IRONWOOD PHARMACEUTICALS INC
Form 424B2
May 22, 2013

Use these links to rapidly review the document
Table of Contents
TABLE OF CONTENTS

Filed Pursuant to Rule 424(b)(2)
Registration No. 333-179430

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per share	Proposed maximum aggregate offering price	Amount of registration fee[(1)]
Class A common stock, $0.001 par value per share, of Ironwood Pharmaceuticals, Inc.	12,075,000	$13.00	$156,975,000	$21,411.39

(1) The filing fee is calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended.

Table of Contents

Prospectus Supplement (to Prospectus Dated February 8, 2012)

10,500,000 Shares

Ironwood Pharmaceuticals, Inc.

Class A Common Stock

We are offering 10,500,000 shares of our Class A common stock. Our Class A common stock is listed on The NASDAQ Global Select Market under the symbol "IRWD." The last reported sale price of our Class A common stock on May 21, 2013 was $13.49 per share.

We have granted the underwriters a 30-day option to purchase up to an additional 1,575,000 shares of Class A common stock at the public offering price less the underwriting discount.

Investing in our Class A common stock involves risks. See "Risk Factors" beginning on page S-12 of this prospectus supplement and "Part II Item 1A Risk Factors" beginning on page 28 of our Quarterly Report on Form 10-Q for the period ended March 31, 2013, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, as that disclosure may be updated by subsequent periodic reports.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	$ 13.00	$ 136,500,000
Underwriting discounts and commissions	$ 0.6825	$ 7,166,250
Proceeds, before expenses, to us	$ 12.3175	$ 129,333,750

The underwriters expect to deliver the Class A common stock on May 24, 2013 only in book-entry form through the facilities of The Depository Trust Company.

Joint Book-Running Managers

J.P. Morgan **BofA Merrill Lynch** **Morgan Stanley**

Co-Managers

Cowen and Company	**Ladenburg Thalmann & Co. Inc.**	**Mizuho Securities**

The date of this prospectus supplement is May 21, 2013.

Table of Contents

PROSPECTUS SUPPLEMENT

PROSPECTUS

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our Class A common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus as well as additional information described under "Where You Can Find More Information" in this prospectus supplement before making an investment decision.

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus supplement or an offer to sell or the solicitation of any offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus supplement and the accompanying prospectus, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

This prospectus supplement may add to, update or change the information in the accompanying prospectus. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus, this prospectus supplement will apply and will supersede that information in the accompanying prospectus.

We use various trademarks and trade names in our business, including without limitation "Ironwood," "Ironwood Pharmaceuticals," "LINZESS®" and "Constella®." This prospectus supplement also contains trademarks and trade names of other businesses that are the property of their respective holders.

Unless otherwise indicated or unless the context requires otherwise, all references in this prospectus supplement to "Ironwood," "we," "us" and "our" refer to Ironwood Pharmaceuticals, Inc.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information incorporated by reference in this prospectus supplement include forward-looking statements. All statements contained in this prospectus supplement and the information incorporated by reference other than statements of historical fact are forward-looking statements. Forward-looking statements include statements regarding our future financial position, business strategy, budgets, projected costs, plans and objectives of management for future operations. The words "may," "continue," "estimate," "intend," "plan," "will," "believe," "project," "expect," "seek," "anticipate" and similar expressions may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, among other things, statements about:

- the market potential for LINZESS® (linaclotide) in the U.S. and Constella® (linaclotide) in the E.U.;
- the timing, investment and associated activities involved in commercializing linaclotide by us and Forest Laboratories, Inc. in the U.S. and by our partners in other countries in the world;
- the timing and execution of the launch of Constella® in the E.U.;
- the ability of our partners and third party manufacturers to manufacture and distribute sufficient amounts of linaclotide on a commercial scale;
- our expectations regarding U.S. and foreign regulatory requirements, including our post-approval, nonclinical and clinical post-marketing plan with the FDA to understand linaclotide's efficacy and safety in pediatric patients;
- our partners' ability to obtain foreign regulatory approval of linaclotide and the ability of all of our product candidates to meet existing or future regulatory standards;
- the safety profile and related adverse events of linaclotide;
- the ability of our partners to perform their obligations under our collaboration and license agreements with them;
- the therapeutic benefits and effectiveness of our product candidates;
- our plans with respect to the development, manufacture or sale of our product candidates, as well as the in-licensing or acquisition of externally discovered programs;
- our expectations as to future financial performance, expense levels, capital raising and liquidity sources;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with our products and product candidates;

the status of government regulation in the life sciences industry, particularly with respect to health care reform;

trends and challenges in our potential markets;

our ability to attract and motivate key personnel; and

other factors discussed elsewhere in this prospectus supplement or information incorporated herein.

Any or all of our forward-looking statements in this prospectus supplement or the information incorporated by reference 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 prospectus

Table of Contents

supplement and "Part II, Item 1A Risk Factors" in our most recent Quarterly Report on Form 10-Q. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus supplement or incorporated herein by reference 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 prospectus supplement or the date of the document incorporated by reference in this prospectus supplement. 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 prospectus supplement.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information you should consider before investing in our Class A common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our Class A common stock discussed under "Risk Factors" beginning on page S-12 of this prospectus supplement and the consolidated financial statements and notes to those consolidated financial statements incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Our Company

We are an entrepreneurial pharmaceutical company focused on the discovery, development and commercialization of medicines that improve patients' lives. We have one marketed product, linaclotide, which is available in the United States, or U.S., under the trademarked name LINZESS and was recently approved in the European Union, or E.U, under the trademarked name Constella. Linaclotide is also being developed in other parts of the world by certain of our partners. We are exploring development opportunities to strengthen the clinical profile of LINZESS within its indicated population and to expand the product label for additional patient populations and indications, as well as exploring the potential for linaclotide-based combination products. In addition to exploring additional development opportunities, we also have a pipeline of early development candidates and discovery research programs in multiple therapeutic areas.

Linaclotide

Linaclotide provides patients and healthcare practitioners with a new therapy for irritable bowel syndrome with constipation, or IBS-C, and chronic idiopathic constipation, or CIC, 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.

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

In November 2012, the European Commission granted marketing authorization to Constella for the symptomatic treatment of moderate to severe IBS-C in adults. Constella is the first and only drug approved in the E.U. for IBS-C. Our European partner, Almirall S.A., or Almirall, has exclusive marketing rights for Constella in Europe (including the Commonwealth of Independent States and Turkey).

Beyond our efforts in the U.S. and Europe, we and our partners continue to advance linaclotide in other parts of the world. In October 2012, Astellas Pharma Inc., or Astellas, our partner in Japan, initiated a double-blind, placebo-controlled, dose-ranging Phase 2 clinical trial of linaclotide in more than 500 Japanese adult patients with IBS-C. In October 2012, we entered into a collaboration agreement with AstraZeneca AB, or AstraZeneca, to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau. In May 2012, we submitted a Clinical Trial Application, or CTA, to China's State Food and Drug Administration for a Phase 3 trial of linaclotide in patients with IBS-C. The CTA has been approved. We continue to assess alternatives to bring linaclotide to IBS-C and CIC sufferers in the parts of the world outside of our partnered territories.

Table of Contents

We are also exploring development opportunities to strengthen the clinical profile of LINZESS within its indicated population and to expand the product label for additional patient populations and indications, and we are exploring the potential for linaclotide-based combination products. As part of this strategy, we and Forest initiated a Phase 3b clinical trial to further characterize the effect of linaclotide on abdominal symptoms in patients with CIC.

Upon FDA-approval of LINZESS in the U.S., we received five years of exclusivity under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which period of exclusivity ends on August 30, 2017. In addition, LINZESS is covered by a U.S. composition of matter patent that expires in 2024, subject to possible patent term extension to 2026. Linaclotide is also covered by E.U. and Japanese composition of matter patents, both of which expire in 2024, subject to possible patent term extension.

Linaclotide Partners

We have pursued a partnering strategy for commercializing linaclotide that has enabled us to retain significant control over linaclotide's development and commercialization worldwide, share the costs with collaborators whose capabilities complement ours, and retain a significant portion of linaclotide's future long-term value. As of December 31, 2012, licensing fees, milestone payments, related equity investments and development, selling and marketing costs received from our linaclotide partners totaled approximately $448.0 million.

In September 2007, we entered into a collaboration agreement with Forest to develop and commercialize linaclotide in North America. Under the terms of the collaboration agreement, we and Forest are jointly and equally funding the development and commercialization of LINZESS in the U.S., with equal share of any profits or losses. Additionally, we granted Forest exclusive rights to develop and commercialize linaclotide in Canada and Mexico in which we receive royalties in the mid-teens on net sales in those countries. In September 2012, Forest sublicensed its commercialization rights in Mexico to Almirall. If linaclotide is successfully commercialized in the U.S., total licensing, milestone payments and related equity investments to us under the Forest collaboration agreement could total up to $330 million, including the $205 million that Forest has already paid to us in license fees and development-related milestones and the $25 million of our capital stock that Forest has already purchased.

In April 2009, we entered into a license agreement with Almirall to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States and Turkey). If linaclotide is successfully commercialized in the Almirall territory, total licensing, milestone payments and related equity investments to us could total up to $95 million, including the $57 million, net of foreign withholding taxes, that Almirall has already paid to us in development-related milestones and the $15 million of our capital stock that Almirall has already purchased. Almirall will pay us gross royalties which escalate based on sales volume in the Almirall territory, beginning in the mid-twenties, less the transfer price paid for the active pharmaceutical ingredient. We are currently in active discussions with Almirall regarding the various financial incentives and structure of our current collaboration, and pending the results of these discussions, this could result in a rebalance of certain short term financial compensation, including the five $4-million launch milestones, in exchange for additional new sales-based incentives and a more favorable royalty structure at certain sales thresholds.

Under our license agreement with Astellas dated November 2009, as amended in March 2013, Astellas, with our cooperation, is to develop and commercialize linaclotide in Japan. If linaclotide is successfully developed and commercialized in Japan, total licensing and milestone payments to us could total up to $75 million, including the $30 million that has already been paid to us. If Astellas receives approval to market and sell linaclotide, Astellas will pay us gross royalties which escalate based on sales

Table of Contents

volume in Japan, beginning in the low-twenties, less the transfer price paid for the active pharmaceutical ingredient.

In October 2012, we entered into a collaboration with AstraZeneca to co-develop and co-commercialize linaclotide in China. Under the terms of the agreement, we and AstraZeneca are jointly funding the development and commercialization of linaclotide in China, Hong Kong and Macau, with AstraZeneca receiving 55% of the net profits or incurring 55% of the net losses until a certain specified commercial milestone is achieved, and profits or losses will be shared equally thereafter. If linaclotide is successfully developed and commercialized in China, total licensing and milestone payments to us under the collaboration agreement could total up to $150 million, including the $25 million that AstraZeneca has already paid to us. As part of the collaboration, in February 2013, Ironwood's sales force began promoting AstraZeneca's NEXIUM® (esomeprazole magnesium) in the U.S.

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

Pipeline

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. In addition to exploring further linaclotide development opportunities, our drugmaking processes have generated a pipeline of early development candidates and discovery research programs in multiple therapeutic areas, including gastrointestinal disease, central nervous system, or CNS, disorders, allergic conditions and cardiovascular disease.

We are also actively engaged in evaluating and licensing rights to externally discovered drug candidates at all stages of development. In evaluating potential assets, we apply the same investment criteria whether the assets are internally or externally discovered. Linaclotide is our only product or product candidate that has demonstrated clinical proof of concept.

In order to successfully grow our business, we will need to overcome the enormous challenges inherent in the pharmaceutical product development model. Developing a novel therapeutic agent can take a decade or more and cost hundreds of millions of dollars, and most drug candidates fail to reach the market profitably. We recognize that most companies undertaking this endeavor fail, yet despite the significant risks and our own experiences with multiple failed drug candidates, we are enthusiastic and passionate about our mission to deliver life-changing 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 and generating substantial returns for our stockholders, we plan to reinvest a portion of our future cash flows into our research and development efforts in order to accelerate and enhance our ability to bring new products to market.

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

Owner-related Business Principles

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

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

Each of our employees also has equity in the business, aligning their interests with their fellow stockholders. As employees and co-owners of Ironwood, our management and employee team seek to

Table of Contents

effectively allocate scarce stockholder capital to maximize the average annual growth of per share value.

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

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

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

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

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

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

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

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

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

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

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

Table of Contents

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

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

Our global operations and commercial teams take a similar approach to capital allocation and decision-making. By ensuring redundancy at each critical node of the linaclotide global supply chain, our global operations team is mitigating against a fundamental risk inherent with pharmaceuticals unanticipated shortages of commercial product. Likewise, we have established a commercial organization dedicated to bringing innovative, highly-valued healthcare solutions to all of our customers. Our commercial organization works closely and methodically with our global commercialization partners, striving to maximize linaclotide's commercial potential through focused efforts aimed at educating patients, payors and healthcare providers.

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

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

If and when we reach profitability, we do not intend to issue quarterly or annual earnings guidance, however we plan to 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:

attracting and incentivizing a team with a singular passion for creating, developing and commercializing medicines that can make a significant difference in patients' lives;

solidifying and expanding our position as the leader in the field of GC-C agonists;

successfully and profitably commercializing LINZESS in collaboration with Forest in the U.S.;

supporting our global partners to commercialize linaclotide outside of the U.S.;

harvesting the maximum value of linaclotide outside of our currently partnered territories;

Table of Contents

exploring development opportunities to strengthen the clinical profile of LINZESS within its indicated population;

seeking ways to expand the product label for LINZESS in additional patient populations and indications, as well as the potential for linaclotide-based combination products;

investing in our pipeline of novel product candidates and evaluating candidates outside of the company for in-licensing or acquisition opportunities;

maximizing the commercial potential of our drugs and playing an active role in their commercialization or find partners who share our vision, values, culture and processes; and

executing our strategy with our stockholders' long-term interests in mind by seeking to maximize long-term per share cash flows.

Risk Factors

For a discussion of the factors you should carefully consider before deciding to purchase any shares, please review "Part II Item 1A Risk Factors" beginning on page 28 of our Quarterly Report on Form 10-Q for the period ended March 31, 2013, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, as that disclosure may be updated by subsequent periodic reports, as well as "Risk Factors" in this prospectus supplement.

Our Principal Executive Offices

The address of our principal executive offices is 301 Binney Street, Cambridge, Massachusetts 02142, and the telephone number at our principal executive offices is (617) 621-7722.

Table of Contents

The Offering

The following summary is qualified in its entirety by reference to the more detailed information appearing elsewhere in this prospectus supplement and the accompanying prospectus. For more information concerning our common stock, see the "Description of Class A Common Stock" section in the accompanying prospectus.

Issuer	Ironwood Pharmaceuticals, Inc.
NASDAQ Global Select Market Symbol	IRWD
Class A Common Stock Offered	10,500,000 shares
Class A Common Stock to be Outstanding After this Offering[(1)]	92,933,724 shares
Use of Proceeds	We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and estimated offering expenses, will be approximately $129.1 million (or approximately $148.5 million if the underwriters exercise in full their option to purchase additional shares), based on a public offering price of $13.00 per share. We intend to use the net proceeds from this offering to support the commercial launch of LINZESS in the U.S. and to fund linaclotide development opportunities to strengthen the clinical profile of LINZESS and expand the product label for additional populations and indications, in addition to general corporate purposes. For more information, see "Use of Proceeds."
Transfer Agent and Registrar	Computershare Trust Company, N.A.

(1) The number of shares of our Class A common stock outstanding after this offering assumes no exercise of the underwriters' option to purchase an additional 1,575,000 shares and is based on 82,433,724 shares outstanding as of May 17, 2013, which excludes:

- options exercisable into 20,746,455 shares of common stock outstanding as of May 17, 2013 at a weighted average exercise price of $8.57 per share; and
- 8,210,772 shares of our common stock reserved as of May 17, 2013 for future issuance under compensation plans.

Table of Contents

RISK FACTORS

Investing in our Class A common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as the other information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference, before making an investment decision. In addition, you should carefully consider, among other things, the matters discussed under "Part II Item 1A Risk Factors" beginning on page 28 of our Quarterly Report on Form 10-Q for the period ended March 31, 2013, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, as that disclosure may be updated by subsequent periodic reports, as well as other documents that we file with the SEC that are incorporated by reference. The risks and uncertainties described in the documents incorporated by reference and those described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. If any of those risks actually occurs, our business, financial condition and results of operations would suffer. In that event, the market price of our Class A common stock could decline, and you may lose all or part of your investment in our Class A common stock. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements. See "Special Note Regarding Forward-Looking Statements."

Risks Related to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return, if any.

Our management will have broad discretion over the use of proceeds from this offering. The net proceeds from this offering will be used to support the commercial launch of LINZESS in the U.S. and to fund linaclotide development opportunities to strengthen the clinical profile of LINZESS and expand the product label for additional populations and indications, in addition to general corporate purposes. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or market value. Until the net proceeds are used, they may be placed in investments that do not produce significant income or investments that lose value.

Investors in this offering will experience immediate dilution in the book value per share of the Class A common stock they purchase.

Because the price per share of our Class A common stock being offered is substantially higher than the book value per share of our common stock (consisting of our Class A common stock and our Class B common stock, assuming a conversion of all Class B common stock to Class A common stock), you will suffer substantial dilution in the net tangible book value of the Class A common stock you purchase in this offering. After giving effect to the sale of 10,500,000 shares of Class A common stock in this offering, and based on a public offering price of $13.00 per share and net tangible book value per share of our common stock (consisting of our Class A common stock and our Class B common stock, assuming a conversion of all Class B common stock to Class A common stock) of $0.48 as of March 31, 2013, if you purchase shares in this offering, you will suffer immediate and substantial dilution of $11.48 per share in the net tangible book value of the Class A common stock purchased.

Investors in this offering may experience future dilution.

In order to raise additional capital, we may in the future offer additional shares of our Class A common stock or other securities convertible into, or exchangeable for, our Class A common stock at prices that may not be the same as the price per share in this offering. We have an effective shelf

Table of Contents

registration statement from which additional shares of Class A common stock can be offered. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering. If the price per share at which we sell additional shares of our Class A common stock or related securities in future transactions is less than the price per share in this offering, investors who purchase our Class A common stock in this offering will suffer a dilution in their investment.

Future sales of our Class A common stock may depress our stock price.

Immediately after this offering, we will have outstanding 92,933,724 shares of Class A common stock and 26,430,272 shares of Class B common stock, based on the number of outstanding shares of Class A common stock and Class B common stock as of May 17, 2013 and assuming no exercise of the underwriters' option to purchase an additional 1,575,000 shares. The shares of Class A common stock that we are selling in connection with this offering may be resold in the public market immediately. We, our directors, certain entities affiliated with our directors, and our executive officers have agreed not to dispose of or hedge any Class A common stock or securities convertible into or exchangeable for shares of Class A common stock during the period from the date of this prospectus supplement continuing through the date 60 days after the date of this prospectus supplement, subject to certain exceptions. The representatives have agreed on behalf of the underwriters that the following transactions, among others, are permissible during the 60-day restricted period: (i) sales pursuant to a trading plan established to provide an affirmative defense pursuant to Rule 10b5-1 that has been disclosed to the representatives of the underwriters prior to or in connection with the execution of lock-up agreements entered into in connection with this offering and (ii) distributions of up to 2,000,000 shares in the aggregate during the 60-day restricted period where the distributee is a limited partner of a signatory of a lock-up agreement and such distributee need not sign a lock-up agreement in connection with such distribution. The representatives of the underwriters may release a holder from restrictions on any such shares provided for in the lock-up agreements under certain circumstances, however, all other holders must be provided with a proportional release except if such a release or releases exceed 100,000 shares in the aggregate or 20,000 shares to an individual holder or if such release occurs in connection with circumstances that the representatives deem in their sole judgment to constitute an emergency or hardship. See "Underwriting."

We have never paid dividends on our capital stock, and because we do not anticipate paying any cash dividends in the foreseeable future, capital appreciation, if any, of our Class A common stock will be your sole source of gain on an investment in our Class A common stock.

We have paid no cash dividends on any of our classes of capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not anticipate paying any cash dividends on our common stock in the foreseeable future. As a result, capital appreciation, if any, of our Class A common stock will be your sole source of gain for the foreseeable future.

Table of Contents

USE OF PROCEEDS

The net proceeds from the sale of the common stock offered hereby are estimated to be approximately $129.1 million (approximately $148.5 million if the underwriters for this common stock offering exercise in full their option to purchase 1,575,000 additional shares of common stock), based on a public offering price of $13.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses.

We intend to use the net proceeds from this common stock offering to support the commercial launch of LINZESS in the U.S. and to fund linaclotide development opportunities to strengthen the clinical profile of LINZESS and expand the product label for additional populations and indications, in addition to general corporate purposes. Pending these uses, we intend to invest the net proceeds of this Class A common stock offering in interest-bearing investment-grade securities.

The foregoing represents our intentions based upon our present plans and business conditions. The occurrence of unforeseen events or changed business conditions, however, could result in the application of the proceeds from this Class A common stock offering in a manner other than as described in this prospectus supplement.

PRICE RANGE OF CLASS A COMMON STOCK

Our Class A common stock is listed on The NASDAQ Global Select Market and trades under the symbol "IRWD." The following table sets forth, for the quarterly periods indicated, the high and low sale price per share of the Class A common stock as reported on The NASDAQ Global Select Market:

	High	Low
Year ended December 31, 2011		
First Quarter	$ 14.39	$ 10.17
Second Quarter	16.50	13.32
Third Quarter	16.49	10.18
Fourth Quarter	14.35	9.97
Year ended December 31, 2012		
First Quarter	$ 15.92	$ 10.65
Second Quarter	15.00	11.24
Third Quarter	14.36	11.29
Fourth Quarter	13.70	10.01
Year ended December 31, 2013		
First Quarter	$ 19.67	$ 11.11
Second Quarter (through May 21, 2013)	18.38	13.16

On May 21, 2013, the last reported sale price of our Class A common stock on the NASDAQ Global Select Market was $13.49 per share. On May 17, 2013, we had 43 holders of record of our Class A common stock.

DIVIDEND POLICY

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.

Table of Contents

WAIVER OF CERTAIN REGISTRATION RIGHTS BY STOCKHOLDERS

On April 30, 2013, the holders of the majority of the registrable securities under the investors' rights agreement entered into an agreement to waive any registration rights and notice rights held by stockholders party to the investors' rights agreement with respect to offerings of our Class A common stock under the shelf registration statement we filed with the SEC on February 8, 2012. Except as modified by this waiver, all other rights under the investors' rights agreement remain the same and are described in the accompanying prospectus. See "Description of Class A Common Stock Registration Rights" in the accompanying prospectus.

SUPPLEMENTAL U.S. FEDERAL TAX CONSIDERATIONS

The following discussion supersedes in its entirety the discussions under the headings "Additional withholding and information reporting requirements" and "Backup Withholding and Information Reporting" beginning on page 14 in the accompanying prospectus. This section should be read together with the remainder of the discussion under the heading "Material U.S. Federal Tax Considerations for Non-U.S. Holders of Common Stock" beginning on page 12 in the accompanying prospectus.

Backup withholding and information reporting

Generally, we must report annually to the Internal Revenue Service and to each Non-U.S. Holder certain information including the Non-U.S. Holder's name, address and taxpayer identification number, the aggregate amount of distributions on our Class A common stock paid to that Non-U.S. Holder during the calendar year and the amount of tax withheld, if any.

Backup withholding tax is imposed on dividends and certain other types of payments to certain U.S. persons (currently at a rate of 28%). In general, backup withholding tax will not apply to payments of dividends on common stock or proceeds from the sale of common stock payable to a Non-U.S. Holder if the certification described under in "Material U.S. Federal Tax Considerations for Non-U.S. Holders of Common Stock Distributions on Our Common Stock" in the accompanying prospectus is duly provided by such Non-U.S. Holder or the Non-U.S. Holder otherwise establishes an exemption, provided that the payor does not have actual knowledge or reason to know that the Non-U.S. Holder is a U.S. person or that the conditions of any claimed exemption are not satisfied. Certain information reporting may still apply to distributions even if an exemption from backup withholding is established. Copies of any information returns reporting the distributions to a Non-U.S. Holder and any withholding also may be made available to the tax authorities in the country in which a Non-U.S. Holder resides under the provisions of an applicable income tax treaty.

Backup withholding is not an additional tax and any amounts withheld under the backup withholding tax rules from a payment to a Non-U.S. Holder will be allowed as a refund or a credit against such Non-U.S. Holder's U.S. federal income tax liability, provided that the requisite procedures are followed.

Non-U.S. Holders are urged to consult their own tax advisors regarding their particular circumstances and the availability of and procedure for obtaining an exemption from backup withholding.

Additional withholding and information reporting requirements

Legislation commonly referred to as the Foreign Accounts Tax Compliance Act or "FATCA" will impose withholding at a rate of 30% on payments to certain foreign entities (including financial intermediaries), including dividends on and the gross proceeds from dispositions of U.S. common stock, unless various U.S. information reporting and due diligence requirements that are different from, and in addition to, the certification requirements described under "Distributions on Our Common Stock"

Table of Contents

beginning on page 12 of the accompanying prospectus have been satisfied (generally relating to ownership by U.S. persons of interests in or accounts with those entities). Under the recently promulgated final regulations, these withholding rules apply to payments of dividends on U.S. common stock beginning January 1, 2014, and to gross proceeds from dispositions of U.S. common stock beginning January 1, 2017. Non-U.S. Holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our Class A common stock.

Table of Contents

DILUTION

If you invest in our Class A common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock (consisting of our Class A common stock and our Class B common stock, assuming a conversion of all Class B common stock to Class A common stock) after this offering. Our net tangible book value as of March 31, 2013 was $51.7 million, or $0.48 per share of our Class A common stock.

After giving effect to the sale by us of 10,500,000 shares of our Class A common stock in this offering at a public offering price of $13.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of March 31, 2013 would have been approximately $180.7 million, or $1.52 per share of our common stock (consisting of our Class A common stock and our Class B common stock, assuming a conversion of all Class B common stock to Class A common stock). This amount represents an immediate increase in our pro forma net tangible book value of $1.04 per share to our existing stockholders and an immediate dilution in our pro forma net tangible book value of $11.48 per share to new investors purchasing shares of our Class A common stock in this offering at the public offering price.

The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 13.00
Historical net tangible book value per share as of March 31, 2013	$ 0.48	
Increase per share attributable to this offering	1.04	
Pro forma net tangible book value per share after this offering		$ 1.52
Dilution per share to new investors		$ 11.48

If the underwriters exercise their option to purchase additional shares in full, the pro forma as adjusted net tangible book value will increase to $1.66 per share, representing an immediate increase to existing stockholders of $1.18 per share and an immediate dilution of $11.34 per share to new investors.

In the discussion and table above, we assume no exercise of outstanding options. As of March 31, 2013, there were 82,236,205 shares of our Class A common stock outstanding and 26,479,272 shares of our Class B common stock outstanding. These amounts exclude:

- options exercisable into 20,838,549 shares of common stock outstanding as of March 31, 2013 at a weighted average exercise price of $8.53 per share; and
- 8,267,197 shares of our common stock reserved as of March 31, 2013 for future issuance under compensation plans.

To the extent that any of these options are exercised, there will be further dilution per share to new investors purchasing shares of our Class A common stock in this offering.

Table of Contents

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2013

- on an actual basis; and
- on an as adjusted basis to give effect to the issuance and sale of 10,500,000 shares of our Class A common stock in this offering at a public offering price of $13.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses (assuming no exercise of the underwriters' option to purchase additional shares).

This table should be read in conjunction with our consolidated financial statements, related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in our quarterly and annual reports filed with the SEC that are incorporated by reference in this prospectus supplement and accompanying prospectus. See "Where You Can Find More Information."

	As of March 31, 2013	
	Actual	As Adjusted
	(unaudited)	
	(in thousands, except share and per share data)	
Cash, cash equivalents and available-for-sale securities	$ 242,029	$ 371,094
Total long-term debt	174,855	174,855
Class A common stock, $0.001 par value: 500,000,000 shares authorized; 82,236,205 shares issued and outstanding, actual; 92,736,205 shares issued and outstanding, as adjusted[(1)]	82	93
Class B common stock, $0.001 par value: 100,000,000 shares authorized; 26,479,272 shares issued and outstanding, actual and as adjusted	27	27
Preferred stock, $0.001 par value: 75,000,000 authorized; no shares issued or outstanding, actual or as adjusted		
Additional paid-in capital	657,320	786,374
Accumulated deficit	(598,918)	(598,918)
Accumulated other comprehensive income	12	12
Total stockholders' equity	58,523	187,588
Total capitalization	$ 233,378	$ 362,443

(1) Includes 10,500,000 shares to be issued pursuant to this offering (assuming no exercise of the underwriters' option to purchase additional shares).

The table above does not include:

- options exercisable into 20,838,549 shares of common stock outstanding as of March 31, 2013 at a weighted average exercise price of $8.53 per share; and
- 8,267,197 shares of our common stock reserved as of March 31, 2013 for future issuance under compensation plans.

Table of Contents

UNDERWRITING

General

We are offering the shares of Class A common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated are acting as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of Class A common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities LLC	4,606,875
Merrill Lynch, Pierce, Fenner & Smith Incorporated	3,794,175
Morgan Stanley & Co. LLC	1,399,650
Cowen and Company, LLC	233,100
Ladenburg Thalmann & Co. Inc.	233,100
Mizuho Securities USA Inc.	233,100
Total	10,500,000

The underwriters are committed to purchase all the shares of Class A common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of Class A common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $0.39 per share. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 1,575,000 additional shares of Class A common stock. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of Class A common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of Class A common stock less the amount paid by the underwriters to us per share of Class A common stock. The underwriting fee is $0.6825 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option exercise	With full option exercise
Per Share	$ 0.6825	$ 0.6825
Total	$ 7,166,250	$ 8,241,188

Table of Contents

We estimate that the total net expenses of this offering, including registration, filing and listing fees, printing fees, financial advisory fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $270,000.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not, subject to limited exceptions, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our Class A common stock or securities convertible into or exchangeable or exercisable for any shares of our Class A common stock (including shares of our Class B Common Stock), or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of any shares of Class A common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of Class A common stock, or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated for a period of 60 days after the date of this prospectus supplement. Notwithstanding the foregoing, if (1) during the last 17 days of the 60-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or (2) prior to the expiration of the 60-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 60-day restricted period, the restrictions described above will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

All of our directors and executive officers, and certain entities affiliated with our directors have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 60 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our Class A common stock or securities convertible into or exchangeable or exercisable for any shares of our Class A common stock (including, without limitation, (i) Class A common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC, (ii) securities which may be issued upon exercise of a stock option or warrant and (iii) shares of our Class B common stock), or publicly disclose the intention to make any offer, sale, lease or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our Class A common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Class A common stock or such other securities, in cash or otherwise or (3) make any demand for, or exercise any right with respect to, the registration of any shares of our Class A common stock or any security convertible into or exercisable or exchangeable for our Class A common stock. Notwithstanding the foregoing, if (1) during the last 17 days of the 60-day restricted period, we issue an earnings release or material news or a material event relating to us occurs; or (2) prior to the expiration of the 60-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 60-day

Table of Contents

restricted period, the restrictions described above will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

The representatives have agreed on behalf of the underwriters that the following transactions are permissible during the 60-day restricted period: (i) sales pursuant to a trading plan established to provide an affirmative defense pursuant to Rule 10b5-1 that has been disclosed to the representatives of the underwriters prior to or in connection with the execution of lock-up agreements entered into in connection with this offering and (ii) distributions of up to 2 million shares in the aggregate during the 60-day restricted period where the distributee is a limited partner of a signatory of a lock-up agreement and such distributee need not sign such a lock-up agreement in connection with such distribution. The representatives of the underwriters may release a holder from restrictions on any such shares provided for in the lock-up agreements under certain circumstances, however, all other holders must be provided with a proportional release except if such a release or releases exceed 100,000 shares in the aggregate or 20,000 shares to an individual holder or if such release occurs in connection with circumstances that the representatives deem in their sole judgment to constitute an emergency or hardship.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our Class A common stock is listed/quoted on the NASDAQ Global Select Market under the symbol "IRWD".

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of Class A common stock in the open market for the purpose of preventing or retarding a decline in the market price of the Class A common stock while this offering is in progress. These stabilizing transactions may include making short sales of the Class A common stock, which involves the sale by the underwriters of a greater number of shares of Class A common stock than they are required to purchase in this offering, and purchasing shares of Class A common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the Class A common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the Class A common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase Class A common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the Class A common stock or preventing or retarding a decline in the market price of the Class A common stock, and, as a result, the price of the Class A common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue

Table of Contents

them at any time. The underwriters may carry out these transactions on the NASDAQ Global Select Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our Class A common stock on The Nasdaq Stock Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Stock Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the Class A common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our Class A common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Member State, from and including the date on which the European Union Prospectus Directive, or the EU Prospectus Directive, was implemented in that Relevant Member State, or the Relevant Implementation Date, an offer of securities described in this prospectus supplement and the accompanying prospectus may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus supplement and the accompanying prospectus may be made to the public in that Relevant Member State at any time:

to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;

Table of Contents

to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or

in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus supplement and the accompanying prospectus shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive. For the purposes of this provision, the expression an "offer of securities to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression "EU Prospectus Directive" means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Switzerland

The Class A common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the Class A common stock or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of Class A common stock will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of Class A common stock.

Dubai

This prospectus supplement and the accompanying prospectus relates to an exempt offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus supplement and accompanying prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on

Table of Contents

by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with exempt offers. The DFSA has not approved this prospectus supplement and the accompanying prospectus nor taken steps to verify the information set forth herein and has no responsibility for this prospectus supplement and the accompanying prospectus. The shares to which this prospectus supplement and the accompanying prospectus relate may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the Class A common stock offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

LEGAL MATTERS

The validity of the shares of Class A common stock offered hereby will be passed upon for us by Ropes & Gray LLP. Pillsbury Winthrop Shaw Pittman LLP, New York, New York will pass upon certain legal matters related to this offering for the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2012, and the effectiveness of our internal control over financial reporting as of December 31, 2012, as set forth in their reports, which are incorporated by reference in this prospectus supplement and the accompanying prospectus and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2012 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN YOU FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any materials that we file with the SEC at its Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Our SEC filings are also available to the public from the SEC's website at http://www.sec.gov.

The SEC's rules allow us to "incorporate by reference" the information we have filed with the SEC, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is a part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede the information included and/or incorporated by reference in this prospectus supplement. We incorporate by reference into this prospectus supplement, the accompanying prospectus, the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 (other than, in each case, any document or portion of a document that is deemed not to be filed) prior to the time that we sell all of the securities offered by this prospectus supplement:

Annual Report on Form 10-K for the year ended December 31, 2012;

Definitive Proxy Statement on Schedule 14A, filed on April 12, 2013 (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2012);

Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2013;

Current Reports on Form 8-K filed on January 8, 2013, March 5, 2013 and May 20, 2013; and

Table of Contents

The description of our Class A common stock contained in our Registration Statement on Form 8-A, originally filed with the SEC on February 1, 2010, as amended by any amendment or report filed for the purpose of updating such description.

You may obtain documents incorporated by reference into this prospectus supplement and the accompanying prospectus at no cost by requesting them in writing or telephoning us at the following address:

Corporate Communications
Ironwood Pharmaceuticals, Inc.
301 Binney Street
Cambridge, MA 02142
(617) 621-7722

These filings are also made available, free of charge, on our website at www.ironwoodpharma.com. The information contained in, and that can be accessed through, our website is not incorporated into and does not form a part of this prospectus supplement or the accompanying prospectus.

PROSPECTUS

IRONWOOD PHARMACEUTICALS, INC.

Class A Common Stock

We may offer and sell, or facilitate the resale of, shares of our Class A common stock from time to time. We will provide specific offering terms in supplements to this prospectus. The prospectus supplements may also add, update or change information contained or incorporated by reference in this document. This prospectus may be used to offer and sell securities only if accompanied by a prospectus supplement. You should read this prospectus and any prospectus supplements, along with the additional information described under the heading "Where You Can Find More Information," before making an investment decision.

The shares of our Class A common stock may be sold directly to our stockholders or to purchasers or through agents on our behalf or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions, or discounts.

Our Class A common stock is listed on The NASDAQ Global Select Market under the symbol "IRWD."

Investing in these securities involves substantial risk. Please see "Risk Factors" on page 3.

The address of our principal executive offices is 301 Binney Street, Cambridge, Massachusetts 02142, and the telephone number at our principal executive offices is (617) 621-7722.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 8, 2012

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

Each time we offer securities using this prospectus, we will provide the number of shares and offering price in a supplement to this prospectus. The prospectus supplements also may add, update or change the information contained or incorporated by reference in this prospectus and also will describe the specific manner in which we will be offering shares. You should read carefully both this prospectus and any prospectus supplement together with the additional information described under the heading "Where You Can Find More Information."

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus, in any accompanying prospectus supplement or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus or incorporated by reference herein is accurate only as of the date on the front of this prospectus or the respective dates of filing of the incorporated documents. Our business, financial condition, results of operations and prospects may have changed since that date.

Unless otherwise indicated or unless the context requires otherwise, all references in this prospectus to "Ironwood," "we," "us" and "our" refer to Ironwood Pharmaceuticals, Inc.

RISK FACTORS

For a discussion of the factors you should carefully consider before deciding to purchase any shares, please review "Part II, Item 1A Risk Factors" in our most recent Quarterly Report on Form 10-Q, which is incorporated by reference in this prospectus, as that disclosure has been updated by subsequent periodic reports, as well as the "Risk Factors" section in the applicable prospectus supplement.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy any materials that we file with the SEC at its Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Our SEC filings are also available to the public from the SEC's website at http://www.sec.gov.

The SEC's rules allow us to "incorporate by reference" the information we have filed with the SEC, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is a part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information included and/or incorporated by reference in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 (other than, in each case, any document or portion of a document that is deemed not to be filed) after the initial filing of the registration statement that contains this prospectus and prior to the time that we sell all of the securities offered by this prospectus:

Annual Report on Form 10-K for the year ended December 31, 2010;

Definitive Proxy Statement on Schedule 14A, filed on April 27, 2011 (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2010);

Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2011, June 30, 2011 and September 30, 2011;

Current Reports on Form 8-K filed on February 7, 2011, March 9, 2011, April 8, 2011, May 25, 2011, May 31, 2011, June 13, 2011, August 11, 2011, September 29, 2011, October 20, 2011 and January 4, 2012; and

The description of our Class A common stock contained in our Registration Statement on Form 8-A, originally filed with the SEC on February 1, 2010, as amended by any amendment or report filed for the purpose of updating such description.

You may obtain documents incorporated by reference into this prospectus at no cost by requesting them in writing or telephoning us at the following address:

Corporate Communications
Ironwood Pharmaceuticals, Inc.
301 Binney Street
Cambridge, MA 02142
(617) 621-7722

These filings are also made available, free of charge, on our website at www.ironwoodpharma.com. The information contained in, and that can be accessed through, our website is not incorporated into and does not form a part of this prospectus.

This prospectus constitutes a part of a registration statement on Form S-3, referred to herein, including all amendments and exhibits, as the Registration Statement, that we have filed with the SEC under the Securities Act of 1933. This prospectus does not contain all of the information contained in the Registration Statement. We refer you to the Registration Statement and related exhibits for further information regarding us and our securities. The Registration Statement may be inspected at the public reference facilities maintained by the SEC at the address set forth above or from the SEC's website at http://www.sec.gov. Statements contained in this prospectus or in a document incorporated or deemed to be incorporated by reference herein concerning the provisions of any document filed as an exhibit to the Registration Statement are not necessarily complete and, in each instance, reference is made to the copy of such document filed as an exhibit to the Registration Statement or otherwise filed with the SEC. Each such statement is qualified in its entirety by such reference.

IRONWOOD PHARMACEUTICALS, INC.

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 and generating substantial returns for our stockholders, we plan to reinvest a portion of our future cash flows into our research and development efforts in order to accelerate and enhance our ability to bring new products to market. If we meet our goals, we hope to earn the right to continue building an enduring pharmaceutical company, an outstanding business that will thrive well beyond our lifetimes.

We are pioneers in the area of guanylate cyclase type-C, or GC-C, agonists and in the science and treatment of gastrointestinal diseases. Our development team has substantial expertise with the pharmacological profile associated with GC-C agonists, and they are complemented by our global

operations and commercial teams that have significant experience in the associated therapeutic modalities. We believe that linaclotide, our GC-C agonist being developed for the treatment of patients with irritable bowel syndrome with constipation, or IBS-C, and 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 is our only product candidate that has demonstrated clinical proof of concept.

USE OF PROCEEDS

The use of proceeds from the disposition of the securities covered by this prospectus will be as set forth in the applicable prospectus supplement.

DESCRIPTION OF CLASS A COMMON STOCK

General

The following is a summary of the material rights of our capital stock and related provisions of our certificate of incorporation and bylaws. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our eleventh amended and restated certificate of incorporation and fifth amended and restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part, as well as our eighth amended and restated investors' rights agreement that is currently in effect and which we have included as an exhibit to the registration statement of which this prospectus is a part.

Our eleventh amended and restated certificate of incorporation provides that we have two series of common stock: one series we call our Class A common stock and the other series we call our Class B common stock. As described below and in our eleventh amended and restated certificate of incorporation, the dual class common stock structure will remain in place at least until 2018 (and potentially until 2038), during the critical period when we expect to be building our commercial capabilities, launching linaclotide, and investing in our development pipeline.

This dual class structure is a fundamental element of our overall strategy to seek to maximize shareholder value over the long-term. Holders of our Class A and Class B common stock have identical rights, except that, in certain circumstances as described below, holders of our Class A common stock are entitled to one vote per share and holders of our Class B common stock are entitled to ten votes per share. The breadth of our Class B stockholder group should ensure that significant decisions about our independence are made within a context of diverse opinions and interests.

Any holder of Class B common stock may convert his or her shares at any time into shares of Class A common stock on a share-for-share basis. Shares of Class B common stock can be sold at any time and, subject to limited exceptions, irrevocably convert to shares of Class A common stock upon sale or transfer. Therefore, we expect that over time, the Class B stockholder class will diminish as a percentage of our total shares outstanding, and that the remaining Class B shares will be concentrated in the hands of our longest term stockholders.

Our authorized capital stock consists of 675,000,000 shares, each with a par value of $0.001 per share, of which:

500,000,000 shares are designated as Class A common stock.

100,000,000 shares are designated as Class B common stock.

75,000,000 shares are designated as preferred stock.

As of February 6, 2012, we had 62,623,097 shares of Class A common stock outstanding and 38,175,539 shares of Class B common stock outstanding.

Voting Rights

Each share of Class A common stock and each share of Class B common stock has one vote per share, except on the following matters (in which each share of Class A common stock has one vote per share and each share of Class B common stock has ten votes per share), if submitted to a vote of stockholders:

adoption of a merger or consolidation agreement involving Ironwood;

a sale, lease or exchange of all or substantially all of Ironwood's assets;

a dissolution or liquidation of Ironwood; or

every matter, if and when any individual, entity or "group" (as such term is used in Regulation 13D of the Exchange Act) has, or has publicly disclosed (through a press release or a filing with the SEC) an intent to have, beneficial ownership of 30% or more of the number of outstanding shares of Class A common stock and Class B common stock, combined.

Holders of shares of Class A common stock and Class B common stock vote together as a single class on all matters (including the election of directors) submitted to a vote of stockholders, unless otherwise required by our certificate of incorporation or bylaws. Our certificate of incorporation provides that any increase in the number of authorized shares of either our Class A common stock or our Class B common stock may be approved by a majority of our Class A common stock and Class B common stock, voting together as a single class. Our certificate of incorporation requires that a majority of the Class B common stock approve further issuances of shares of Class B common stock, subject to certain exceptions, or any amendment to our certificate of incorporation. Delaware law could require either our Class A common stock or Class B common stock to vote separately as a single class in the following circumstances:

If we amended our certificate of incorporation to increase or decrease the par value of a class of stock, then that class would be required to vote separately to approve the proposed amendment.

If we amended our certificate of incorporation in a manner that altered or changed the powers, preferences or special rights of a class of stock in a manner that affects them adversely then that class would be required to vote separately to approve the proposed amendment.

We have not provided for cumulative voting for the election of directors in our certificate of incorporation. Because our certificate of incorporation does provide for plurality voting for the election of directors, a director may be elected even if less than a majority of the votes cast are in favor of such election.

Dividends

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 will be 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.

Liquidation Rights

Upon our liquidation, dissolution or winding-up, the holders of Class A common stock and Class B common stock will be entitled to share equally all assets remaining after the payment of any liabilities and the liquidation preferences on any outstanding preferred stock.

Conversion

Our Class A common stock is not convertible into any other shares of our capital stock.

Each share of Class B common stock is convertible at any time at the option of the holder into one share of Class A common stock.

In addition, each share of Class B common stock will convert automatically into one share of Class A common stock upon any transfer, whether or not for value, except for certain transfers described in our certificate of incorporation, including the following:

- transfers for tax and estate planning purposes, including to trusts, corporations, partnerships or other legal entities in which the holder of Class B common stock retains the voting control over such shares;
- transfers to a family member or to another legal entity for the benefit of the family member;
- transfers to any person directly or indirectly controlling, controlled by or under common control with the holder of Class B common stock; and
- if the holder of Class B common stock is a partnership, transfers to any general partner of the partnership who also is a director of Ironwood at that time.

The death of any holder of Class B common stock who is a natural person will result in the conversion of his or her shares of Class B common stock into Class A common stock unless, as a result of the death of such holder, the shares of Class B common stock transfer to one or more of the entities described in the preceding bulleted list.

Furthermore, each share of Class B common stock will convert automatically into one share of Class A common stock upon the earliest of the following:

- the later of (1) the first date on which the number of shares of Class B common stock then outstanding is less than 19,561,556, or (2) December 31, 2018;
- December 31, 2038; or
- a date agreed to in writing by the holders of at least a majority of then outstanding shares of Class B common stock.

Once converted into Class A common stock, the Class B common stock will be retired and will not be reissued.

Preferred Stock

Our board of directors has the authority, without approval by the stockholders, to issue up to a total of 75,000,000 shares of preferred stock in one or more series. Our board of directors may establish the number of shares to be included in each such series and may fix the designations, preferences, powers and other rights of the shares of a series of preferred stock. Our board could authorize the issuance of preferred stock with voting or conversion rights that could dilute the voting power or rights of the holders of common stock. However, such shares of preferred stock would not convert into shares of Class B common stock without the prior consent of our board. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of Ironwood and might harm the market price of our common stock. We have no current plans to issue any shares of preferred stock.

Registration Rights

The holders of our Class B common stock issued upon conversion of our preferred stock at our initial public offering are entitled to rights with respect to the registration under the Securities Act of shares of Class A common stock into which their shares of Class B common stock converts. These registration rights are contained in our eighth amended and restated investors' rights agreement and are described below. The registration rights under the investors' rights agreement will expire five years following the completion of our initial public offering, or, with respect to an individual holder, when such holder holds less than 1% of the number of outstanding shares of Class B common stock and is able to sell all of its shares pursuant to Rule 144 under the Securities Act in any 90 day period.

Demand Registration Rights

The holders of shares of common stock having demand registration rights under the investors' rights agreement have the right to require that we register their shares of Class A common stock into which their shares of Class B common stock converts, provided such registration relates to not less than 20% in aggregate of our then outstanding shares of Class B common stock having demand registration rights and the anticipated aggregate offering price to the public is at least $5,000,000. In response to these demand registration rights, we are only obligated to effect two registrations for each series of our outstanding preferred stock that were converted into Class B common stock upon the completion of our initial public offering. We may postpone the filing of a registration statement for up to 90 days once in any 12-month period if our board of directors determines in good faith that the filing would be seriously detrimental to our stockholders or us. The underwriters of any underwritten offering have the right to limit the number of shares to be included in a registration statement filed in response to the exercise of these demand registration rights. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with the exercise of these demand registration rights.

Piggyback Registration Rights

If we register any securities for public sale, the stockholders with piggyback registration rights under the investors' rights agreement have the right to include their shares in the registration, subject to specified exceptions. In accordance with the terms of the investors' rights agreement, we have received a waiver of these piggyback registration rights with respect to the registration for this offering. The underwriters of any underwritten offering have the right to limit the number of shares registered by these stockholders due to marketing reasons. We must pay all expenses, except for underwriters' discounts and commissions, incurred in connection with the exercise of these piggyback registration rights.

S-3 Registration Rights

If we are eligible to file a registration statement on Form S-3, the stockholders with S-3 registration rights under the investors' rights agreement can request that we register their shares, provided that the total price of the shares of common stock offered to the public is at least $500,000. These S-3 registration rights are wholly distinct from the demand registration rights and piggyback registration rights described above. A holder of S-3 registration rights may not require us to file a registration statement on Form S-3 if we have already effected two registrations on Form S-3 at the request of such holder in the last 12-month period. We may postpone the filing of a Form S-3 registration statement for up to 90 days once in any 12-month period if our board of directors determines in good faith that the filing would be seriously detrimental to our stockholders or us. The holders of S-3 registration rights must pay all expenses associated with any registrations on Form S-3 after the first six registrations on Form S-3.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Certain provisions of Delaware law, our certificate of incorporation and our bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. In particular, our dual class common stock structure will concentrate ownership of our voting stock in the hands of our founders, board members and pre-initial public offering employees. These provisions, which are summarized below, encourage persons seeking to acquire control of us to first negotiate with our board of directors and the holders of our capital stock.

Dual Class Common Stock Structure

As discussed above, our Class B common stock has ten votes per share in change of control transactions, while our Class A common stock has one vote per share. Because of our dual class common stock structure, holders of our Class B common stock (and their affiliates) will continue to be able to control all matters submitted to our stockholders for approval even if they come to own significantly less than 50% of the shares of our outstanding common stock. This concentrated control could discourage others from initiating any potential merger, takeover or other change of control transaction that other stockholders may view as beneficial.

Undesignated Preferred Stock

The ability to authorize undesignated 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. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Limits on Ability of Stockholders to Act by Written Consent

We have provided in our certificate of incorporation that our stockholders may not act by written consent other than in matters that require a separate series vote of the Class B common stock. In addition, our certificate of incorporation also requires that special meetings of stockholders be called only by our board of directors, our chairman, our chief executive officer or our president if there is no chief executive officer. This limit on the ability of our stockholders to act by written consent or to call a special meeting may lengthen the amount of time required to take stockholder actions. As a result, a holder controlling a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a stockholders meeting.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. The bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding business to be conducted at a special or annual meeting of the stockholders. However, our bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Staggered Board of Directors

Nine individuals currently serve on our board of directors, which is divided into three classes. At each annual meeting of stockholders, a class of directors is to be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result, a portion of our board of directors will be elected each year. Our certificate of incorporation authorizes our board of directors to fix the number of directors from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control. Between stockholder meetings, directors may be removed by our stockholders only for cause, and the board of directors may appoint new directors to fill the vacancies. These provisions may prevent a stockholder from removing incumbent directors and simultaneously gaining control of the board of directors by filling the resulting vacancies with its own nominees. Consequently, the existence of these provisions may have the effect of deterring hostile takeovers, which could depress the market price of our Class A common stock.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law. This statute regulating corporate takeovers prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for three years following the date that the stockholder became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon completion of the transaction that resulted in the interested stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers, and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66^{2}/_{3}$% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is any person who, together with such person's affiliates and associates (i) owns 15% or more of a corporation's voting securities or (ii) is an affiliate or associate of a corporation and was the owner of 15% or more of the corporation's voting securities at any time within the three year period immediately preceding a business combination of the corporation governed by Section 203. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage takeover attempts that might result in a premium over the market price for the shares of Class A common stock held by our stockholders.

Transfer Agent and Registrar

The transfer agent and registrar for our Class A common stock is Computershare Trust Company, N.A.

Listing

Our Class A common stock is listed on The NASDAQ Global Select Market under the symbol "IRWD."

MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a summary of certain material U.S. federal income and estate tax considerations relating to the purchase, ownership and disposition of our common stock by Non-U.S. Holders (defined below), but does not purport to be a complete analysis of all the potential tax considerations. This summary is based upon the Internal Revenue Code of 1986, as amended (the "Code"), the Treasury regulations promulgated or proposed thereunder and administrative and judicial interpretations thereof, all as of the date hereof and all of which are subject to change at any time, possibly on a retroactive basis. This summary is limited to the tax consequences to those persons who hold our common stock as capital assets within the meaning of Section 1221 of the Code.

This summary does not purport to deal with all aspects of U.S. federal income and estate taxation that might be relevant to particular Non-U.S. Holders in light of their particular investment circumstances or status, nor does it address specific tax considerations that may be relevant to particular persons (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain U.S. expatriates, tax-exempt organizations, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, or persons in special situations, such as those who have elected to mark securities to market or those who hold common stock as part of a straddle, hedge, conversion transaction or other integrated investment). In addition, this summary does not address U.S. federal alternative minimum, certain estate and gift tax considerations or considerations under the tax laws of any state, local or non-U.S. jurisdiction.

This summary is for general information only. Non-U.S. Holders are urged to consult their tax advisors concerning the U.S. federal income and estate taxation, state, local and non-U.S. taxation and other tax consequences to them of the purchase, ownership and disposition of our common stock, as well as the application of state, local and non-U.S. income and other tax laws.

For purposes of this summary, a "Non-U.S. Holder" means a beneficial owner of common stock that for U.S. federal income tax purposes is not:

- an individual who is a citizen or resident of the U.S.,
- a corporation (or other entity taxable as a corporation) created or organized under the laws of the U.S., any state thereof, or the District of Columbia,
- an estate the income of which is subject to U.S. federal income tax regardless of its source, or
- a trust if (a) a court within the U.S. is able to exercise primary supervision over the administration of the trust, and one or more U.S. persons have the authority to control all substantial decisions of the trust, or (b) a valid election to be treated as a U.S. person is in effect with respect to such trust.

If a partnership, or an entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds common stock, the tax treatment of a partner in the partnership generally will depend upon the partner's tax status and upon the activities of the partnership. Accordingly, partnerships and other entities that are classified as partnerships for U.S. federal income tax purposes that hold our common stock and partners in such partnerships should consult their tax advisors.

Distributions on Our Common Stock

As discussed under "Dividends" above, we do not currently expect to pay dividends. In the event that we do make a distribution of cash or property with respect to our common stock, any such distributions will be treated as a dividend for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits (as determined under U.S. federal income tax

principles). If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated first as a tax-free return of capital to the extent of the Non-U.S. Holder's tax basis in our common stock and thereafter as capital gain from the sale or exchange of such stock. Any such distribution would also be subject to the discussion below under the section titled "Additional withholding and information reporting requirements." Dividends paid to a Non-U.S. Holder generally will be subject to a 30% U.S. federal withholding tax unless such Non-U.S. Holder provides us or our agent, as the case may be, with a properly executed:

1. IRS Form W-8BEN (or successor form) claiming, under penalties of perjury, a reduction in withholding under an applicable income tax treaty, or

2. IRS Form W-8ECI (or successor form) stating that a dividend paid on common stock is not subject to withholding tax because it is effectively connected with a U.S. trade or business of the Non-U.S. Holder (in which case such dividend generally will be subject to regular graduated U.S. tax rates as described below).

The certification requirement described above also may require a Non-U.S. Holder that provides an IRS form or that claims treaty benefits to provide its U.S. taxpayer identification number. Special certification and other requirements apply in the case of certain Non-U.S. Holders that are intermediaries or pass-through entities for U.S. federal income tax purposes.

Each Non-U.S. Holder is urged to consult its own tax advisor about the specific methods for satisfying these requirements. A claim for exemption will not be valid if the person receiving the applicable form has actual knowledge or reason to know that the statements on the form are false.

If dividends are effectively connected with a U.S. trade or business of the Non-U.S. Holder (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment), the Non-U.S. Holder, although exempt from the withholding tax described above (provided that the certifications described above are satisfied), will be subject to U.S. federal income tax on such dividends on a net income basis in the same manner as if it were a resident of the United States. In addition, if such Non-U.S. Holder is a non-U.S. corporation and dividends are effectively connected with its U.S. trade or business (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment), such Non-U.S. Holder may be subject to an additional "branch profits tax" equal to 30% (unless reduced by an applicable income treaty) in respect of such effectively-connected income.

If a Non-U.S. Holder is eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, such holder may obtain a refund or credit of any excess amount withheld by timely filing an appropriate claim for refund with the IRS.

Disposition of Our Common Stock

Subject to the discussion below under the section titled "Additional withholding and information reporting requirements", in general, a Non-U.S. Holder will not be subject to U.S. federal income tax or withholding tax on gain recognized on a sale, exchange or other taxable disposition of a share of our common stock, unless:

the gain is effectively connected with a trade or business of the Non-U.S. Holder in the United States (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment);

the Non-U.S. Holder is a nonresident alien who is present in the United States for 183 days or more in the taxable year of the disposition and meets certain other conditions; or

we are or have been a "United States real property holding corporation," as defined in the Code (a "USRPHC"), at any time within the shorter of the five-year period preceding the disposition and the Non-U.S. Holder's holding period in the share of our common stock.

We believe that we are not, and do not anticipate becoming, a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, a Non-U.S. Holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock so long as our common stock continues to be regularly traded on an established securities market and such Non-U.S. Holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our common stock at any time during the shorter of the five year period ending on the date of disposition and the holder's holding period.

If a Non-U.S. Holder is engaged in a trade or business in the U.S. and gain recognized by the Non-U.S. Holder on a sale or other disposition of our common stock is effectively connected with the conduct of such trade or business, the Non-U.S. Holder will generally be subject to regular U.S. income tax as if the Non-U.S. Holder were a U.S. person, subject to an applicable income tax treaty providing otherwise. Additionally, a non-U.S. corporation may also, under certain circumstances, be subject to an additional "branch profits tax" imposed at a rate of 30% (or, if applicable, a lower income tax treaty rate). Non-U.S. Holders whose gain from dispositions of our common stock may be effectively connected with the conduct of a trade or business in the United States are urged to consult their own tax advisors with respect to the U.S. tax consequences of the purchase, ownership and disposition of our common stock.

A nonresident alien who is subject to U.S. federal income tax because such individual was present in the United States for 183 days or more in the taxable year of the taxable disposition of our common stock will be subject to a flat 30% tax on the gain derived from such disposition, which may be offset by U.S. source capital loss.

Additional withholding and information reporting requirements

Recent legislation generally will impose withholding at a rate of 30% on payments to certain foreign entities (including financial intermediaries), including dividends on and the gross proceeds from dispositions of U.S. common stock, unless various U.S. information reporting and due diligence requirements that are different from, and in addition to, the certification requirements described above under "Distributions on Our Common Stock" have been satisfied (generally relating to ownership by U.S. persons of interests in or accounts with those entities). The withholding rules apply to payments of dividends on U.S. common stock beginning January 1, 2014, and to gross proceeds from dispositions of U.S. common stock beginning January 1, 2015. The IRS's guidance with respect to these rules is only preliminary, and the scope of these rules remains unclear and potentially subject to material changes. Non-U.S. Holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS and to each Non-U.S. Holder certain information including the Non-U.S. Holder's name, address and taxpayer identification number, the aggregate amount of distributions on our common stock paid to that Non-U.S. Holder during the calendar year and the amount of tax withheld, if any.

Backup withholding tax is imposed on dividends and certain other types of payments to certain U.S. persons (currently at a rate of 28% and scheduled to increase to 31% for taxable years 2013 and thereafter). In general, backup withholding tax will not apply to payments of dividends on common stock or proceeds from the sale of common stock payable to a Non-U.S. Holder if the certification described above in "Distributions on Our Common Stock" is duly provided by such Non-U.S. Holder or the Non-U.S. Holder otherwise establishes an exemption, provided that the payor does not have

actual knowledge or reason to know that the Non-U.S. Holder is a U.S. person or that the conditions of any claimed exemption are not satisfied. Certain information reporting may still apply to distributions even if an exemption from backup withholding is established. Copies of any information returns reporting the distributions to a Non-U.S. Holder and any withholding also may be made available to the tax authorities in the country in which a Non-U.S. Holder resides under the provisions of an applicable income tax treaty.

Backup withholding is not an additional tax and any amounts withheld under the backup withholding tax rules from a payment to a Non-U.S. Holder will be allowed as a refund or a credit against such Non-U.S. Holder's U.S. federal income tax liability, provided that the requisite procedures are followed.

Non-U.S. Holders are urged to consult their own tax advisors regarding their particular circumstances and the availability of and procedure for obtaining an exemption from backup withholding.

U.S. Federal Estate Tax

Common stock owned or treated as owned by an individual who is a Non-U.S. Holder at the time of death generally will be included in the individual's gross estate for U.S. federal estate tax purposes and may be subject to U.S. federal estate tax unless an applicable estate or other tax treaty provides otherwise.

PLAN OF DISTRIBUTION

General

The shares may be sold:

- to or through underwriting syndicates represented by managing underwriters;
- to or through one or more underwriters without a syndicate;
- through dealers or agents; or
- to investors directly in negotiated sales or in competitively bid transactions.

The prospectus supplement for each offering will describe, to the extent required, information with respect to that offering, including:

- the name or names of any underwriters and the respective amounts underwritten;
- the sale price and the proceeds from the sale;
- any underwriting discounts and other items constituting underwriters' compensation;
- any public offering price and any discounts or concessions allowed or reallowed or paid to dealers; and
- any material relationships with the underwriters.

Underwriters

If underwriters are used in the sale, we will execute an underwriting agreement with those underwriters relating to the sale of the shares. Unless otherwise set forth in the applicable prospectus supplement, the obligations of the underwriters to purchase these shares will be subject to conditions, and the underwriters will be obligated to purchase all of these shares if any are purchased.

The shares subject to an underwriting agreement will be acquired by the underwriters for their own account and may be resold by them from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may be deemed to have received compensation in the form of underwriting discounts or commissions and may also receive commissions from the purchasers of these shares for whom they may act as agent. Underwriters may sell these shares to or through dealers. These dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agent. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

Agents

We may sell shares through agents designated by us from time to time. We will name any agent involved in the offer or sale of these shares and will list commissions payable by us to these agents in the applicable prospectus supplement. These agents will be acting on a best efforts basis to solicit purchases for the period of its appointment, unless we state otherwise in the applicable prospectus supplement.

Direct Sales

We may sell shares directly to purchasers. In this case, we will not engage underwriters or agents in the offer and sale of the applicable shares.

Indemnification

We may indemnify underwriters, dealers or agents who participate in the distribution of shares against certain liabilities, including liabilities under the Securities Act, and agree to contribute to payments which these underwriters, dealers or agents may be required to make.

Secondary Sales

Shares of our Class A common stock may be sold from time to time by selling stockholders, through public or private transactions at prevailing market prices or at privately negotiated prices, as described in the applicable prospectus supplement.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, our counsel Ropes & Gray, LLP, Boston Massachusetts, will pass upon the validity of the shares of Class A common stock offered by this prospectus.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2010, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements as of December 31, 2010 are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

Table of Contents