extend the initial term for two additional terms of five years each. The Company's occupancy of the space occurred in four distinct phases, and rent for each phase commenced at the earlier of a contractually set date or the occupancy date. Base rent for the space ranges from $49.25 to $60.50 per rentable square foot per year. Base rent escalates in January 2012 based upon a formula that is tied to the Consumer Price Index. The space was delivered to the Company in September 2007, and rent payments for the first phase of occupancy commenced in January 2008. The rent expense, inclusive of the escalating rent payments and free rent period is recognized on a straight-line basis over the term of the lease agreement. In accordance with the terms of the lease agreement, in the second quarter of 2010 the Company increased the letter of credit securing its obligations under the lease agreement by approximately $2.3 million.

The Company entered into two amendments to the lease agreement in February 2010 and July 2010, respectively (together "the Amendments"). Pursuant to the Amendments, the Company leased an additional 57,033 rentable square feet of the 301 Binney Street building, comprising (a) an initial phase of 35,444 rentable square feet (the "Initial Phase"), and (b) a second phase of up to 24,556 rentable square feet (the "Second Phase"). The Fourth Amendment to the lease (Note 24), signed in February 2011, clarified the Second Phase to consist of 21,589 rentable square feet. Rent for the Initial Phase commenced on July 1, 2010 and rent for the Second Phase will commence no later than July 1, 2011. Initial base rent for the Initial Phase is $42.00 per rentable square foot per year and the initial base rent for the Second Phase will be $42.50 per rentable square foot per year. Base rent for both the Initial Phase and the Second Phase will increase annually by $0.50 per rentable square foot. The rent expense, inclusive of the escalating rent payments, is recognized on a straight-line basis over the term of the lease agreement. The Amendments do not change the expiration date of the lease agreement.

The landlord has reimbursed the Company for its tenant improvements for the initial four phases occupied under the lease agreement at a set rate per rentable square foot. Under the terms of the Amendments, the landlord has or will provide the Company with an allowance of $55.00 per rentable square foot for tenant improvements in the Initial Phase and the Second Phase. As of December 31, 2010, approximately $14.4 million has been paid to the Company as reimbursement for tenant

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

improvements under the lease agreement, including its amendments. 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 term of the lease agreement.

The Company elected not to renew its lease of approximately 39,000 square feet of space at 320 Bent Street, Cambridge, Massachusetts, which expired in December 2010.

In June 2010, the Company entered into a commercial supply agreement with a contract manufacturing organization for the purchase of a portion of the linaclotide API that will be used to seek regulatory approval of linaclotide in the U.S., Canada and/or Mexico, and, depending on any such approval, that would be used for commercial sale in such countries. The commercial supply agreement contains minimum purchase requirements that commence with the commercial launch of linaclotide and that are dependent upon forecasted commercial requirements. Since, at this time, linaclotide has not yet been approved for commercialization and future commercial demand for linaclotide is unknown, the Company cannot estimate its future minimum purchase requirements under the commercial supply agreement.

In the years ended December 31, 2010, 2009 and 2008, the Company entered into capital leases totaling approximately $1.0 million for certain computer and office equipment. The capital leases expire at various times through June 2015. At December 31, 2010 and 2009, the weighted average interest rate on the outstanding capital lease obligations was 10.6% and 10.3%, respectively.

At December 31, 2010, future minimum lease payments under all non-cancelable lease arrangements are as follows (in thousands):

	Operating Leases	Capital Leases
2011	$ 8,671	$ 248
2012	9,871	188
2013	9,912	145
2014	9,942	85
2015	9,971	35
Thereafter	168	—
Total future minimum lease payments	$ 48,535	701
Less amounts representing interest		(111)
Capital lease obligations at December 31, 2010		590
Less current portion of capital lease obligations		(197)
Capital lease obligations, net of current portion		$ 393

Rent expense of approximately $8.9 million, $9.1 million and $10.7 million was charged to continuing operations for the years ended December 31, 2010, 2009 and 2008, respectively. Rent expense of approximately $1.3 million, $2.7 million and $2.1 million related to Microbia for the years ended December 31, 2010, 2009 and 2008, respectively, is included in net income (loss) from discontinued operations. Sublease income of approximately $0.4 million related to Microbia is recorded as a reduction to rent expense for the year ended December 31, 2008 and is included in net income

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

12. Commitments and Contingencies (Continued)

(loss) from discontinued operations. The sublease agreement was terminated in November 2008. The Company did not record any sublease income for the years ended December 31, 2010 and 2009.

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 should limit its exposure and enable it to recover a portion of any future amounts paid.

The Company is a party to a number of agreements entered into in the ordinary course of business that contain typical provisions that obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain.

The Company leases office space under a non-cancelable operating lease. The Company has a standard indemnification arrangement under the lease that requires it to indemnify its landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation or nonperformance of any covenant or condition of the Company's lease.

As of December 31, 2010 and 2009, the Company had not experienced any material losses related to these indemnification obligations and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible. As a result, the Company has not established any related reserves.

13. Litigation

In February 2008, Microbia and Teva Pharmaceutical Works, Rt., formerly known as Biogal Pharmaceutical Works, Rt. ("Teva"), entered into a Settlement Agreement (the "Settlement Agreement") related to a dispute under two of the Company's development agreements for Teva. Pursuant to the Settlement Agreement, Teva remitted a payment of approximately $1.2 million to Microbia in March 2008, in settlement of all outstanding litigation. The settlement amount is included in net income (loss) from discontinued operations for the year ended December 31, 2008 in the consolidated statement of operations.

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 other legal matters will have a material adverse effect on the Company's consolidated financial statements.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

14. Convertible Preferred Stock

On February 2, 2010, upon the closing of the Company's initial public offering, 69,904,843 shares outstanding of the Company's convertible preferred stock automatically converted into 70,391,620 shares of its Class B common stock. As of December 31, 2010, the Company does not have any convertible preferred stock authorized, issued or outstanding.

Prior to the closing of the initial public offering, the Company's Convertible Preferred Stock consisted of the following (in thousands, except share and per share amounts):

	December 31,	
	2010	2009
Series A Convertible Preferred Stock, $0.001 par value: 8,904,567 shares authorized, issued and outstanding (liquidation value of approximately $18.4 million) at December 31, 2009	$ —	$ 9,795
Series B Convertible Preferred Stock, $0.001 par value: 7,419,355 shares authorized, issued and outstanding (liquidation value of approximately $40.3 million) at December 31, 2009	—	23,000
Series C Convertible Preferred Stock, $0.001 par value: 6,401,523 shares authorized, issued and outstanding (liquidation value of approximately $42.6 million) at December 31, 2009	—	26,223
Series D Convertible Preferred Stock, $0.001 par value: 12,618,296 shares authorized, issued and outstanding (liquidation value of approximately $58.2 million) at December 31, 2009	—	39,906
Series E Convertible Preferred Stock, $0.001 par value: 20,500,000 shares authorized, 19,633,531 shares issued and outstanding (liquidation value of approximately $98.2 million) at December 31, 2009	—	74,927
Series F Convertible Preferred Stock, $0.001 par value: 8,000,000 shares authorized, issued and outstanding (liquidation value of approximately $61.6 million) at December 31, 2009	—	49,951
Series G Convertible Preferred Stock, $0.001 par value: 2,083,333 shares authorized, issued and outstanding (liquidation value of approximately $25.7 million) at December 31, 2009	—	16,200
Series H Convertible Preferred Stock, $0.001 par value: 8,333,333 shares authorized, 4,162,419 issued and outstanding (liquidation value of approximately $55.1 million) at December 31, 2009	—	49,848
Series I Convertible Preferred Stock, $0.001 par value: 681,819 shares authorized, issued and outstanding (liquidation value of approximately $15.2 million) at December 31, 2009	—	8,500
	$ —	$ 298,350

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

14. Convertible Preferred Stock (Continued)

In September 2008, the Company issued 4,141,586 shares of Series H Convertible Preferred Stock at a price of $12.00 per share for cash proceeds of approximately $49.6 million, net of issuance costs of approximately $0.1 million.

In August 2009, the Company issued 20,833 shares of Series H Convertible Preferred Stock at a price of $12.00 per share for cash proceeds of approximately $0.2 million.

In September 2009, the Company issued 2,083,333 shares of Series G Convertible Preferred Stock at a price of $12.00 per share for cash proceeds of $25.0 million. In July 2009, upon the settlement of the Forest forward purchase contract, $8.8 million was reclassified from the forward purchase contract asset to convertible preferred stock to offset the $25.0 million of proceeds received.

In November 2009, the Company settled the Almirall forward purchase contract by selling Almirall 681,819 shares of Series I Convertible Preferred Stock at a price of $22.00 per share for cash proceeds of $15.0 million. Upon the settlement of the Almirall forward purchase contract, $6.5 million was reclassified from the forward purchase contract asset to convertible preferred stock to offset the $15.0 million of proceeds received.

15. Stockholders' Equity (Deficit)

Common Stock

In February 2010, in conjunction with the Company's initial public offering (Note 3), the Company amended its certificate of incorporation to authorize it to issue 500,000,000 shares of Class A common stock, 100,000,000 shares of Class B common stock and 75,000,000 shares of preferred stock.

The Company has designated two series of common stock, Series A Common Stock ($0.001 par value per share), which is referred to as "Class A Common Stock," and Series B Common Stock ($0.001 par value per share), 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 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 converts to Class A Common Stock, on a one-for-one basis, if transferred or sold after the completion of a public offering. Class B Common Stock can be sold at any time and irrevocably converts to Class A Common Stock upon sale or transfer.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

15. Stockholders' Equity (Deficit) (Continued)

The Class B Common Stock will be 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 25% of the number of shares of Class B Common Stock outstanding immediately following the completion of an initial public offering 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.

Restricted Stock

In 2005 and 2006, the Company sold an aggregate of 520,000 shares of common stock at par value ($0.001 per share) to independent members of the board of directors under restricted stock agreements in accordance with the terms of the Company's 2002 Stock Incentive Plan ("2002 Plan"). The restricted stock was fully vested as of December 31, 2009.

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 Company's 2005 Stock Incentive Plan ("2005 Plan") and the Company's director compensation program. 115,549 shares of restricted common stock granted in 2009 vested on December 31, 2009 and the remainder vest ratably over four years beginning in January 2010. In the event that a member of the board of directors ceases to serve on the Company's board prior to December 31, 2013, the member shall forfeit all unvested shares in accordance with the terms of the restricted stock agreement.

A summary of the unvested shares of restricted stock as of December 31, 2010 is presented below:

	Shares	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2009	400,000	$ 5.67
Granted	—	—
Vested	(90,000)	$ 5.69
Forfeited	(40,000)	$ 5.48
Unvested at December 31, 2010	270,000	$ 5.69

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans

The Company has several share-based compensation plans. Under the 1998 Amended and Restated Stock Option Plan ("1998 Plan"), options to purchase 3,405,000 shares of common stock were available for grant to employees, directors, and consultants of the Company. The options were granted under the 1998 Plan at fair market value on the grant date, generally vest over a period of four years, and expire ten years from the grant date. There are no shares available for future grant under this plan, as it expired in accordance with its terms in 2008. At December 31, 2010 and 2009, options for 200,500 and 550,633 shares, respectively, were outstanding under the 1998 Plan.

Under the Company's 2002 Stock Incentive Plan ("2002 Plan") and 2005 Plan, stock awards may be granted to employees, officers, directors, consultants, or advisors of the Company. The 2002 Plan and 2005 Plan provide for the granting of stock options, restricted stock, restricted stock units, and other share-based awards. At December 31, 2010, there were 4,700,000 shares of common stock reserved for issuance under the 2002 Plan and 12,200,000 shares reserved under the 2005 Plan. The 2002 Plan allows for the transfer of unused shares from the 1998 Plan. Upon the expiration of the 1998 Plan on July 10, 2008, 382,438 unused shares were transferred to the 2002 Plan. At December 31, 2010, there were 61,831 shares available for future grant under the 2002 Plan and 23,657 shares available for future grant under the 2005 Plan.

On January 21, 2010, the Company's stockholders approved the 2010 Employee, Director and Consultant Equity Incentive Plan ("2010 Plan") and (together with the 2002 Plan and 2005 Plan, the "Plans") which became effective upon the closing of the Company's initial public offering on February 8, 2010. Under the 2010 Plan, stock awards may be granted to employees, officers, directors, or consultants of the Company. There are 6,000,000 shares of common stock initially reserved for issuance under the 2010 Plan. The number of shares available for future grant under the 2010 Plan 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 Class A 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 1998 Plan, 2002 Plan and 2005 Plan as a result of their expiration, cancellation, termination or repurchase are automatically made available for issuance under the 2010 Plan. At December 31, 2010, there were 5,489,369 shares available for future grant under the 2010 Plan.

On January 21, 2010, the Company's stockholders approved the 2010 Employee Stock Purchase Plan ("Purchase Plan") which became effective upon the closing of the Company's initial public offering on February 8, 2010. The Purchase Plan allows eligible employees the right to purchase shares of common stock at the lower of 85% of the fair market value of a share of common stock 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 Purchase Plan. The number of shares available for future grant under the 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 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. At December 31, 2010, there were 369,562 shares available for future grant under the Purchase Plan. The initial offering period, under which 30,438 shares were issued, began on July 1, 2010 and ran through December 31, 2010. During the year ended December 31, 2010, approximately $0.1 million of share-based compensation expense was recognized related to the Purchase Plan.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans (Continued)

Each plan, other than the Purchase Plan, provides for the granting of stock awards whereby the Company's Class B common stock is issuable upon exercise of options granted prior to the closing of the Company's initial public offering and Class A common stock is issuable upon exercise of options granted after the closing of the Company's initial public offering. At December 31, 2010, options exercisable into 11,881,229 shares of Class B common stock and 2,722,000 shares of Class A common stock were outstanding.

The option price at the date of grant is determined by the board of directors and, in the case of incentive stock options, may not be less than the fair market value of the common stock at the date of grant. Due to the absence of an active market for the Company's common stock, prior to the Company's initial public offering on February 2, 2010, the board of directors was required to determine the fair value of the common stock for consideration in setting exercise prices for the options granted and in valuing the options granted. In determining the fair value, the board of directors considered both quantitative and qualitative factors including prices at which the Company sold shares of its convertible preferred stock, the rights, preferences and liquidity of the Company's convertible preferred and common stock, the Company's historical operating and financial performance and the status of its research and product development efforts, achievement of enterprise milestones, including the Company entering into collaboration agreements where third parties agree to purchase shares of the Company's convertible preferred stock at fixed prices sometime in the future, external market conditions affecting the biotechnology industry sector, and financial market conditions and, commencing in 2006, contemporaneous valuations provided by management.

The option exercise period may not extend beyond ten years from the date of grant. The Plans provide that, subject to approval by the board of directors, option grantees may have the right to exercise an option prior to vesting. Shares purchased upon the exercise of unvested options will be subject to the same vesting schedule as the underlying options, and are subject to repurchase at the original exercise price by the Company should the employee be terminated or leave the Company prior to becoming fully vested in such shares. At December 31, 2010 and 2009, there were 14,960 and 34,156 shares, respectively, that had been issued pursuant to the exercise of unvested options that remain unvested and subject to repurchase by the Company. At December 31, 2010, the Company does not hold any treasury shares. Upon stock option exercise, the Company issues new shares and delivers them to the participant. 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 and was not material to the consolidated financial statements at December 31, 2010 and 2009.

The Company, from time to time, issues certain time-accelerated stock options to certain employees under the Plans. The vesting of these time-accelerated stock 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, and expire at the end of ten years. During the years ended December 31, 2010 and 2009, 52,500 and 100,000 shares vested as a result of milestone or service period achievements, respectively. At December 31, 2010 and 2009, there were 2,279,000 and 2,481,500 shares, respectively, issuable under outstanding and 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 for the respective stock option over the implicit service period. At December 31, 2010,

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans (Continued)

the Company has approximately $1.1 million in unrecognized share-based compensation, net of estimated forfeitures, related to these options.

During 2005, the Company granted to employees options to purchase 97,500 shares of common stock at an exercise price of $0.60 per share, which represented the fair value of the stock at that time. These options are subject to performance-based milestone vesting and expire ten years from the date of grant. The options were deemed to be variable upon grant because the number of shares that will vest was not fixed on the date of grant. The options are therefore remeasured at each reporting period until settlement of the option. During 2006, 37,500 shares vested as a result of milestone achievements. In the year ended December 31, 2009, the remaining 60,000 options vested. During the year ended December 31, 2010, 37,500 shares were exercised and will no longer be remeasured. The Company recorded share-based compensation related to these performance-based options of approximately ($43,000), $0.7 million and $0.3 million during the years ended December 31, 2010, 2009 and 2008.

During 2010 and 2009, the Company granted to employees options to purchase a total of 67,500 and 1,060,000 shares of common stock subject to performance-based milestone vesting, respectively. The vesting of these stock options will occur upon the achievement of certain performance-based milestones. During 2010, 5,000 shares vested as a result of milestone achievements and the Company recorded related share-based compensation expense of approximately $31,000 for these options. As of December 31, 2010, the Company concluded that one additional performance-based milestone is probable of achievement, and as a result recognized approximately $0.1 million of share-based compensation expense related to options subject to this performance-based milestone. At December 31, 2010, the unrecognized share-based compensation related to performance-based milestone options was approximately $3.9 million.

The Company also grants options to external consultants. During the years ended December 31, 2010 and 2009, the Company granted options for the purchase of 25,000 and 37,000 shares, respectively, to external consultants. The weighted-average grant date fair value per share of options granted to external consultants during the years ended December 31, 2010 and 2009 was $7.22 and $4.97, respectively. Most grants made to external consultants vest over a period of one year, and the expense related to these options is being charged to share-based compensation expense over the vesting period of the options. The amount of share-based compensation expense that may be recognized for outstanding, unvested options as of December 31, 2010 was approximately $0.1 million. The amount of share-based compensation expense that will ultimately be recorded will depend on the remeasurement of the outstanding awards through their vesting date. This remaining compensation expense will be recognized over a weighted-average amortization period of 1.2 years at December 31, 2010.

In calculating share-based compensation costs, the Company estimated the fair value of stock options using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model was developed for use in estimating the fair value of short-lived, exchange-traded options that have no vesting restrictions and are fully transferable. The Company estimates the number of awards that will be forfeited in calculating compensation costs. Such costs are then recognized over the requisite service period of the awards on a straight-line basis.

Determining the fair value of share-based awards using the Black-Scholes option-pricing model requires the use of highly subjective assumptions, including the expected term of the award, expected stock price volatility and, up to the date of the Company's initial public offering, the fair value of the Company's common stock. The weighted average assumptions used to estimate the fair value of the

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans (Continued)

stock options using the Black-Scholes option pricing model were as follows for the years ended December 31, 2010, 2009 and 2008:

	Years Ended December 31,		
	2010	2009	2008
Weighted-average fair value of common stock	$ 11.23	$ 5.19	$ 3.94
Expected volatility	57.4%	62.3%	64.0%
Expected term (in years)	6.5	6.5	6.5
Risk-free interest rate	2.9%	2.7%	3.1%
Expected dividend yield	—%	—%	—%

Expected Volatility

Volatility measures the amount that a stock price has fluctuated or is expected to fluctuate during a period. As the Company was not publicly traded prior to February 3, 2010 and therefore had no trading history, stock price volatility was estimated based on an analysis of historical and implied volatility of comparable public companies.

Expected Term

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. As a result, for stock option grants made during the years ended December 31, 2010, 2009 and 2008, the expected term was estimated using the "simplified method." The simplified method is based on the average of the vesting tranches and the contractual life of each grant.

Risk-Free Interest Rate

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.

Expected Dividend Yield

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.

Forfeitures

Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from the Company's estimates. Subsequent changes in estimated forfeitures are recognized through a cumulative adjustment in the period of change, and will also impact the amount of share-based compensation expense in future periods. The Company uses historical data to estimate forfeiture rates. The Company's forfeiture rates were 5.5%, 5.8% and 4.4% as of December 31, 2010, 2009 and 2008, respectively.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans (Continued)

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

	Years Ended December 31,		
	2010	2009	2008
Ironwood:			
Employee stock options	$ 6,545	$ 4,010	$ 2,293
Restricted stock awards	469	784	—
Non-employee stock options	123	301	300
ESPP	100	—	—
Stock award	259	—	25
	7,496	5,095	2,618
Microbia Stock Plan (included in discontinued operations)	59	149	176
	$ 7,555	$ 5,244	$ 2,794

Share-based compensation is reflected in the consolidated statements of operations as follows for the years ended December 31, 2010, 2009 and 2008 (in thousands):

	Years Ended December 31,		
	2010	2009	2008
Research and development	$ 4,112	$ 2,372	$ 1,627
General and administrative	3,384	2,723	991
Net income (loss) from discontinued operations	59	149	176

At December 31, 2010, there were 5,574,857 shares available for future grant under the Plans.

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

	Shares of Common Stock Attributable to Options	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2009	13,691,579	$ 2.45	6.24	$ 131,459
Granted	2,752,000	$ 11.23		
Exercised	(1,746,184)	$ 1.01		
Cancelled	(94,166)	$ 6.45		
Outstanding at December 31, 2010	14,603,229	$ 4.25	6.44	$ 91,575
Vested or expected to vest at December 31, 2010	13,322,107	$ 4.17	6.34	$ 84,577
Exercisable at December 31, 2010 (1)	6,779,369	$ 2.20	4.96	$ 55,457

(1) All stock options granted under the 1998 Plan, 2002 Plan and 2005 Plan contain provisions allowing for the early exercise of such options into restricted stock. The exercisable shares disclosed above represent those that are vested as of December 31, 2010.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

16. Stock Option Plans (Continued)

The weighted-average grant date fair value per share of options granted to employees during the years ended December 31, 2010, 2009 and 2008 was $6.48, $3.17 and $2.44, respectively. The total intrinsic value of options exercised during the years ended December 31, 2010, 2009 and 2008 was approximately $18.6 million, $1.6 million and $0.4 million, respectively. Prior to the Company's initial public offering, the intrinsic value was calculated as the difference between the estimated fair value of the Company's common stock and the exercise price of the option issued. The fair value of the Company's common stock was $10.35, $12.05 and $4.89 per share at December 31, 2010, 2009 and 2008, respectively.

The grant-date fair value of the options granted to employees during the years ended December 31, 2010, 2009 and 2008 was approximately $17.7 million, $9.1 million and $4.7 million, respectively.

As of December 31, 2010, there was approximately $1.4 million and $17.2 million of unrecognized share-based compensation, net of estimated forfeitures, related to restricted stock awards and unvested stock option grants with time-based vesting, respectively which are expected to be recognized over a weighted average period of 3.36 years. The total unrecognized share-based compensation cost will be adjusted for future changes in estimated forfeitures.

Microbia Stock Plan

Under the Microbia Stock Plan, 16,000 options were granted to employees during 2010. The grant date fair value of the options granted to employees during the years ended December 31, 2010, 2009 and 2008 was approximately $1,000, $0.1 million and $0.2 million, respectively. As a result of the sale of the Company's interest in Microbia to DSM in September 2010 the Microbia Stock Plan was cancelled, resulting in the cancellation of all existing shares.

17. Income Taxes

The Company has not recorded a provision for federal or state income taxes as it has had cumulative net operating losses since inception. However, because of the intra-period income tax allocation requirements, the Company recorded a benefit for income taxes from continuing operations of $2.9 million for the year ended December 31, 2010, offset by an identical and corresponding income tax provision from discontinued operations. The intra-period income tax allocation considers income (loss) from discontinued operations for purposes of determining the amount of tax benefit that results from the loss from continuing operations. The Company recognized a federal income tax benefit of approximately $0.3 million for the year ending December 31, 2009 related to refundable research and development tax credits, resulting from a provision in the Housing Assistance Tax Act of 2008 that allowed the Company to claim a refund for a portion of its unused pre-2006 research tax credits on its 2008 U.S. federal income tax return.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

17. Income Taxes (Continued)

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

	Years Ended December 31,		
	2010	2009	2008
Income tax benefit using U.S. federal statutory rate	$ (20,181)	$ (20,500)	$ (16,119)
Permanent differences	(3,126)	2,047	79
State income taxes, net of federal benefit	(3,427)	(3,282)	(2,973)
Stock compensation	(243)	1,300	923
Tax credits	(2,041)	(4,633)	(609)
Expiring net operating losses and tax credits	912	570	501
Effect of change in state tax rate on deferred tax assets and deferred tax liabilities	613	1,744	—
Change in the valuation allowance	27,608	22,400	18,190
Other	(115)	58	8
Total before intra-period allocation	—	(296)	—
Intra-period tax allocation	(2,944)	—	—
	$ (2,944)	$ (296)	$ —

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

	December 31,	
	2010	2009
Deferred tax assets:		
Net operating loss carryforwards	$ 57,257	$ 33,479
Tax credit carryforwards	14,534	12,492
Capitalized research and development	27,874	51,542
Deferred revenue	35,758	17,092
Other	12,424	7,257
Deferred tax assets of discontinued operations	—	10,016
Total deferred tax assets	147,847	131,878
Valuation allowance	(147,847)	(131,878)
Net current 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, 2010 and 2009. Management reevaluates the positive and negative evidence on a quarterly basis.

The valuation allowance increased approximately $16.0 million during the year ended December 31, 2010, due primarily to the increase in the net operating loss carryforwards and deferred revenue. The valuation allowance increased approximately $27.9 million during the year ended

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

17. Income Taxes (Continued)

December 31, 2009, due primarily to the increase in the net operation loss carryforwards, capitalized research and development expenses and tax credits. The valuation allowance increased $21.6 million during the year ended December 31, 2008, due primarily to the increase in the net operating loss carryforwards and research and development tax credits.

Subject to the limitations described below at December 31, 2010 and 2009, the Company has net operating loss carryforwards of approximately $153.2 million and $111.3 million, respectively, to offset future federal taxable income, which expire beginning in 2018 continuing through 2030. As of December 31, 2010 and 2009, the Company has state net operating loss carryforwards of approximately $97.7 million and $82.3 million, respectively, to offset future state taxable income, which have begun to expire and will continue to expire through 2020. The Company also has tax credit carryforwards of approximately $15.8 million and $14.7 million as of December 31, 2010 and 2009, respectively, to offset future federal and state income taxes, which expire at various times through 2030.

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, 2009 and December 31, 2010, 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 January 1, 2009 and December 31, 2009 and December 31, 2010, 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, 2007, 2008 and 2009, although carryforward attributes that were generated prior to tax year 2007 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 audits in progress.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

17. Income Taxes (Continued)

The Company has not, as yet, conducted a study of its research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforward and the valuation allowance.

18. 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 Internal Revenue Code 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. In 2008, the Company instituted a matching contribution of 50% of the employee's first $6,000 of contributions. During the years ended December 31, 2010, 2009 and 2008, the Company recorded approximately $0.5 million, $0.4 million and $0.3 million in net income (loss) from continuing operations related to its 401(k) company match. Included in net income (loss) from discontinued operations for each of the years ended December 31, 2010, 2009 and 2008 is approximately $0.1 million related to the 401(k) company match.

19. 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 $0.3 million, $0.1 million and $0.1 million in legal fees to this investor during the years ended December 31, 2010, 2009, and 2008, respectively.

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 5). Additional related party disclosure related to Microbia and T&L is included in Note 22.

20. Segment Reporting

Prior to the sale of its interest in Microbia in September 2010, the Company had two reportable business segments: human therapeutics and biomanufacturing. The Company had no inter-segment revenues.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

20. Segment Reporting (Continued)

The following table reports revenue and loss from operations for the Company's reportable segments for the years ended December 31, 2010, 2009 and 2008 (in thousands):

	Years Ended December 31,		
	2010	2009	2008
Revenue:			
Human therapeutics	$ 43,857	$ 34,321	$ 18,383
Biomanufacturing (included in discontinued operations)	1,985	1,781	3,833
Total	$ 45,842	$ 36,102	$ 22,216
Loss from operations:			
Human therapeutics	$ (60,766)	$ (60,816)	$ (48,307)
Biomanufacturing (included in discontinued operations)	(4,532)	(13,161)	(7,614)
Total	$ (65,298)	$ (73,977)	$ (55,921)

	December 31,		
	2010	2009	2008
Total assets:			
Human therapeutics	$ 301,365	$ 160,105	$ 134,554
Biomanufacturing (included in discontinued operations)	—	2,346	3,817
Total	$ 301,365	$ 162,451	$ 138,371

At December 31, 2010, all of the Company's accounts receivable related to the human therapeutics segment. At December 31, 2009 approximately $15,000 of the Company's accounts receivable related to the Company's biomanufacturing segment and is included in current assets of discontinued operations and approximately $5.2 million of the Company's accounts receivable related to the human therapeutics segment.

21. Federal Grant

In October 2010, the Company was notified that it was awarded approximately $1.0 million in grants under the Qualifying Therapeutic Discovery Project Program which was created in March 2010 as part of the Patient Protection and Affordability Care Act. The total amount awarded was recognized in the fourth quarter of 2010 and is recorded as other income on the Company's consolidated statements of operations.

22. Microbia, Inc.

On September 21, 2010, the Company sold its interest in Microbia to DSM in exchange for cash proceeds of $9.5 million, the payment of approximately $1.1 million of Microbia debt and interest by DSM and future contingent consideration based on the sale of products incorporating Microbia's technology (See Note 2).

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

22. Microbia, Inc. (Continued)

Tate & Lyle Investments, Ltd.

In September 2006, the Company entered into a collaboration agreement with T&L. The collaboration agreement had a five-year term with a one-year notice of termination. In connection with the execution of the collaboration agreement, the Company also issued T&L 1,823,529 shares of common stock of Microbia, the Company's wholly owned subsidiary, at the aggregate purchase price of approximately $2,000, and issued 7,000,000 shares of convertible preferred stock of Microbia at the aggregate purchase price of $7.0 million. After the sale of stock to T&L, the Company retained an 85% majority ownership interest, and T&L had a 15% noncontrolling interest in Microbia. The Company's ownership interest in Microbia was entirely comprised of convertible preferred stock with the same preferences to that held by T&L. The ownership of the convertible preferred and common stock by T&L is recorded as noncontrolling interest in the consolidated financial statements.

In evaluating whether or not T&L's investment in Microbia's convertible preferred stock should have been classified as noncontrolling interest, the Company had to determine whether or not the convertible preferred stock was in fact in-substance common stock. In-substance common stock is an investment in an entity that has risk and reward characteristics that are substantially similar to that entity's common stock. After reviewing the criteria for treatment as in-substance common stock, the Company concluded that the liquidation preference of the convertible preferred stock was not substantive as Microbia had little subordinated equity, in the form of common stock, from a fair value perspective. As a result, in the event of liquidation, the convertible preferred stock would participate in substantially all of Microbia's losses. The Company also concluded that T&L's investment in Microbia's convertible preferred stock had the risks and rewards of ownership. T&L had the ability to convert the convertible preferred stock into Microbia common stock without any significant restrictions or contingencies that prohibited them from participating in the capital appreciation of Microbia in a manner that was substantially similar to Microbia's common stock. Therefore, this conversion feature was an indicator that the convertible preferred stock was substantially similar to common stock. Additionally, Microbia's preferred stock did not require Microbia to transfer substantive value to T&L in a manner in which the common stockholders did not participate similarly, for example, the preferred stock was not redeemable. As a result, the Company concluded that T&L's investment in Microbia's convertible preferred stock was in fact an investment in in-substance common stock and accordingly attributed Microbia's losses based on the relative ownership interests in Microbia, represented by T&L's common and preferred stock ownership. This resulted in attributing 15% of Microbia's losses to the noncontrolling interest in the Company's consolidated financial statements.

On June 15, 2010, T&L and Microbia entered into an agreement to terminate their collaboration. The terms and conditions of the agreement included an exchange of intellectual property and a one-time payment to Microbia of approximately $1.8 million. All current and future obligations between Microbia and T&L were terminated as a result of this agreement.

Revenue earned from the T&L collaboration agreement totaled approximately $1.9 million, $1.8 million and $2.2 million during the years ended December 31, 2010, 2009 and 2008, respectively. This revenue is included in net income (loss) from discontinued operations for all periods presented. There was no accounts receivable from T&L at December 31, 2010. Accounts receivable from T&L was approximately $10,000 at December 31, 2009 and is included in current assets of discontinued operations.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

22. Microbia, Inc. (Continued)

In conjunction with the sale of Microbia to DSM in September 2010, the Company sold its interest in Microbia, resulting in the deconsolidation of its former subsidiary. As such, the non-controlling interest balance was reduced to zero in conjunction with the sale of the entity (Note 2).

Strategic Restructuring Plan

In November 2009, Microbia implemented a strategic restructuring plan that included an immediate reduction of its workforce by approximately 40% of its existing workforce, and a reduced workweek for an additional 12% of its existing workforce. Microbia took this action to focus on its proprietary strain-development platform and existing service agreements.

In connection with the strategic restructuring plan, Microbia recorded restructuring charges of approximately $1.2 million in the year ended December 31, 2009. Provisions associated with the strategic restructuring are included in net income (loss) from discontinued operations in the consolidated statements of operations. Activities against Microbia's restructuring accrual, which is included in current liabilities of discontinued operations in the consolidated balance sheets, were as follows for the years ended December 31, 2010 and 2009 (in thousands):

	Balance at December 31, 2009	Provisions	Payments	Asset Impairments	Balance at December 31, 2010
Termination benefits	$ 2	$ —	$ (2)	$ —	$ —
Asset impairment	—	—	—	—	—
Other charges	—	—	—	—	—
Total	$ 2	$ —	$ (2)	$ —	$ —

	Balance at December 31, 2008	Provisions	Payments	Asset Impairments	Balance at December 31, 2009
Termination benefits	$ —	$ 287	$ (285)	$ —	$ 2
Asset impairment	—	890	—	(890)	—
Other charges	—	30	(30)	—	—
Total	$ —	$ 1,207	$ (315)	$ (890)	$ 2

The Company accounts for restructuring costs in accordance with ASC 420, *Exit or Disposal Cost Obligations.* ASC 420 requires that a liability for a cost associated with an exit or disposal activity be recognized and measured initially at its fair value in the period in which the liability is incurred, except for one-time termination benefits that meet specific requirements.

Termination benefits related to severance and continuation of benefit costs associated with Microbia's workforce reduction.

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

23. Restatement and Selected Quarterly Financial Data (Unaudited)

The unaudited quarterly financial information of the Company for the quarter ended September 30, 2010 has been restated in order to correctly reflect a benefit to income taxes from continuing operations and an identical income tax provision from discontinued operations for an intra-period income tax allocation. The intra-period income tax allocation considers discontinued operations for purposes of determining the amount of tax benefit that results from the Company's loss from continuing operations. The accounts affected were income tax benefit, net loss from continuing operations and net income (loss) from discontinued operations. This error did not impact net loss, net loss attributable to Ironwood Pharmaceuticals, Inc., or net cash used in operations for the quarter ended September 30, 2010. The Company determined that the incorrect amounts identified were material in the quarter ended September 30, 2010. Accordingly, the Company has restated its unaudited quarterly financial information for this quarter in order to correct the error for the tax benefit. The impact of the error to the three and nine months ended September 30, 2010 is reflected below:

	Three Months Ended September 30, 2010		
	As Originally Reported	As Restated	Change
	(in thousands, except per share data)		
Income tax benefit	$ —	$ (2,944)	$ 2,944
Net loss from continuing operations	(16,058)	(13,114)	2,944
Net income (loss) from discontinued operations	9,311	6,367	(2,944)
Net loss per share from continuing operations	$ (0.16)	$ (0.13)	$ 0.03
Net income (loss) per share from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	0.08	0.05	(0.03)

	Nine Months Ended September 30, 2010		
	As Originally Reported	As Restated	Change
	(in thousands, except per share data)		
Income tax benefit	$ —	$ (2,944)	$ 2,944
Net loss from continuing operations	(47,704)	(44,760)	2,944
Net income (loss) from discontinued operations	7,495	4,551	(2,944)
Net loss per share from continuing operations	$ (0.55)	$ (0.52)	$ 0.03
Net income (loss) per share from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	0.07	0.04	(0.03)

The following table contains quarterly financial information for 2010 and 2009. 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. Amounts associated with the Company's former

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

23. Restatement and Selected Quarterly Financial Data (Unaudited) (Continued)

subsidiary, Microbia, which was sold in September 2010, have been presented as discontinued operations for all periods shown in the information below.

	First Quarter	Second Quarter	Third Quarter (Restated)	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2010					
Collaborative arrangements revenue	$ 8,838	$ 9,188	$ 9,059	$ 16,772	$ 43,857
Total operating expenses	23,334	26,498	25,224	29,567	104,623
Other income (expense), net	15	145	107	1,144	1,411
Net loss from continuing operations	(14,481)	(17,165)	(13,114)	(11,651)	(56,411)
Net income (loss) from discontinued operations	(1,772)	(44)	6,367	—	4,551
Net loss	(16,253)	(17,209)	(6,747)	(11,651)	(51,860)
Net (income) loss from discontinued operations attributable to noncontrolling interest	329	73	(1,523)	—	(1,121)
Net loss attributable to Ironwood Pharmaceuticals, Inc.	(15,924)	(17,136)	(8,270)	(11,651)	(52,981)
Net loss per share from continuing operations	$ (0.23)	$ (0.18)	$ (0.13)	$ (0.12)	$ (0.63)
Net income (loss) per share from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	(0.02)	—	0.05	—	0.04
Net loss per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	$ (0.25)	$ (0.18)	$ (0.08)	$ (0.12)	$ (0.59)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2009					
Collaborative arrangements revenue	$ 4,450	$ 6,210	$ 15,257	$ 8,404	$ 34,321
Total operating expenses	20,327	21,495	23,544	29,771	95,137
Other income (expense), net	200	(300)	(44)	666	522
Net loss from continuing operations	(15,677)	(15,585)	(8,178)	(20,558)	(59,998)
Net income (loss) from discontinued operations	(2,723)	(3,332)	(3,243)	(4,016)	(13,314)
Net loss	(18,400)	(18,917)	(11,421)	(24,574)	(73,312)
Net loss from discontinued operations attributable to noncontrolling interest	432	532	519	644	2,127
Net loss attributable to Ironwood Pharmaceuticals, Inc.	(17,968)	(18,385)	(10,902)	(23,930)	(71,185)
Net loss per share from continuing operations	$ (2.24)	$ (2.21)	$ (1.15)	$ (2.83)	$ (8.43)
Net income (loss) per share from discontinued operations attributable to Ironwood Pharmaceuticals, Inc.	(0.32)	(0.40)	(0.38)	(0.47)	(1.57)
Net loss per share attributable to Ironwood Pharmaceuticals, Inc.—basic and diluted	$ (2.56)	$ (2.61)	$ (1.53)	$ (3.30)	$ (10.00)

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

24. Subsequent Events

State Grant

In December 2010, the Company was notified that it was awarded an approximately $1.0 million tax incentive from the Massachusetts Life Sciences Center as part of the Life Sciences Tax Incentive Program. 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 credit can be recovered by the Massachusetts Department of Revenue if the Company does not meet and maintain its job creation commitments. At December 31, 2010, the Company had not recognized the credit in its consolidated financial statements because the award was not finalized until 2011.

Protagonist Therapeutics, Inc.

The Company entered into a collaboration agreement with Protagonist Therapeutics, Inc. and Protagonist Pty Ltd. (collectively "Protagonist") in January 2011. Under this agreement, Protagonist will use its proprietary technology platform to discover peptides against certain targets and the Company has the rights to develop and commercialize these peptides. In connection with entering into the agreement, the Company made an up-front payment to Protagonist. The Company will also fund full-time equivalents for Protagonist's drug discovery activities, and will make certain milestone and royalty payments pending the achievement of certain development and commercialization milestones.

Lease Amendment

In February 2011, the Company entered into a Fourth Amendment to its lease for 301 Binney Street. Under the amended lease, the Company leases an additional 23,307 square feet of the 301 Binney Street building. Rent for the additional space commences no later than February 15, 2012 and base rent will be $42.50 per rentable square foot per year, and will increase annually by $0.50 per rentable square foot. The landlord will provide the Company with a finish work allowance of $40.00 per rentable square foot of additional space rented pursuant to this amendment. The Amendment does not change the January 31, 2016 expiration date of the original lease.

Commercial Supply Agreement

In March 2011, the Company, along with its collaboration partner Forest, entered into a commercial supply agreement with Roche Colorado Corporation for the purchase of a portion of the linaclotide API that will be used to support regulatory approval of linaclotide in the United States and/or Canada, and, pending any such approval, that will be sold commercially in such country. The commercial supply agreement contains a minimum purchase requirement for the Company and Forest that commences in 2012. Since, at this time, linaclotide has not yet been approved for commercialization and future commercial demand for linaclotide is unknown, the Company cannot estimate its actual future purchase requirements under the commercial supply agreement.

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
10.1#	1998 Amended and Restated Stock Option 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 2002 Stock Incentive Plan and form agreements thereunder	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.3#	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
10.4#	2010 Employee, Director and Consultant Equity Incentive Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 20, 2010
10.4.1#	Form agreement under the 2010 Employee, Director and Consultant Equity Incentive Plan	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
10.5#	2010 Employee Stock Purchase Plan	Registration Statement on Form S-8 (File No. 333-165230)	March 5, 2010
10.6#	Change of Control Severance Benefit Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.7#	Director Compensation Plan	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.8#	Form of Indemnification Agreement with directors and officers	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009

Number	Description	Incorporated by reference herein	
		Form	Date
10.9#	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
10.10+	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
10.11+	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
10.12+	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
10.13+	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	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
10.14.1	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
10.14.2*	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		

Number	Description	Incorporated by reference herein	
		Form	Date
10.14.3*	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		
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		

* 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 with the SEC pursuant to the confidential treatment request.

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

(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).

Exhibit 10.14.2

THIRD AMENDMENT TO LEASE

THIS THIRD AMENDMENT TO LEASE (this " Amendment ") is dated and effective as of July 1, 2010 (the " Effective Date "), by and between BMR-ROGERS STREET LLC, a Delaware limited liability company (" Landlord ," as successor-in-interest to Rogers Street, LLC (" Original Landlord ")), and IRONWOOD PHARMACEUTICALS, INC., a Delaware corporation (formerly known as Microbia, Inc.) (" Tenant ").

RECITALS

A. WHEREAS, Original Landlord and Tenant entered into that certain Lease dated as of January 12, 2007 (collectively with the First Amendment and the Second Amendment, the " Original Lease "), as amended by that certain First Amendment to Lease dated as of April 9, 2009 (the " First Amendment ") and that certain Second Amendment to Lease dated as of February 9, 2010 (the " Second Amendment "), whereby Tenant leases certain premises from Landlord at 301 Binney Street in Cambridge, Massachusetts;

B. WHEREAS, Landlord and Tenant desire to enter into this Amendment to, among other things, memorialize the size of the Additional Premises Initial Phase, the Additional Premises Initial Phase Rent Commencement Date, an appropriate adjustment to Tenant's Pro Rata Share and the Additional Premises Finish Work Allowance with respect to the Additional Premises Initial Phase, as required pursuant to Section 5 of the Second Amendment; and

C. WHEREAS, Landlord and Tenant desire to modify and amend the Original Lease only in the respects and on the conditions hereinafter stated.

AGREEMENT

NOW, THEREFORE, Landlord and Tenant, in consideration of the mutual promises contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, agree as follows:

1. Definitions . For purposes of this Amendment, capitalized terms shall have the meanings ascribed to them in the Original Lease unless otherwise defined herein.

2. Additional Premises Initial Phase . The Additional Premises Initial Phase consists of thirty-five thousand four hundred forty-four (35,444) rentable square feet on the third floor of the Building, as depicted on Exhibit A attached hereto, and includes shaft and/or mechanical space in the basement and on the first, second, third, fourth, fifth and penthouse levels of the Building. The Additional Premises Initial Phase consists of thirty thousand seven hundred fifty-eight (30,758) useable square feet of space. The Additional Premises Initial Phase Rent Commencement Date is July 1, 2010.

3. Tenant's Pro Rata Share . Effective as of the Effective Date, Tenant's Pro Rata Share shall be 37.61%.

4. Additional Premises Finish Work Allowance . The amount of the Additional Premises Finish Work Allowance allocated to the Additional Premises Initial Phase shall be One Million Nine Hundred Forty-Nine Thousand Four Hundred Twenty and 00/100 Dollars ($1,949,420).

5. Completion of Landlord's Work . The work referenced on Exhibit B to the Second Amendment was completed by Landlord on or before March 1, 2010. Tenant hereby acknowledges that it has approved and accepted such work and acknowledges that Landlord has satisfied its obligations set to complete all such work referenced in Section 10 of the Second Amendment, except for any latent defects not visually discoverable by Tenant upon a reasonably diligent inspection and which are identified in writing to Landlord on or before March 1, 2011. Landlord shall repair all such latent defects upon receipt of written notice thereof.

6. Measurement Standard . Effective as of the Effective Date, pursuant to Section 2.01(e)(ii) of the Original Lease, the rentable area of the Premises has been remeasured in accordance with the Measurement Standard and the remeasured rentable square footage of the Premises is set forth on Exhibit B attached hereto. Exhibit 2.01 (e) to the Original Lease is hereby deleted in its entirety and replaced with Exhibit B attached hereto. Landlord and Tenant acknowledge and agree that the measurements reflected in this Amendment, including Exhibit B , are the final and conclusive measurements for the Building, Premises and each Phase (except for the Additional Premises Second Phase) under the Lease. Notwithstanding anything herein to the contrary, to the extent that there is a conflict between the rentable area set forth in this Amendment and that set forth on Exhibit B hereto, the information set forth in this Amendment shall supersede. For clarification purposes, effective as of the Effective Date but not prior to such Effective Date, the measurements reflected in Sections 7, 8 and 9 and Exhibit B of this Amendment, supersede the measurements set forth in the First Amendment, including Exhibit A attached thereto.

7. Premises . Effective as of the Effective Date, the rentable square footage of the Premises (except for the Additional Premises Second Phase) in its entirety is one hundred forty-nine thousand ninety (149,090) rentable square feet. Effective as of the Effective Date, the Premises depiction attached as Exhibit C hereto supersedes that which was attached as Exhibit 1.07 to the Original Lease pursuant to Section 4 of the First Amendment.

8. Phases . The Office Space consists of nineteen thousand nine hundred twenty-three (19,923) rentable square feet on the second floor of the Building. The First Floor Space consists of eighteen thousand (18,000) rentable square feet of space on the first floor of the Building and includes shaft and/or mechanical space in the basement and on the first, second, third, fourth, fifth and penthouse levels of the Building. The First Lab Space consists of thirty-seven thousand seventy-two (37,072) rentable square feet on the second floor of the Building and includes shaft and/or mechanical space in the basement and on the first, second, third, fourth, fifth and penthouse levels of the Building. The Final Lab Space consists of thirty-eight thousand six hundred fifty-one (38,651) rentable square feet on the second floor of the Building and includes shaft and/or mechanical space on the second, third, fourth, fifth and penthouse levels of the Building.

9. Base Rent and Pro Rata Share True-Up . Effective as of the Effective Date, Base Rent for the Office Space, the First Floor Space and the First Lab Space shall be calculated based on the Measurement Standard attached hereto as Exhibit B and a credit shall be given to Tenant for overpayments of Base Rent from and after the Effective Date through the date of the October rent statement. Tenant shall receive such credit on the October rent statement. Effective as of the Effective Date, Base Rent for the Additional Premises Initial Phase shall be calculated based on the Measurement Standard attached hereto as Exhibit B and the amount of such Base Rent from and after the Effective Date through the date of the October rent statement shall also be reflected in the October rent statement. All amounts owed from and after the Effective Date through the date of the October rent statement for Tenant's Pro Rata Share of estimated (i) Operating Expenses, (ii) Taxes, and (iii) Landlord's utilities and insurance expenses that result from the increase in the Tenant's Pro Rata Share between the First Amendment and this Amendment shall also be reflected on the October rent statement.

10. Building . The rentable square footage of the Building is four hundred seventeen thousand two hundred ninety (417,290) rentable square feet.

11. Finish Work Allowance . The parties hereby agree that the Finish Work Allowance allocable to the Premises (other than the Additional Premises Initial Phase and the Additional Premises Second Phase) shall not change as a result of the revised measurements set forth in this Amendment and shall remain as set forth in Section 10 of the First Amendment.

12. Letter of Credit . The parties hereby agree that the amount of the Letter of Credit currently due shall not change as a result of the revised measurements set forth in this Amendment and shall remain as set forth in Section 11 of the First Amendment. Landlord hereby confirms that, pursuant to Section 11 of the First Amendment, Tenant has delivered to Landlord, and Landlord currently holds, a Letter of Credit in the amount of Seven Million Six Hundred Sixteen Thousand Eight Hundred Thirty-Three Dollars ($7,616,833.00).

13. Broker . Tenant and Landlord each represents and warrants to the other that it has not dealt with any broker or agent in the negotiation for or the obtaining of this Amendment and agrees to indemnify, defend and hold the other harmless from any and all cost or liability for compensation claimed by any such broker or agent employed or engaged by it or claiming to have been employed or engaged by it for such purposes.

14. Effect of Amendment . Except as modified by this Amendment, the Original Lease and all the covenants, agreements, terms, provisions and conditions thereof shall remain in full force and effect and are hereby ratified and affirmed. The covenants, agreements, terms, provisions and conditions contained in this Amendment shall bind and inure to the benefit of the parties hereto and their respective successors and, except as otherwise provided in the Original Lease, as amended hereby, their respective assigns. In the event of any conflict between the terms contained in this Amendment and the Original Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties. From and after the date hereof, the term " Lease " as used in

the Original Lease and this Amendment shall mean the Original Lease, as modified by this Amendment.

15. Miscellaneous . This Amendment becomes effective only upon execution and delivery hereof by Landlord and Tenant. The captions of the paragraphs and subparagraphs in this Amendment are inserted and included solely for convenience and shall not be considered or given any effect in construing the provisions hereof. All exhibits hereto are incorporated herein by reference.

16. Counterparts . This Amendment may be executed in one or more counterparts that, when taken together, shall constitute one original.

17. Authority . Landlord and Tenant have all necessary and proper authority, without the need for the consent of any other person or entity, other than any consents that have been obtained, to enter into and perform under this Amendment.

IN WITNESS WHEREOF, Landlord and Tenant have hereunto set their hands as of the date and year first above written, and acknowledge that they possess the requisite authority to enter into this transaction and to execute this Amendment.

LANDLORD :

BMR-ROGERS STREET LLC ,
a Delaware limited liability company

By: /s/ Kevin Simonsen
Name: Kevin Simonsen
Title: Vice President, Real Estate Counsel

TENANT :

IRONWOOD PHARMACEUTICALS, INC. ,
a Delaware corporation

By: /s/ J DeTore
Name: J DeTore
Title: VP, Finance

Exhibit 10.14.3

FOURTH AMENDMENT TO LEASE

THIS FOURTH AMENDMENT TO LEASE (this " Amendment ") is entered into as of this 3rd day of February, 2011 (the " Execution Date "), by and between BMR-ROGERS STREET LLC, a Delaware limited liability company (" Landlord ," as successor-in-interest to Rogers Street, LLC (" Original Landlord ")), and IRONWOOD PHARMACEUTICALS, INC., a Delaware corporation (formerly known as Microbia, Inc.) (" Tenant ").

RECITALS

A. WHEREAS, Original Landlord and Tenant entered into that certain Lease dated as of January 12, 2007, as amended by that certain First Amendment to Lease dated as of April 9, 2009, that certain Second Amendment to Lease dated as of February 9, 2010 (the " Second Amendment "), and that certain Third Amendment to Lease dated as of July 1, 2010 (collectively, as the same may have been otherwise amended, supplemented or modified from time to time, the " Lease "), whereby Tenant leases certain premises (the " Original Premises ") from Landlord at 301 Binney Street in Cambridge, Massachusetts (the " Building ");

B. WHEREAS, Landlord and Tenant desire to memorialize the size of the Additional Premises Second Phase, an appropriate adjustment to Tenant's Pro Rata Share and the Additional Premises Finish Work Allowance with respect to the Additional Premises Second Phase, as required pursuant to Section 6 of the Second Amendment;

C. WHEREAS, Tenant desires to lease additional premises from Landlord; and

D. WHEREAS, Landlord and Tenant desire to modify and amend the Lease only in the respects and on the conditions hereinafter stated.

AGREEMENT

NOW, THEREFORE, Landlord and Tenant, in consideration of the mutual promises contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, agree as follows:

1. Definitions . For purposes of this Amendment, capitalized terms shall have the meanings ascribed to them in the Lease unless otherwise defined herein.

2. Additional Premises Second Phase . The Additional Premises Second Phase consists of Twenty-One Thousand Five Hundred Eighty-Nine (21,589) rentable square feet on the third floor of the Building, as depicted on Exhibit A attached hereto, and includes shaft and/or mechanical space on the first, third, fourth, fifth and penthouse levels of the Building. The Additional Premises Second Phase consists of Eighteen Thousand Six Hundred Sixty-Seven (18,667) useable square feet of space. The Additional Premises Second Phase Rent Commencement Date shall be determined in accordance with the Second Amendment. Once the Additional Premises Second Phase Rent Commencement Date is determined, Landlord and Tenant shall execute a notice, as a confirmation only, setting forth the Additional Premises Second Phase Rent Commencement Date.

3. Tenant's Pro Rata Share . Effective as of the Additional Premises Second Phase Rent Commencement Date, Tenant's Pro Rata Share shall be 43.05%.

4. Additional Premises Finish Work Allowance . The amount of the Additional Premises Finish Work Allowance allocated to the Additional Premises Second Phase shall be One Million One Hundred Eighty-Seven Thousand Three Hundred Ninety-Five and 00/100 Dollars ($1,187,395).

5. Rights of Building Tenants in Additional Premises Third Phase . As of the Execution Date, Landlord represents and warrants that no other person or entity has any enforceable rights with respect to the leasing or occupancy of the Additional Premises Third Phase (as defined below) as a tenant.

6. Additional Premises Third Phase . As of the Execution Date, Landlord hereby leases to Tenant approximately 23,307 contiguous rentable square feet of additional premises located on the third floor of the Building, as depicted on Exhibit B attached hereto (the " Additional Premises Third Phase "). The actual rentable square footage and actual useable square footage of the Additional Premises Third Phase will be adjusted and mutually agreed to between Landlord and Tenant based upon the actual constructed rentable square footage and actual constructed usable square footage determined in accordance with the Measurement Standard.

7. Term Commencement Date. The term with respect to the Additional Premises Third Phase shall commence upon the Execution Date and shall terminate, subject to any extension options granted pursuant to the Lease, simultaneous with the expiration of the Term. From and after the Execution Date, the term " Premises ," as used in the Lease, shall mean the Original Premises plus the Additional Premises Third Phase and, except as otherwise provided herein, all provisions of the Lease, including (without limitation) the option to extend the Term as set forth in Section 3.03 of the Lease, shall apply to such Premises.

8. Additional Premises Third Phase Rent Commencement Date. Rent with respect to the Additional Premises Third Phase shall commence upon the earlier of (a) February 15, 2012 and (b) substantial completion of the Finish Work with respect to the Additional Premises Third Phase and Tenant's occupancy thereof for the conduct of its business (the " Additional Premises Third Phase Rent Commencement Date "). Following the Additional Premises Third Phase Rent Commencement Date, Landlord and Tenant shall enter into an amendment to the Lease, as amended hereby, memorializing the actual useable square footage and the actual rentable square footage of the Additional Premises Third Phase, the Additional Premises Third Phase Rent Commencement Date, an appropriate adjustment to Tenant's Pro Rata Share and the Additional Premises Third Phase Finish Work Allowance (as defined below) with respect thereto.

9. Tenant's Pro Rata Share . Tenant's Pro Rata Share shall be increased on the Additional Premises Third Phase Rent Commencement Date to include the actual rentable square footage of the Additional Premises Third Phase in the calculation of Tenant's Pro Rata Share.

10. Base Rent/Annual Adjustments : The initial Base Rent for the Additional Premises Third Phase shall be $42.50 per rentable square foot per year commencing on the Additional Premises Third Phase Rent Commencement Date. Base Rent for the Additional Premises Third

Phase shall be increased during the initial Term on each annual anniversary of the Additional Premises Initial Phase Rent Commencement Date beginning with the first such annual anniversary after the Additional Premises Third Phase Rent Commencement Date by fifty cents ($0.50) per rentable square foot per year. Base Rent for the Additional Premises Third Phase shall not be increased on the Interim Date as provided in Section 1.16 of the Lease. Base Rent for the Additional Premises Third Phase for any Extension Term or Terms shall be determined in accordance with Section 1.16 of the Lease. Commencing on the Additional Premises Third Phase Rent Commencement Date, the Base Rent for the Additional Premises Third Phase shall be paid in equal monthly installments in advance on the first day of each and every calendar month during the Term as set forth in Section 4.01 of the Lease. To the extent the Additional Premises Third Phase Rent Commencement Date occurs before the actual rentable square footage of such phase is determined in accordance with Section 6 of this Amendment, the parties hereto agree to true up all payments of Rent for such phase made prior to the date such actual square footage is determined within thirty (30) days of the date such actual rentable square footage is determined. The parties will also make any appropriate adjustments and true ups for payments of the Additional Premises Third Phase Finish Work Allowance for such phase within thirty (30) days of the date such actual rentable square footage is determined.

11. Finish Work Allowance . Landlord shall provide to Tenant an additional Finish Work Allowance of Forty Dollars ($40.00) per rentable square foot of Additional Premises Third Phase (the " Additional Premises Third Phase Finish Work Allowance ") in order to fund, pursuant to the terms and procedures set forth in Sections 10.04(c) and 10.05 of the Lease (including, without limitation, Tenant's rights under the last paragraph of Section 10.04(c)-2 of Exhibit 10.04(c)), the design and construction by Tenant of the Finish Work with respect to the Additional Premises Third Phase; provided that, notwithstanding anything in Sections 10.04(c) or 10.05 of the Lease to the contrary, (i) Tenant shall have no obligation to pay or reimburse Landlord for any costs or expenses to review or supervise the construction of the Finish Work with respect to the Additional Premises Third Phase, to review the Construction Documents related thereto or to assist with government filings and (ii) Landlord's approval of the Construction Documents related to the Finish Work with respect to the Additional Premises Third Phase shall not be unreasonably withheld, conditioned or delayed. The Additional Premises Third Phase Finish Work Allowance shall be determined based on the actual constructed rentable square footage of the Additional Premises Third Phase. The Additional Premises Third Phase Finish Work Allowance must be utilized for Finish Work constructed within the Additional Premises Third Phase. Tenant will not be required to remove the Finish Work constructed within the Additional Premises Third Phase at the end of the Term.

12. Condition of Premises . Tenant acknowledges that, other than as set forth below or in the Lease, neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of the Additional Premises Third Phase, the Building or the Property, or with respect to the suitability of the Additional Premises Third Phase, the Building or the Property for the conduct of Tenant's business. Tenant acknowledges that (a) it is fully familiar with the condition of the Additional Premises Third Phase and agrees to take the same in its condition "as is" as of the Execution Date and (b) Landlord shall have no obligation to alter, repair or otherwise prepare the Additional Premises Third Phase for Tenant's occupancy or to pay for or construct any improvements to the Additional Premises Third Phase, except that Landlord shall provide the Additional Premises Third Phase Finish Work Allowance as described in Section 11 above.

Landlord hereby represents and warrants that, as of the Execution Date, the common area of the Building and the Additional Premises Third Phase are in compliance with all Legal Requirements.

13. Parking . In addition to any existing Tenant rights to parking spaces under the Lease, commencing on the date requested by Tenant, but in any event, no later than the Additional Premises Third Phase Rent Commencement Date, Landlord shall provide Tenant with 1.0 parking spaces per 1,000 useable square feet (exclusive of any mechanical space) of Additional Premises Third Phase at Landlord's then-current prevailing monthly rate for parking spaces. Tenant's use of the parking spaces provided hereunder and Tenant's rights with respect thereto (including (without limitation) limitations on increases in the prevailing monthly rate for parking spaces) shall otherwise be in accordance with the terms of Section 2.01(d) of the Lease.

14. Broker . Tenant represents and warrants that it has had no dealings with any real estate broker or agent in connection with the negotiation of this Amendment other than CB Richard Ellis, Inc. (" Broker "), and that it knows of no other real estate broker or agent that is or might be entitled to a commission in connection with the representation of Tenant in connection with this Amendment. Landlord shall compensate Broker in relation to this Amendment pursuant to a separate agreement between Landlord and Broker.

14.1 Tenant represents and warrants that no broker or agent has made any representation or warranty relied upon by Tenant in Tenant's decision to enter into this Amendment, other than as contained in this Amendment.

14.2 Tenant acknowledges and agrees that the employment of brokers by Landlord is for the purpose of solicitation of offers of leases from prospective tenants and that no authority is granted to any broker to furnish any representation (written or oral) or warranty from Landlord unless expressly contained within this Amendment. Landlord is executing this Amendment in reliance upon Tenant's representations, warranties and agreements contained within Section 14 , Section 14.1 and this Section 14.2 .

14.3 Tenant agrees to indemnify, save, defend and hold Landlord harmless from any and all cost or liability for compensation claimed by any other broker or agent, other than Broker, employed or engaged by Tenant or claiming to have been employed or engaged by Tenant.

14.4 Landlord shall pay any commission, fee or other compensation due to any Landlord broker(s) in connection with this Amendment. Landlord agrees to indemnify, save, defend and hold Tenant harmless from any and all cost or liability for compensation claimed by any broker or agent employed or engaged by Landlord or claiming to have been employed or engaged by Landlord.

15. Effect of Amendment . Except as modified by this Amendment, the Lease and all the covenants, agreements, terms, provisions and conditions thereof shall remain in full force and effect and are hereby ratified and affirmed. The covenants, agreements, terms, provisions and conditions contained in this Amendment shall bind and inure to the benefit of the parties hereto and their respective successors and, except as otherwise provided in the Lease, as amended hereby, their respective assigns. In the event of any conflict between the terms contained in this Amendment and

the Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties. From and after the Execution Date, the term " Lease " as used in the Lease shall mean the Lease, as modified by this Amendment.

16. Miscellaneous . This Amendment becomes effective only upon execution and delivery hereof by Landlord and Tenant. The captions of the paragraphs and subparagraphs in this Amendment are inserted and included solely for convenience and shall not be considered or given any effect in construing the provisions hereof. All exhibits hereto are incorporated herein by reference.

17. Counterparts . This Amendment may be executed in one or more counterparts that, when taken together, shall constitute one original.

18. Authority . Landlord and Tenant have all necessary and proper authority, without the need for the consent of any other person or entity, other than any consents that have been obtained, to enter into and perform under this Amendment.

IN WITNESS WHEREOF, Landlord and Tenant have hereunto set their hands as of the date and year first above written, and acknowledge that they possess the requisite authority to enter into this transaction and to execute this Amendment.

LANDLORD :

BMR-ROGERS STREET LLC ,
a Delaware limited liability company

By: /s/ John Bonanno
Name: John Bonanno
Title: Senior Vice President, Leasing & Development

TENANT :

IRONWOOD PHARMACEUTICALS, INC. ,
a Delaware corporation

By: /s/ J DeTore
Name: J DeTore
Title: VP, Finance

Exhibit 21.1

List of Registrant's Subsidiaries

Ironwood Pharmaceuticals Securities Corporation, incorporated in Massachusetts, a wholly owned subsidiary.

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EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Form S-8 Nos. 333-165227, 333-165228, 333-165229, 333-165230, and 333-165231) of our report dated March 30, 2011, with respect to the consolidated financial statements of Ironwood Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2010.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 30, 2011

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EXHIBIT 23.1

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 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: March 30, 2011

/s/ PETER M. HECHT

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

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EXHIBIT 31.1

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 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: March 30, 2011

/s/ MICHAEL J. HIGGINS

Michael J. Higgins
Chief Financial Officer

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EXHIBIT 31.2

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, 2010 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
March 30, 2011

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.

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EXHIBIT 32.1

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, 2010 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
March 30, 2011

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.

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EXHIBIT 32.2