April 29, 2014

Ironwood Pharmaceuticals Provides First Quarter 2014 Investor Update

- First quarter LINZESS® (linaclotide) net product sales of $60.8 million, as reported by Forest Laboratories, Inc. -

- Multi-channel Direct-to-Consumer awareness campaign launched -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) today provided an update on its first quarter 2014 and recent business activities.

"During the first fifteen months of the LINZESS launch, we have established a strong foundation of physician experience and payer coverage for LINZESS. Now, while we continue advancing with prescribers and payers, we are intensifying our efforts to educate appropriate patients about LINZESS through a multi-channel, direct-to-consumer patient awareness campaign," said Peter Hecht, chief executive officer of Ironwood. "With commercial momentum, significant progress in our R&D pipeline and the close of a $190 million equity offering, Ironwood continues to grow into a leader in gastrointestinal therapeutics as we work to maximize value for patients, health care providers and our fellow shareholders."

First Quarter 2014 and Recent Highlights

LINZESS® (linaclotide)

- LINZESS net product sales, as reported by Forest Laboratories, Inc., were $60.8 million in the first quarter of 2014, an increase of approximately 19% quarter over quarter.
- Nearly 240,000 LINZESS prescriptions were filled in the first quarter of 2014, according to IMS Health, resulting in approximately 11% growth in total prescriptions quarter over quarter. More than 800,000 LINZESS prescriptions have been filled by more than 260,000 unique adult patients since the product's launch in December 2012, according to IMS Health.
- The total number of unique healthcare practitioners prescribing LINZESS since launch reached more than 63,000 in the first quarter of 2014, according to IMS Health. This includes approximately 92% of high prescribing gastroenterologists and approximately 76% of other high prescribing healthcare practitioners, mostly primary care physicians.
- More than 70% of people with commercial insurance and Medicare Part D plans had unrestricted access to LINZESS as of March 2014. Additionally, in March 2014, more than 70% of people with commercial insurance had a copay of $30 or less, through formulary coverage or the LINZESS Instant Savings Program.
- Ironwood and Forest launched a DTC patient awareness campaign for LINZESS designed to help adults suffering from IBS-C or CIC recognize the symptoms of these disorders, describe their symptoms to their doctor, and ask their doctor about LINZESS to help proactively manage their disease. The extensive multi-channel campaign includes television, print and online advertising; social media elements; an updated brand website (www.linzess.com); brochures in doctors' offices and pharmacies; and a waiting room TV program.
- Ironwood and Forest received Notices of Allowance from the United States Patent and Trademark Office (USPTO) for two separate patent applications covering the commercial formulation of LINZESS and methods of using the product to treat patients with IBS-C or CIC. Both of these patent applications are expected to issue in mid-2014 and extend LINZESS patent protection by an additional five years into 2031. In addition, Ironwood was successful in defending a separate linaclotide patent that was subject to an inter partes reexamination. The USPTO confirmed that all claims in the patent are patentable, concluding the review in Ironwood's favor and affirming the strength of Ironwood's intellectual property around LINZESS.

Linaclotide (Rest of World)

- Almirall, S.A., Ironwood's European partner, continues to commercialize CONSTELLA® (linaclotide) in Europe, where it is the first and only prescription product approved by the European Medicines Agency for the symptomatic treatment of moderate to severe IBS-C in adult patients. CONSTELLA has been approved for adult patients with moderate to severe IBS-C and has been launched in 10 countries in Europe, including the United Kingdom, Germany and most recently Italy, with additional country launches expected in 2014. Almirall recently announced that it intends to suspend

commercialization of CONSTELLA in Germany in May 2014, following an inability to reach agreement with the German National Association of Statutory Health Insurance Funds on a reimbursement price that reflects the innovation and value of CONSTELLA. Almirall is assessing all possibilities to facilitate continued access to CONSTELLA for appropriate patients in Germany.

- Forest received marketing approval for linaclotide in Canada and Mexico; launches in both countries are expected in mid-2014. Forest has the rights to commercialize CONSTELLA in Canada and, through a sublicense from Forest, Almirall has the rights to commercialize LINZESS in Mexico.
- Ironwood and AstraZeneca AB continue to enroll patients in a Phase III clinical trial of linaclotide in adult patients with IBS-C in China. The trial is expected to be completed in the first half of 2015.
- Astellas Pharma Inc. completed a Phase II double-blind, placebo-controlled, dose-ranging clinical trial of linaclotide in adult patients with IBS-C in Japan. Preliminary top level data from Astellas indicate higher responder rates for all linaclotide dose groups versus placebo in the primary endpoint, although the difference was not statistically significant. Linaclotide was well tolerated in all dose groups within this study.

Research & Development

- Ironwood continues to explore opportunities to evaluate linaclotide in additional indications such as opioid-induced constipation, colorectal cancer prevention, and pediatrics, as well as in combination with a proton pump inhibitor and in a colonic delivery formulation. Ironwood also is leveraging its gastrointestinal and guanylate cyclase expertise to advance a robust pipeline of additional potential product candidates, including IW‑3718 which is being studied for refractory GERD, IW-9179 which is being studied for functional dyspepsia (FD) and gastroparesis, and a soluble guanylate cyclase (sGC) program. Research and development highlights for the quarter include:
  - Ironwood initiated dosing of its investigational bile acid sequestrant, IW‑3718, in a Phase IIa clinical study for patients with GERD symptoms who have not responded adequately to treatment with a proton pump inhibitor. Data from this trial are expected in the first half of 2015.
  - Ironwood ended its exploratory Phase IIa study of IW-9179 in FD prior to completing enrollment, due to challenges with the rigorous enrollment exclusion criteria in the trial. Data analysis is ongoing but preliminary data support continued development. Ironwood continues to define a path forward for IW-9179 in FD. In parallel, Ironwood plans to initiate a Phase IIa clinical trial of IW-9179 in patients with gastroparesis in the first half of 2015.
  - Ironwood identified a development candidate in its sGC program, which targets a proven mechanism for treating pulmonary arterial hypertension (PAH) and other cardiovascular diseases with the potential for broad therapeutic utility both inside and outside of the CV therapeutic category. Preclinical development is ongoing.

Corporate and Financials

- **Collaborative Arrangements Revenue.** Collaborative arrangements revenue was approximately $14.6 million in the first quarter of 2014 compared with approximately $5.0 million in the fourth quarter of 2013. The collaborative arrangements revenue consisted of $8.4 million in revenue associated with Ironwood's share of the net profits and losses from the sales of LINZESS in the U.S., as well as $6.2 million in sales of linaclotide active pharmaceutical ingredient (API), amortization of deferred revenue associated with consideration received from Ironwood's collaboration with Astellas, revenue recognized under the collaboration with AstraZeneca, and milestone and royalty payments based on sales of CONSTELLA in Europe from Almirall.
- **Operating Expenses.** Operating expenses were approximately $57.1 million in the first quarter of 2014, including non-reoccurring charges totaling $4.3 million associated with Ironwood's headcount reduction in January 2014, as compared to approximately $51.2 million in the fourth quarter of 2013. Operating expenses consisted of approximately $27.1 million in research and development (R&D) expenses, which included $2.7 million in non-cash share-based compensation expense, and approximately $30.0 million in selling, general and administrative (SG&A) expenses, which included $3.4 million in non-cash share-based compensation expense.
- **Collaboration Expense.** Ironwood records its share of the net profits and losses from the sales of LINZESS in the U.S. on a net basis and presents the settlement payments from and to Forest as collaborative arrangements revenue or collaboration expense, respectively. In the first quarter of 2014 and the fourth quarter of 2013, Ironwood recorded the settlement payments from Forest of approximately $8.4 million and $2.9 million, respectively, as collaborative arrangements revenue, and no collaboration expense was recorded.
- **Interest Expense.** Interest expense was approximately $5.3 million in the first quarter of 2014 in connection with the $175 million debt financing executed in January 2013.
- **Net Loss.** Net loss was approximately $49.6 million, or $0.38 per share, in the first quarter of 2014, as compared to approximately $52.0 million, or $0.43 per share, in the fourth quarter of 2013.
- **Cash Position.** Ironwood ended the first quarter of 2014 with approximately $332 million of cash, cash equivalents and

available-for-sale securities, up from approximately $198 million as of the end of 2013. Ironwood used approximately $58 million of cash for operations during the first quarter of 2014.

- **Public Equity Offering.** In the first quarter of 2014, Ironwood sold 15,784,325 shares of its Class A common stock through a firm commitment, underwritten public offering at a price to the public of $12.75 per share. As a result of the offering, Ironwood received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $190.4 million.
- **2014 Financial Guidance.** Ironwood today reiterated its financial guidance for 2014. Total operating expenses are expected to be in the range of $215 to $245 million, consisting of $105 to $120 million in R&D expenses and $110 to $125 million in SG&A expenses. Non-linaclotide R&D expenses are expected to be approximately 45% of total R&D expenses. In addition, Ironwood today reiterated its financial guidance for the Forest and Ironwood total 2014 marketing and sales expenses for LINZESS, which it continues to expect to be in the range of $240 to $270 million.

Conference Call Information

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time, on Tuesday, April 29, to discuss its first quarter 2014 and recent business activities. Individuals interested in participating in the call should dial (877) 643-7155 (U.S. and Canada) or (914) 495-8552 (international) using conference ID number 3733415. To access the webcast, please visit the Investors section of Ironwood's website at www.ironwoodpharma.com at least 15 minutes prior to the start of the call to ensure adequate time for any software downloads that may be required. The call will be available for replay via telephone starting today at approximately 11:30 a.m. Eastern Time, on April 29, running through 11:59 p.m. Eastern Time on May 6, 2014. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 3733415. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the call has completed.

About LINZESS (linaclotide)

LINZESS is the first and only guanylate cyclase-C (GC-C) agonist approved by the FDA and is indicated for the treatment of both irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) in adults. LINZESS is a once-daily capsule that helps relieve the abdominal pain and constipation associated with IBS-C, as well as the constipation, infrequent stools, hard stools and incomplete evacuation associated with CIC. The recommended dose is 290 mcg for IBS-C patients and 145 mcg for CIC patients. LINZESS should be taken at least 30 minutes before the first meal of the day.

LINZESS is thought to work in two ways based on nonclinical studies. LINZESS binds to the GC-C receptor locally, within the intestinal epithelium. Activation of GC-C results in increased intestinal fluid secretion and accelerated transit and a decrease in the activity of pain-sensing nerves in the intestine. The clinical relevance of the effect on pain fibers, which is based on nonclinical studies, has not been established.

In placebo-controlled Phase III clinical trials of more than 2,800 adults, LINZESS was shown to reduce abdominal pain in IBS-C patients and increase bowel movement frequency in both IBS-C patients and CIC patients. Improvement in abdominal pain and constipation occurred in the first week of treatment and was maintained throughout the 12-week treatment period. Maximum effect on abdominal pain was seen at weeks 6-9 and maximum effect on constipation occurred during the first week. When a subset of LINZESS-treated patients in the trials were switched to placebo, they reported their symptoms returned toward pretreatment levels within one week, while placebo-treated patients switched to LINZESS reported symptom improvements. LINZESS is contraindicated in pediatric patients up to 6 years of age. The use of LINZESS in pediatric patients 6 through 17 years of age should be avoided. In nonclinical studies, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths in young juvenile mice. LINZESS has not been studied in pediatric patients. In adults with IBS-C or CIC treated with LINZESS, the most commonly reported adverse event was diarrhea.

Ironwood and Forest Laboratories, Inc. are co-promoting LINZESS in the United States. Linaclotide is marketed by Almirall, S.A. for the treatment of adults with moderate to severe IBS-C in Europe under the brand name CONSTELLA®. Ironwood also has partnered with Astellas Pharma Inc. for development and commercialization of linaclotide in Japan and with AstraZeneca for development and commercialization in China.

About CONSTELLA (linaclotide)

Linaclotide is a Guanylate Cyclase-C receptor agonist (GCCA) with visceral analgesic and secretory activities. Linaclotide is a 14-amino acid synthetic peptide structurally related to the endogenous guanylin peptide family. Both linaclotide and its active metabolite bind to the Guanylate Cyclase-C receptor, on the luminal surface of the intestinal epithelium. Through its action at GC-C, linaclotide has been shown to reduce visceral pain and increase GI transit in animal models and increase colonic transit in humans. Activation of GC-C results in an increase in concentrations of cyclic guanosine monophosphate (cGMP), both extracellularly and intracellularly. Extracellular cGMP decreases pain-fiber activity, resulting in reduced visceral pain in animal models. Intracellular cGMP causes secretion of chloride and bicarbonate into the intestinal lumen, through activation of the cystic fibrosis transmembrane conductance regulator (CFTR), which results in increased intestinal fluid and accelerated transit.

Linaclotide was discovered by scientists at Ironwood and is marketed by Almirall, S.A. for the treatment of adults with moderate to severe IBS-C in Europe under the brand name CONSTELLA, through a license agreement between the two companies.

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is focused on creating medicines that make a difference for patients, building value to earn the continued support of our fellow shareholders, and empowering our team to passionately pursue excellence. We discovered, developed and are commercializing linaclotide, which is approved in the United States and a number of other countries. Our pipeline priorities include exploring further opportunities for linaclotide, as well as leveraging our therapeutic expertise in gastrointestinal disorders and our pharmacologic expertise in guanylate cyclases to address patient needs across the upper and lower gastrointestinal tract. Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. Connect with us at www.ironwoodpharma.com or on Twitter at www.twitter.com/ironwoodpharma; information that may be important to investors will be routinely posted in both these locations.

Important Safety Information

WARNING: PEDIATRIC RISK
LINZESS is contraindicated in pediatric patients up to 6 years of age. Use should be avoided in pediatric patients 6 through 17 years of age. In nonclinical studies, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths in young juvenile mice.

Contraindications

- LINZESS is contraindicated in pediatric patients up to 6 years of age.
- LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions

Pediatric Risk

- LINZESS is contraindicated in pediatric patients up to 6 years of age. In nonclinical studies, deaths occurred within 24 hours in young juvenile mice (1 to 3 week-old mice; approximately equivalent to human pediatric patients less than 2 years of age) following administration of one or two daily oral doses of linaclotide.
- Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. Linaclotide did not cause deaths in older juvenile mice (approximately equivalent to humans age 12 to 17 years). Although there were no deaths in older juvenile mice, given the deaths in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients, use of LINZESS should be avoided in pediatric patients 6 through 17 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction of LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. Severe diarrhea was reported in 2% of LINZESS-treated patients. The incidence of diarrhea was similar in the IBS-C and CIC populations.
- Patients should be instructed to stop LINZESS if severe diarrhea occurs and to contact their healthcare provider, who should consider dose suspension.

Adverse Reactions

- In IBS-C clinical trials, the most common adverse reactions in LINZESS-treated patients (incidence ≥2% and greater than placebo) were diarrhea (20% vs 3% placebo), abdominal pain (7% vs 5%), flatulence (4% vs 2%), headache (4% vs 3%), viral gastroenteritis (3% vs 1%) and abdominal distension (2% vs 1%).
- In CIC clinical trials, the most common adverse reactions in LINZESS-treated patients (incidence ≥2% and greater than placebo) were diarrhea (16% vs 5% placebo), abdominal pain (7% vs 6%), flatulence (6% vs 5%), upper respiratory tract infection (5% vs 4%), sinusitis (3% vs 2%) and abdominal distension (3% vs 2%).

Please see full Prescribing Information including Boxed Warning: http://www.frx.com/pi/linzess_pi.pdf.

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including, but not limited to, statements about our development and commercialization plans for linaclotide, our product candidates and the programs in our pipeline, including statements regarding our LINZESS patient awareness campaign; the launch and commercialization of linaclotide in additional countries and the timing thereof, as well as expectations regarding the continued commercialization of CONSTELLA in Germany; the anticipated timing of pre-clinical and clinical developments; the timing and results of clinical and pre-clinical trials; the expected issuance of patents and the period of patent protection associated therewith, if issued; the strength of the intellectual property protection for our product and product candidates; and our company's financial performance and results and guidance related thereto, including our projected 2014 operating expenses (including certain research and development expenses and selling, general and administrative expenses) and marketing and sales expense for LINZESS. Each forward‐looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include, but are not limited to, those related to pre-clinical and clinical development, manufacturing, and formulation development; decisions made by regulatory authorities; decisions made by the USPTO and its foreign counterparts; intellectual property rights of competitors or potential competitors; efficacy, safety and tolerability; competition in disease states; the commercial potential of LINZESS and our product candidates; the risk that we may never get sufficient patent protection for our product and product candidates; the risk that our planned investments do not have the anticipated effect on LINZESS or our company revenues; the risk that we are unable to manage our operating expenses over the year due to foreseeable or unforeseeable events or occurrences; and the risk that we and our partner, Forest Laboratories, Inc., are unable to commercialize LINZESS within the guided range of expenses. Applicable risks also include those that are listed under the heading "Risk Factors" and elsewhere in Ironwood's Annual Report on Form 10‐K for the year ended December 31, 2013, in addition to the risk factors that are listed from time to time in Ironwood's Annual Reports on Form 10‐K, Quarterly Reports on Form 10‐Q and any other subsequent SEC filings. Ironwood undertakes no obligation to update these forward-looking statements to reflect events or circumstances occurring after this press release. Except as otherwise noted, these forward-looking statements speak only as of the date of this press release. All forward‐looking statements are qualified in their entirety by this cautionary statement.

Condensed Consolidated Balance Sheets
(In thousands)
(unaudited)

	March 31, 2014	December 31, 2013
Assets		
Cash, cash equivalents and available-for-sale securities	$ 332,269	$ 197,602
Accounts receivable, net	10,337	3,213
Inventory	23,413	22,145
Prepaid expenses and other current assets	5,286	6,168
Total current assets	371,305	229,128
Property and equipment, net	35,524	37,376
Other assets	12,042	12,458
Total assets	$ 418,871	$ 278,962
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 24,032	$ 32,037
Current portion of capital lease obligations	1,156	1,139
Current portion of deferred rent	2,803	2,790
Current portion of deferred revenue	6,128	5,074
Current portion of notes payable	4,381	—
Total current liabilities	38,500	41,040
Capital lease obligations	2,842	3,134
Deferred rent	8,127	8,822
Deferred revenue	10,147	11,416
Notes payable	170,312	174,672
Other liabilities	—	1,653
Total stockholders' equity	188,943	38,225
Total liabilities and stockholders' equity	$ 418,871	$ 278,962

Condensed Consolidated Statements of Operations
(In thousands, except per share amounts)
(unaudited)

	Three Months Ended March 31,	
	2014	**2013**
Revenue	$ 14,605	$ 3,255
Cost and expenses:		
Cost of revenue	1,924	1,231
Research and development (1)	27,144	32,753
Selling, general and administrative (1)	29,924	33,374
Collaboration expense	—	24,730
Total cost and expenses	58,992	92,088
Loss from operations	(44,387)	(88,833)
Other income (expense), net	(5,239)	(5,069)
Net loss	$ (49,626)	$ (93,902)
Net loss per share—basic and diluted	$ (0.38)	$ (0.87)
Weighted average number of common shares used in net loss per share — basic and diluted	129,745	108,073
(1) Non-cash compensation expenses reflected in the condensed consolidated statements of operations are as follows:		
Research and development	$ 2,690	$ 2,224
Selling, general and administrative	$ 3,384	$ 3,051

LINZESS U.S. Collaboration Revenue/Expense Calculation[1]
(in thousands)
(unaudited)

	Three Months Ended March 31,	
	2014	**2013**
LINZESS net sales	$ 60,812	$ 4,502
Commercial costs and expenses[2]	59,916	71,040
Net profit (loss) on sales of LINZESS	$ 896	$ (66,538)
Ironwood's share of net profit (loss)	$ 448	$ (33,269)
Ironwood's selling, general and administrative expenses[3]	$ 7,999	$ 8,539
Ironwood's collaboration expense	$ —	$ (24,730)
Ironwood's collaborative arrangement revenue	$ 8,447	$ —

[1] Ironwood collaborates with Forest on the development and commercialization of linaclotide in North America. Under the terms of the collaboration agreement, Ironwood receives 50% of the net profits and bears 50% of the net losses from the commercial sale of LINZESS in the U.S. The purpose of this table is to present calculations of Ironwood's share of net profit (loss) generated from the sales of LINZESS in the U.S. and Ironwood's collaboration revenue/expense; however, the table does not present the research and development expenses related to LINZESS in the U.S. that are shared equally between the parties under the collaboration agreement.

[2] Includes cost of goods sold incurred by Forest as well as selling, general and administrative expenses incurred by Forest and Ironwood that are attributable to the cost-sharing arrangement between the parties.

[3] Includes Ironwood's selling, general and administrative expenses attributable to the cost-sharing arrangement with Forest.

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